## Disclaimer

The following report(s) provides findings from an FDA-initiated query using Sentinel. While Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Sentinel, and seeking to better understand Sentinel capabilities.

Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

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**Overview for Request: cder_mpl2p_wp021**

**Request ID:** cder_mpl2p_wp021

**Request Description:** In this request, we assessed the risk of angioedema associated with sacubitril/valsartan (SV) compared to angiotensin-converting enzyme inhibitors (ACEIs) or to angiotensin II receptor blockers (ARBs, excluding SV) among heart failure patients in the Sentinel Distributed Database (SDD).

**Sentinel Routine Querying Module:** Cohort Identification and Descriptive Analysis (CIDA) and Propensity Score Analysis (PSA) tools, version 9.7.0, with ad hoc programming

**Data Source:** The study period spanned from July 7, 2015 to February 29, 2020. We distributed the analytic package to five Data Partners (DP) on January 13, 2021. This report contains aggregated data from five DPs for which the propensity score estimation models converged across all comparisons. See Appendix A for a list of the latest dates of available data for each DP included in this report.

**Study Design:** We identified individuals with incident use of SV, ACEIs, and ARBs who were 18 years or older with a history of heart failure and evaluated the occurrence of angioedema and serious angioedema during exposure episodes. We then conducted a PSA comparing the SV users to the ACEI or ARB users, matching and stratifying on propensity score. This is a Type 2 analysis using the Propensity Score Analysis module in the Query Request Package (QRP) documentation.

**Exposure and Comparator:** We defined exposures of interest as new use of SV, ACEIs, and ARBs. The exposure drugs were defined using National Drug Codes (NDCs). For a list of generic and brand names of medical products used to define the exposure and comparator drugs, please see Appendix B.

**Outcomes of Interest:** We defined our main outcome of interest, angioedema, as an angioedema diagnosis code recorded in any diagnostic position of an inpatient, emergency department, or outpatient encounter. We defined our secondary outcome of interest, serious angioedema, as an angioedema diagnosis recorded in any diagnostic position of an inpatient or emergency department encounter with evidence of an intensive care unit admission, intubation, tracheostomy, or laryngoscopy occurring within two days of the hospital admission or emergency department visit. We defined our outcomes using International Classification of Diseases, Ninth and Tenth Revisions, Clinical Modification (ICD-9-CM and ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS), Current Procedural Terminology, Fourth Edition (CPT-4), and Healthcare Common Procedure Coding System, Level II (HCPCS). For a list of codes used to define outcomes, please see Appendix C.

**Cohort Eligibility Criteria:** We required patients 18 years or older to be enrolled in plans with both medical and drug coverage for at least 183 days before index dispensing, during which gaps in coverage of up to 45 days were allowed and treated as continuous enrollment. New use of ACEI or ARB was defined as no use of SV, ACEIs, or ARBs in the 183 days preceding the index dispensing (index date). New use of SV was defined as no use of SV in the 183 days preceding the index date, in addition to prior or ongoing use of the comparator (ACEIs or ARBs, evidenced by dispensing date or days supply) in the 183 days preceding and including the index date; a sensitivity analysis alternatively required prior or ongoing use of the comparator in the 14 days preceding and including the index date. We included patients with evidence of heart failure in the 183 days preceding and including index date. We excluded patients from the cohort if they had evidence of a dispensing for the other two exposures on their index date. Incidence, inclusion, and exclusion criteria were defined using ICD-9-CM and ICD-10-CM diagnosis codes. For a list of generic and brand names of medical products and specific diagnosis codes used to define cohort eligibility, please see Appendices D and E.

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**Follow-up:** We determined follow-up time based on the length of the exposure episodes and censored upon prespecified criteria. We created exposure episodes using outpatient pharmacy dispensing data. We bridged together exposure episodes less than 14 days apart and added 14 days at the end of each exposure episodes to create continuous treatment episodes. A sensitivity analysis shortened the episode gap and episode extension to 7 days. Follow-up began on the day of exposure initiation and continued until the earliest of any of the following: 1) outcome occurrence; 2) requester-defined censoring criteria -- initiation of any of the other two study drugs or after 365 days of continuous exposure; 3) disenrollment; 4) recorded death; 5) end of exposure episode; 6) end of query period; or 7) end of available data. Only the first valid exposure episode that occurred during the study period was included per patient, with the exception for one-time cohort reentry from the comparator to SV group upon initiation of SV during the first comparator exposure episode *plus* when new use criteria of SV was satisfied.

**Baseline Covariates:** Please refer to Appendices F, G, and I for a list of covariates, codes, and evaluation windows used to defined covariates.

**Propensity Score Estimation:** For each comparison, we fit a logistic regression model to estimate the propensity score (PS) based on potential confounders and risk factors outlined in Appendix J. The matching ratio for the PS was 1:1 and the matching caliper was 0.05. Exposure and comparator episodes were nearest neighbor-matched without replacement. We also used PS stratification (deciles) for our main analyses comparing SV to ACEIs and ARBs and risk of angioedema. For each comparison, we used risk set-based approach to estimate the hazard ratio and 95% confidence intervals for the unadjusted analyses, unconditional and conditional matched analyses, and PS-stratified analyses. Subgroup analyses for effect estimation included angioedema diagnosis in 183 days prior to index date and separately, angioedema diagnosis in entire enrollment history prior to index date; serious allergies diagnosis in the 183 days prior to index date; sex; age group; race; and follow-up time.

**See Appendices H and I for the specifications of parameters used in the analyses for this request.**

**Limitations:** As with all observational studies, this evaluation was limited in its ability to control for all sources of potential bias. Algorithms used to define exposures, outcomes, inclusion and exclusion criteria, and covariates are imperfect and may be misclassified. Therefore, data should be interpreted with this limitation in mind.

**Notes:** Please contact the e Sentinel Operations Center (info@sentinelsystem.org) for questions and to provide comments/suggestions for future enhancements to this document. For more information on Sentinel's routine querying modules, please refer to the documentation (https://dev.sentinelsystem.org/projects/SENTINEL/repos/sentinel-routine-queryingtooldocumentation/browse).

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## Glossary of Terms for Analyses Using
## Cohort Identification and Descriptive Analysis (CIDA) Module*

**Amount Supplied -** number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing.
**Blackout Period -** number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.
**Care Setting -** type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA). For laboratory results, possible care settings include: Emergency Department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). The Care Setting, along with the Principal Diagnosis Indicator (PDX), forms the Care Setting/PDX parameter.

- **Ambulatory Visit (AV) -** includes visits at outpatient clinics, same-day surgeries, urgent care visits, and other same-day ambulatory hospital encounters, but excludes emergency department encounters.
- **Emergency Department (ED) -** includes ED encounters that become inpatient stays (in which case inpatient stays would be a separate encounter). Excludes urgent care visits.
- **Inpatient Hospital Stay (IP) -** includes all inpatient stays, same-day hospital discharges, hospital transfers, and acute hospital care where the discharge is after the admission date.
- **Non-Acute Institutional Stay (IS) -** includes hospice, skilled nursing facility (SNF), rehab center, nursing home, residential, overnight non-hospital dialysis and other non-hospital stays.
- **Other Ambulatory Visit (OA) -** includes other non overnight AV encounters such as hospice visits, home health visits, skilled nursing facility visits, other non-hospital visits, as well as telemedicine, telephone and email consultations.

**Charlson/Elixhauser Combined Comorbidity Score -** calculated based on comorbidities observed during a requester-defined window around the exposure episode start date (e.g., in the 183 days prior to index).
**Code Days -** the minimum number of times the diagnosis must be found during the evaluation period in order to fulfill the algorithm to identify the corresponding patient characteristic.
**Cohort Definition (drug/exposure) -** indicates how the cohort will be defined: 01: Cohort includes only the first valid treatment episode during the query period; 02: Cohort includes all valid treatment episodes during the query period; 03: Cohort includes all valid treatment episodes during the query period until an event occurs.
**Computed Start Marketing Date -** represents the first observed dispensing date among all valid users within a GROUP (scenario) within each Data Partner site.
**Days Supplied -** number of days supplied for all dispensings in qualifying treatment episodes.
**Eligible Members -** number of members eligible for an incident treatment episode (defined by the drug/exposure and event washout periods) with drug and medical coverage during the query period.
**Enrollment Gap -** number of days allowed between two consecutive enrollment periods without breaking a “continuously enrolled” sequence.
**Episodes -** treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.
**Episode Gap -** number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.
**Event Deduplication -** specifies how events are counted by the Modular Program (MP) algorithm: 0: Counts all occurrences of a health outcome of interest (HOI) during an exposure episode; 1: de-duplicates occurrences of the same HOI code and code type on the same day; 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).

**Exposure Episode Length -** number of days after exposure initiation that is considered "exposed time."
**Exposure Extension Period -** number of days post treatment period in which the outcomes/events are counted for a treatment episode. Extensions are added after any episode gaps have been bridged.
**Lookback Period -** number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).
**Maximum Episode Duration -** truncates exposure episodes after a requester-specified number of exposed days. Applied after any gaps are bridged and extension days added to the length of the exposure episode.

**Member-Years -** sum of all days of enrollment with medical and drug coverage in the query period preceded by an exposure washout period all divided by 365.25.
**Minimum Days Supplied -** specifies a minimum number of days in length of the days supplied for the episode to be considered.

**Minimum Episode Duration -** specifies a minimum number of days in length of the episode for it to be considered. Applied after any gaps are bridged and extension days added to the length of the exposure episode.
**Monitoring Period -** used to define time periods of interest for both sequential analysis and simple cohort characterization requests.
**Principal Diagnosis (PDX) -** diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.
**Query Period -** period in which the modular program looks for exposures and outcomes of interest.
**Switch Evaluation Step Value -** value used to differentiate evaluation step. Each switch pattern can support up to 2 evaluation steps (0 = switch pattern evaluation start; 1 = first evaluation; 2 = second evaluation).
**Switch Gap Inclusion Indicator - i**ndicator for whether gaps in treatment episodes that are included in a switch episode will be counted as part of the switch episode duration.
**Switch Pattern Cohort Inclusion Date -** indicates which date to use for inclusion into the switch pattern cohort of interest as well as optionally as the index date of the treatment episode initiating the switch pattern. Valid options are the product approval date, product marketing date, other requester defined date, or computed start marketing date.

**Switch Pattern Cohort Inclusion Strategy -** indicates how the switch pattern cohort inclusion date will be used: 01: used only as a switch cohort entry date. First treatment episode dispensing date is used as index for computing time to first switch; 02: used as switch cohort entry date and as initial switch step index date for computing time to first switch.

**Treatment Episode Truncation Indicator -** indicates whether the exposure episode will be truncated at the occurrence of a requester-specified code.
**Washout Period (drug/exposure) -** number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.
**Washout Period (event/outcome) -** number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.
**Years at Risk -** number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

*all terms may not be used in this report

## Glossary of Terms for Analyses Using Propensity Score Analysis (PSA) Tool*

**Covariate -** requester defined binary variable to include in the propensity score estimation model (e.g., diabetes, heart failure, etc.) during requester-defined lookback period. Requester may also choose to add any of the following categorical, continuous, or count

1. Age (continuous)
2. Sex
3. Time period (i.e., monitoring period for sequential analyses)
4. Year of exposure
5. Comorbidity score
6. Medical utilization – number of inpatient stays
7. Medical utilization – number of institutional stays
8. Medical utilization – number of emergency department visits
9. Medical utilization – number of outpatient visits
10. Health care utilization – number of other ambulatory encounters (e.g., telemedicine, email consults)
11. Drug utilization – number of dispensings
12. Drug utilization – number of unique generics dispensed
13. Drug Utilization – number of unique drug classes dispensed

**Covariate Evaluation Window -** specified number of days relative to index date to evaluate the occurrence of covariates of interest. Note: members are required to have continuous enrollment during the covariate evaluation window, regardless of the value

**Individual Level Data Return -** program may return individual-level, de-identified datasets to the Sentinel Operations Center (SOC). While the datasets contain a single row per patient for each specified analysis, patient identifiers such as a patient ID are not included in the output. Individual-level datasets are returned to the SOC, aggregated, and used to calculate effect estimates via Cox

**Mahalanobis Distance -** provides a measure of balance across all variables while accounting for their correlation.

**Matching Caliper -** maximum allowed difference in propensity scores between treatment and control patients. Requester may select any caliper (e.g., 0.01, 0.025, and 0.05).

**Matching Ratio -** patients in exposed and comparator groups are nearest neighbor matched by a 1:1 or 1:n (up to 10) matching

**Matched Conditional and Unconditional Analysis -** in a conditional matched analysis, a Cox model, stratified by Data Partner site and matched set, is run on the matched population. This can be done for both the both 1:1 and 1:n matched cohorts. In an unconditional analysis, a Cox model, stratified by Data Partner site only, is run on the matched population. This can be done for the

**Propensity Score Stratification -** option to stratify propensity scores based on requester-defined percentiles in the unmatched population. In a stratified analysis, a Cox model, stratified by Data Partner site, is run on the stratified population. Note that all

**PSM Tool -** performs effect estimation by comparing exposure propensity-score matched parallel new user cohorts. Propensity score estimation and matching are conducted within each Sentinel Data Partner site via distributed programming code; data are

**Risk-set Level Data Return -** alternative to the patient-level data return approach. In this approach, the PSM tool will produce de-identified, risk-set level datasets instead of or in addition to individual-level output. Whereas each observation in the patient-level datasets represents one patient in the cohort, each observation in the risk set dataset represents one event. Risk sets are created at the Data Partner site, returned to the SOC, aggregated, and used to calculate effect estimates via case-centered logistic regression.

**Subgroup Analysis -** may be conducted using any requester-defined covariates. Subgroup analyses may be performed in the

**Zero Cell Correction -** indicator for whether to screen variables with a zero correction added to each cell in the confounder/outcome 2x2 table. Recommended when the number of exposed outcomes is fewer than 150.

*all terms may not be used in this report

**Table 1a. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Patients (Number) | 69,639 | 100.0% | 694,882 | 100.0% | - | - |
| **Demographics** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean age (years) | 70.2 | 11.2 | 72.7 | 12.5 | -2.563 | -0.216 |
| Age | **Number** | **Percent** | **Number** | **Percent** | | |
| 18-44 years | 2,412 | 3.5% | 21,587 | 3.1% | 0.357 | 0.020 |
| 45-54 years | 5,115 | 7.3% | 45,057 | 6.5% | 0.861 | 0.034 |
| 55-64 years | 11,494 | 16.5% | 97,244 | 14.0% | 2.511 | 0.070 |
| 65+ years | 50,618 | 72.7% | 530,994 | 76.4% | -3.729 | -0.086 |
| Sex | | | | | | |
| Female | 21,199 | 30.4% | 341,867 | 49.2% | -18.757 | -0.390 |
| Male | 48,440 | 69.6% | 353,015 | 50.8% | 18.757 | 0.390 |
| Race | | | | | | |
| American Indian or Alaska Native | 242 | 0.3% | 4,525 | 0.7% | -0.304 | -0.043 |
| Asian | 666 | 1.0% | 7,871 | 1.1% | -0.176 | -0.017 |
| Black or African American | 9,015 | 12.9% | 92,098 | 13.3% | -0.308 | -0.009 |
| Native Hawaiian or Other Pacific Islander | 66 | 0.1% | 741 | 0.1% | -0.012 | -0.004 |
| Unknown | 11,656 | 16.7% | 99,645 | 14.3% | 2.398 | 0.066 |
| White | 47,994 | 68.9% | 490,002 | 70.5% | -1.598 | -0.035 |
| Hispanic Origin | 1,351 | 1.9% | 15,586 | 2.2% | -0.303 | -0.021 |
| Year | | | | | | |
| 2015 | 1,349 | 1.9% | 87,092 | 12.5% | -10.596 | -0.418 |
| 2016 | 10,510 | 15.1% | 172,880 | 24.9% | -9.787 | -0.247 |
| 2017 | 16,864 | 24.2% | 156,573 | 22.5% | 1.684 | 0.040 |
| 2018 | 19,077 | 27.4% | 142,979 | 20.6% | 6.818 | 0.160 |
| 2019 | 21,511 | 30.9% | 133,608 | 19.2% | 11.662 | 0.272 |
| 2020 | 328 | 3.6% | 1,750 | 2.4% | 1.194 | 0.070 |
| **Recorded History of:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Charlson/Elixhauser Combined Comorbidity Score[3] | 5.2 | 2.7 | 5.8 | 3.0 | -0.610 | -0.214 |
| | **Number** | **Percent** | **Number** | **Percent** | | |
| *Ambulatory allergies or allergy treatment* | *33,754* | *48.5%* | *320,699* | *46.2%* | *2.318* | *0.046* |
| Angioedema (-183, -1) | 83 | 0.1% | 864 | 0.1% | -0.005 | -0.001 |
| *Angioedema (ever, -1)* | *494* | *0.7%* | *7,317* | *1.1%* | *-0.344* | *-0.037* |
| Diabetes | 35,071 | 50.4% | 326,005 | 46.9% | 3.446 | 0.069 |
| Ischemic heart disease | 55,067 | 79.1% | 432,968 | 62.3% | 16.767 | 0.375 |
| Renal disorders | 27,364 | 39.3% | 289,746 | 41.7% | -2.403 | -0.049 |
| Serious allergies | 8,047 | 11.6% | 110,960 | 16.0% | -4.413 | -0.128 |

**Table 1a. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Ambulatory allergies or treatment and not serious allergies | 28,444 | 40.8% | 252,983 | 36.4% | 4.438 | 0.091 |
| **History of Use:** | | | | | | |
| Diuretics (thiazides, potassium sparing, loop diuretics) | 60,338 | 86.6% | 458,102 | 65.9% | 20.719 | 0.502 |
| Everolimus | 11 | 0.0% | 183 | 0.0% | -0.011 | -0.007 |
| Nonsteroidal anti-inflammatory drugs (NSAIDs) | 7,793 | 11.2% | 88,957 | 12.8% | -1.611 | -0.050 |
| Sirolimus | ***** | ***** | 208 | 0.0% | -0.018 | -0.013 |
| **Health Service Utilization Intensity:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean number of ambulatory encounters | 17.9 | 13.7 | 17.4 | 19.7 | 0.531 | 0.031 |
| Mean number of emergency room encounters | 0.7 | 1.4 | 0.9 | 1.8 | -0.188 | -0.115 |
| Mean number of inpatient hospital encounters | 0.8 | 1.1 | 1.0 | 1.2 | -0.211 | -0.186 |
| Mean number of non-acute institutional encounters | 0.2 | 0.8 | 0.4 | 1.1 | -0.217 | -0.235 |
| Mean number of other ambulatory encounters | 8.1 | 12.2 | 12.8 | 18.0 | -4.732 | -0.308 |
| *Mean number of filled prescriptions* | *31.3* | *19.8* | *26.9* | *23.0* | *4.408* | *0.205* |
| *Mean number of generics* | *13.1* | *5.1* | *11.5* | *5.7* | *1.614* | *0.297* |
| Mean number of unique drug classes | 11.4 | 4.5 | 10.8 | 5.0 | 0.626 | 0.131 |

[1]Covariates in italics were not included in the propensity score logistic regression model

[2]Covariates in blue show a standardized difference greater than 0.1

[3]The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 1b. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Adjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05**

| Characteristic[1,2] | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Patients (Number) | 69,639 | 100.0% | 69,639 | 10.0% | - | - |
| **Demographics** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean age (years) | 70.2 | 11.2 | 70.2 | 12.2 | -0.019 | -0.002 |
| Age | **Number** | **Percent** | **Number** | **Percent** | | |
| 18-44 years | 2,412 | 3.5% | 2,717 | 3.9% | -0.438 | -0.024 |
| 45-54 years | 5,115 | 7.3% | 5,694 | 8.2% | -0.831 | -0.032 |
| 55-64 years | 11,494 | 16.5% | 11,900 | 17.1% | -0.583 | -0.016 |
| 65+ years | 50,618 | 72.7% | 49,328 | 70.8% | 1.852 | 0.044 |
| Sex | | | | | | |
| Female | 21,199 | 30.4% | 21,398 | 30.7% | -0.286 | -0.006 |
| Male | 48,440 | 69.6% | 48,241 | 69.3% | 0.286 | 0.006 |
| Race | | | | | | |
| American Indian or Alaska Native | 242 | 0.3% | 242 | 0.3% | 0.000 | 0.000 |
| Asian | 666 | 1.0% | 662 | 1.0% | 0.006 | 0.001 |
| Black or African American | 9,015 | 12.9% | 9,043 | 13.0% | -0.040 | -0.001 |
| Native Hawaiian or Other Pacific Islander | 66 | 0.1% | 75 | 0.1% | -0.013 | -0.004 |
| Unknown | 11,656 | 16.7% | 11,662 | 16.7% | -0.009 | -0.000 |
| White | 47,994 | 68.9% | 47,955 | 68.9% | 0.056 | 0.001 |
| Hispanic Origin | 1,351 | 1.9% | 1,521 | 2.2% | -0.244 | -0.017 |
| Year | | | | | | |
| 2015 | 1,349 | 1.9% | 1,255 | 1.8% | 0.135 | 0.010 |
| 2016 | 10,510 | 15.1% | 10,469 | 15.0% | 0.059 | 0.002 |
| 2017 | 16,864 | 24.2% | 16,928 | 24.3% | -0.092 | -0.002 |
| 2018 | 19,077 | 27.4% | 19,069 | 27.4% | 0.011 | 0.000 |
| 2019 | 21,511 | 30.9% | 21,555 | 31.0% | -0.063 | -0.001 |
| 2020 | 328 | 3.6% | 363 | 4.0% | -0.385 | -0.020 |
| **Recorded History of:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Charlson/Elixhauser Combined Comorbidity Score[3] | 5.2 | 2.7 | 5.2 | 2.6 | -0.017 | -0.006 |
| | **Number** | **Percent** | **Number** | **Percent** | | |
| *Ambulatory allergies or allergy treatment* | *33,754* | *48.5%* | *33,596* | *48.2%* | *0.227* | *0.005* |
| Angioedema (-183, -1) | 83 | 0.1% | 92 | 0.1% | -0.013 | -0.004 |
| *Angioedema (ever, -1)* | *494* | *0.7%* | *723* | *1.0%* | *-0.329* | *-0.035* |
| Diabetes | 35,071 | 50.4% | 34,906 | 50.1% | 0.237 | 0.005 |
| Ischemic heart disease | 55,067 | 79.1% | 55,153 | 79.2% | -0.123 | -0.003 |
| Renal disorders | 27,364 | 39.3% | 27,495 | 39.5% | -0.188 | -0.004 |
| Serious allergies | 8,047 | 11.6% | 8,038 | 11.5% | 0.013 | 0.000 |

**Table 1b. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Adjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Ambulatory allergies or treatment and not serious allergies | 28,444 | 40.8% | 28,475 | 40.9% | -0.045 | -0.001 |
| **History of Use:** | | | | | | |
| Diuretics (thiazides, potassium sparing, loop diuretics) | 60,338 | 86.6% | 60,422 | 86.8% | -0.121 | -0.004 |
| Everolimus | 11 | 0.0% | 12 | 0.0% | -0.001 | -0.001 |
| Nonsteroidal anti-inflammatory drugs (NSAIDs) | 7,793 | 11.2% | 7,766 | 11.2% | 0.039 | 0.001 |
| Sirolimus | ***** | ***** | 14 | 0.0% | -0.009 | -0.007 |
| **Health Service Utilization Intensity:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean number of ambulatory encounters | 17.9 | 13.7 | 17.9 | 20.5 | -0.041 | -0.002 |
| Mean number of emergency room encounters | 0.7 | 1.4 | 0.7 | 1.2 | -0.003 | -0.002 |
| Mean number of inpatient hospital encounters | 0.8 | 1.1 | 0.8 | 0.9 | -0.011 | -0.010 |
| Mean number of non-acute institutional encounters | 0.2 | 0.8 | 0.2 | 0.7 | -0.006 | -0.008 |
| Mean number of other ambulatory encounters | 8.1 | 12.2 | 8.2 | 11.0 | -0.062 | -0.005 |
| *Mean number of filled prescriptions* | *31.3* | *19.8* | *28.2* | *22.9* | *3.118* | *0.146* |
| *Mean number of generics* | *13.1* | *5.1* | *12.2* | *5.7* | *0.922* | *0.170* |
| Mean number of unique drug classes | 11.4 | 4.5 | 11.4 | 5.0 | -0.041 | -0.009 |

[1]Covariates in italics were not included in the propensity score logistic regression model

[2]Covariates in blue show a standardized difference greater than 0.1

[3]The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity sc ore predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 1c. Weighted Baseline Characteristics of Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Propensity Score Stratified,**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Patients (Number) | 69,639 | 100.0% | 694,882 | 100.0% | - | - |
| **Demographics** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean age (years) | 72.1 | 11.4 | 72.6 | 12.5 | -0.466 | -0.039 |
| Age | **Number** | **Percent** | **Number** | **Percent** | | |
| 18-44 years | 1,968 | 2.8% | 21,875 | 3.1% | -0.321 | -0.019 |
| 45-54 years | 4,182 | 6.0% | 45,805 | 6.6% | -0.587 | -0.025 |
| 55-64 years | 9,832 | 14.1% | 98,637 | 14.2% | -0.076 | -0.002 |
| 65+ years | 53,657 | 77.0% | 528,564 | 76.1% | 0.984 | 0.025 |
| Sex | | | | | | |
| Female | 33,257 | 47.8% | 330,693 | 47.6% | 0.167 | 0.003 |
| Male | 36,382 | 52.2% | 364,189 | 52.4% | -0.167 | -0.003 |
| Race | | | | | | |
| American Indian or Alaska Native | 396 | 0.6% | 4,349 | 0.6% | -0.057 | -0.007 |
| Asian | 724 | 1.0% | 7,777 | 1.1% | -0.079 | -0.008 |
| Black or African American | 8,622 | 12.4% | 92,009 | 13.2% | -0.860 | -0.026 |
| Native Hawaiian or Other Pacific Islander | 58 | 0.1% | 732 | 0.1% | -0.023 | -0.007 |
| Unknown | 11,379 | 16.3% | 99,758 | 14.4% | 1.984 | 0.092 |
| White | 48,459 | 69.6% | 490,256 | 70.6% | -0.966 | -0.025 |
| Hispanic Origin | 1,327 | 1.9% | 15,544 | 2.2% | -0.332 | -0.023 |
| Year | | | | | | |
| 2015 | 7,015 | 10.1% | 80,407 | 11.6% | -1.498 | -0.048 |
| 2016 | 15,676 | 22.5% | 166,839 | 24.0% | -1.499 | -0.035 |
| 2017 | 15,798 | 22.7% | 158,018 | 22.7% | -0.055 | -0.001 |
| 2018 | 15,486 | 22.2% | 147,402 | 21.2% | 1.025 | 0.025 |
| 2019 | 15,371 | 22.1% | 140,377 | 20.2% | 1.871 | 0.046 |
| 2020 | 293 | 3.2% | 1,839 | 2.5% | 0.682 | 0.041 |
| **Recorded History of:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Charlson/Elixhauser Combined Comorbidity Score[3] | 5.9 | 3.2 | 5.8 | 3.0 | 0.115 | 0.037 |
| | **Number** | **Percent** | **Number** | **Percent** | | |
| *Ambulatory allergies or allergy treatment* | *33,199* | *47.7%* | *322,089* | *46.4%* | *1.321* | *0.027* |
| Angioedema (-183, -1) | 76 | 0.1% | 860 | 0.1% | -0.015 | -0.004 |
| *Angioedema (ever, -1)* | *501* | *0.7%* | *7,303* | *1.1%* | *-0.331* | *-0.035* |
| Diabetes | 32,924 | 47.3% | 328,219 | 47.2% | 0.045 | 0.001 |
| Ischemic heart disease | 45,178 | 64.9% | 443,528 | 63.8% | 1.046 | 0.022 |
| Renal disorders | 29,955 | 43.0% | 288,849 | 41.6% | 1.446 | 0.029 |
| Serious allergies | 11,113 | 16.0% | 108,563 | 15.6% | 0.334 | 0.009 |

**Table 1c. Weighted Baseline Characteristics of Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Propensity Score Stratified,**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Ambulatory allergies or treatment and not serious allergies | 25,967 | 37.3% | 255,647 | 36.8% | 0.497 | 0.010 |
| **History of Use:** | | | | | | |
| Diuretics (thiazides, potassium sparing, loop diuretics) | 48,928 | 70.3% | 471,272 | 67.8% | 2.439 | 0.053 |
| Everolimus | 33 | 0.0% | 177 | 0.0% | 0.022 | 0.011 |
| Nonsteroidal anti-inflammatory drugs (NSAIDs) | 8,966 | 12.9% | 88,045 | 12.7% | 0.204 | 0.006 |
| Sirolimus | 21 | 0.0% | 195 | 0.0% | 0.001 | 0.001 |
| **Health Service Utilization Intensity:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean number of ambulatory encounters | 18.0 | 14.6 | 17.4 | 19.8 | 0.600 | 0.035 |
| Mean number of emergency room encounters | 1.0 | 3.4 | 0.8 | 1.7 | 0.152 | 0.056 |
| Mean number of inpatient hospital encounters | 1.1 | 1.5 | 1.0 | 1.1 | 0.091 | 0.067 |
| Mean number of non-acute institutional encounters | 0.5 | 1.3 | 0.4 | 1.0 | 0.063 | 0.055 |
| Mean number of other ambulatory encounters | 13.1 | 20.5 | 12.4 | 17.6 | 0.699 | 0.037 |
| *Mean number of filled prescriptions* | *30.6* | *20.9* | *27.0* | *23.0* | *3.589* | *0.164* |
| *Mean number of generics* | *12.8* | *5.5* | *11.6* | *5.7* | *1.224* | *0.218* |
| Mean number of unique drug classes | 11.1 | 4.8 | 10.8 | 5.0 | 0.239 | 0.049 |

[1]Covariates in italics were not included in the propensity score logistic regression model

[2]Covariates in blue show a standardized difference greater than 0.1

[3]The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 1d. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ARBs | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Patients (Number) | 49,140 | 100.0% | 337,083 | 100.0% | - | - |
| **Demographics** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean age (years) | 72.6 | 10.7 | 73.8 | 12.0 | -1.241 | -0.109 |
| Age | **Number** | **Percent** | **Number** | **Percent** | | |
| 18-44 years | 1,164 | 2.4% | 8,502 | 2.5% | -0.153 | -0.010 |
| 45-54 years | 2,653 | 5.4% | 18,293 | 5.4% | -0.028 | -0.001 |
| 55-64 years | 5,990 | 12.2% | 40,547 | 12.0% | 0.161 | 0.005 |
| 65+ years | 39,333 | 80.0% | 269,741 | 80.0% | 0.021 | 0.001 |
| Sex | | | | | | |
| Female | 19,226 | 39.1% | 187,871 | 55.7% | -16.609 | -0.337 |
| Male | 29,914 | 60.9% | 149,212 | 44.3% | 16.609 | 0.337 |
| Race | | | | | | |
| American Indian or Alaska Native | 133 | 0.3% | 1,948 | 0.6% | -0.307 | -0.047 |
| Asian | 1,070 | 2.2% | 7,811 | 2.3% | -0.140 | -0.009 |
| Black or African American | 6,989 | 14.2% | 55,801 | 16.6% | -2.331 | -0.065 |
| Native Hawaiian or Other Pacific Islander | 61 | 0.1% | 478 | 0.1% | -0.018 | -0.005 |
| Unknown | 8,082 | 16.4% | 47,793 | 14.2% | 2.268 | 0.063 |
| White | 32,805 | 66.8% | 223,252 | 66.2% | 0.528 | 0.011 |
| Hispanic Origin | 1,135 | 2.3% | 9,032 | 2.7% | -0.370 | -0.024 |
| Year | | | | | | |
| 2015 | 878 | 1.8% | 32,231 | 9.6% | -7.775 | -0.341 |
| 2016 | 6,685 | 13.6% | 70,696 | 21.0% | -7.369 | -0.196 |
| 2017 | 11,072 | 22.5% | 73,800 | 21.9% | 0.638 | 0.015 |
| 2018 | 13,611 | 27.7% | 81,657 | 24.2% | 3.474 | 0.079 |
| 2019 | 16,598 | 33.8% | 77,594 | 23.0% | 10.758 | 0.240 |
| 2020 | 296 | 4.9% | 1,105 | 3.2% | 1.652 | 0.084 |
| **Recorded History of:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Charlson/Elixhauser Combined Comorbidity Score[3] | 5.4 | 2.7 | 5.8 | 3.0 | -0.374 | -0.133 |
| | **Number** | **Percent** | **Number** | **Percent** | | |
| *Ambulatory allergies or allergy treatment* | *26,106* | *53.1%* | *169,522* | *50.3%* | *2.835* | *0.057* |
| Angioedema (-183, -1) | 58 | 0.1% | 825 | 0.2% | -0.127 | -0.030 |
| *Angioedema (ever, -1)* | *750* | *1.5%* | *7,357* | *2.2%* | *-0.656* | *-0.049* |
| Diabetes | 26,110 | 53.1% | 173,497 | 51.5% | 1.664 | 0.033 |
| Ischemic heart disease | 38,297 | 77.9% | 203,944 | 60.5% | 17.432 | 0.385 |
| Renal disorders | 21,237 | 43.2% | 154,620 | 45.9% | -2.653 | -0.053 |
| Serious allergies | 6,466 | 13.2% | 54,435 | 16.1% | -2.991 | -0.085 |

**Table 1d. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ARBs | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Ambulatory allergies or treatment and not serious allergies | 21,703 | 44.2% | 134,451 | 39.9% | 4.279 | 0.087 |
| **History of Use:** | | | | | | |
| Diuretics (thiazides, potassium sparing, loop diuretics) | 42,889 | 87.3% | 222,859 | 66.1% | 21.165 | 0.517 |
| Everolimus | 15 | 0.0% | 98 | 0.0% | 0.001 | 0.001 |
| Nonsteroidal anti-inflammatory drugs (NSAIDs) | 5,633 | 11.5% | 44,187 | 13.1% | -1.645 | -0.050 |
| Sirolimus | ***** | ***** | 142 | 0.0% | -0.030 | -0.018 |
| **Health Service Utilization Intensity:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean number of ambulatory encounters | 19.2 | 14.8 | 20.4 | 22.5 | -1.228 | -0.064 |
| Mean number of emergency room encounters | 0.6 | 1.3 | 0.8 | 1.7 | -0.169 | -0.112 |
| Mean number of inpatient hospital encounters | 0.8 | 1.1 | 0.8 | 1.1 | -0.079 | -0.071 |
| Mean number of non-acute institutional encounters | 0.2 | 0.7 | 0.4 | 1.0 | -0.174 | -0.192 |
| Mean number of other ambulatory encounters | 8.1 | 11.6 | 11.7 | 17.4 | -3.639 | -0.246 |
| *Mean number of filled prescriptions* | *32.5* | *20.9* | *27.8* | *22.3* | *4.697* | *0.217* |
| *Mean number of generics* | *13.8* | *5.4* | *12.0* | *5.8* | *1.857* | *0.331* |
| Mean number of unique drug classes | 12.0 | 4.7 | 11.2 | 5.1 | 0.812 | 0.164 |

[1]Covariates in italics were not included in the propensity score logistic regression model

[2]Covariates in blue show a standardized difference greater than 0.1

[3]The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 1e. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020, Fixed Ratio 1:1, Caliper: 0.05**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ARBs | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Patients (Number) | 49,137 | 100.0% | 49,137 | 14.6% | - | - |
| **Demographics** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean age (years) | 72.6 | 10.7 | 72.6 | 11.5 | -0.016 | -0.001 |
| Age | **Number** | **Percent** | **Number** | **Percent** | | |
| 18-44 years | 1,164 | 2.4% | 1,231 | 2.5% | -0.136 | -0.009 |
| 45-54 years | 2,652 | 5.4% | 2,977 | 6.1% | -0.661 | -0.029 |
| 55-64 years | 5,988 | 12.2% | 6,682 | 13.6% | -1.412 | -0.043 |
| 65+ years | 39,333 | 80.0% | 38,247 | 77.8% | 2.210 | 0.058 |
| Sex | | | | | | |
| Female | 19,226 | 39.1% | 19,287 | 39.3% | -0.124 | -0.003 |
| Male | 29,911 | 60.9% | 29,850 | 60.7% | 0.124 | 0.003 |
| Race | | | | | | |
| American Indian or Alaska Native | 133 | 0.3% | 144 | 0.3% | -0.022 | -0.004 |
| Asian | 1,070 | 2.2% | 1,059 | 2.2% | 0.022 | 0.002 |
| Black or African American | 6,988 | 14.2% | 7,004 | 14.3% | -0.033 | -0.001 |
| Native Hawaiian or Other Pacific Islander | 61 | 0.1% | 53 | 0.1% | 0.016 | 0.005 |
| Unknown | 8,080 | 16.4% | 8,091 | 16.5% | -0.022 | -0.001 |
| White | 32,805 | 66.8% | 32,786 | 66.7% | 0.039 | 0.001 |
| Hispanic Origin | 1,135 | 2.3% | 1,221 | 2.5% | -0.175 | -0.011 |
| Year | | | | | | |
| 2015 | 878 | 1.8% | 822 | 1.7% | 0.114 | 0.009 |
| 2016 | 6,685 | 13.6% | 6,735 | 13.7% | -0.102 | -0.003 |
| 2017 | 11,072 | 22.5% | 11,079 | 22.5% | -0.014 | -0.000 |
| 2018 | 13,611 | 27.7% | 13,558 | 27.6% | 0.108 | 0.002 |
| 2019 | 16,595 | 33.8% | 16,643 | 33.9% | -0.098 | -0.002 |
| 2020 | 296 | 4.9% | 300 | 5.0% | -0.066 | -0.003 |
| **Recorded History of:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Charlson/Elixhauser Combined Comorbidity Score[3] | 5.4 | 2.7 | 5.4 | 2.7 | 0.001 | 0.000 |
| | **Number** | **Percent** | **Number** | **Percent** | | |
| *Ambulatory allergies or allergy treatment* | *26,103* | *53.1%* | *26,126* | *53.2%* | *-0.047* | *-0.001* |
| Angioedema (-183, -1) | 58 | 0.1% | 56 | 0.1% | 0.004 | 0.001 |
| *Angioedema (ever, -1)* | *750* | *1.5%* | *1,084* | *2.2%* | *-0.680* | *-0.050* |
| Diabetes | 26,109 | 53.1% | 25,978 | 52.9% | 0.267 | 0.005 |
| Ischemic heart disease | 38,294 | 77.9% | 38,161 | 77.7% | 0.271 | 0.007 |
| Renal disorders | 21,235 | 43.2% | 21,281 | 43.3% | -0.094 | -0.002 |
| Serious allergies | 6,466 | 13.2% | 6,500 | 13.2% | -0.069 | -0.002 |

**Table 1e. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020, Fixed Ratio 1:1, Caliper: 0.05**

| Characteristic[1,2] | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ARBs | | | |
| | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Ambulatory allergies or treatment and not serious allergies | 21,700 | 44.2% | 21,734 | 44.2% | -0.069 | -0.001 |
| **History of Use:** | | | | | | |
| Diuretics (thiazides, potassium sparing, loop diuretics) | 42,886 | 87.3% | 42,937 | 87.4% | -0.104 | -0.003 |
| Everolimus | 15 | 0.0% | 19 | 0.0% | -0.008 | -0.004 |
| Nonsteroidal anti-inflammatory drugs (NSAIDs) | 5,633 | 11.5% | 5,752 | 11.7% | -0.242 | -0.008 |
| Sirolimus | ***** | ***** | ***** | ***** | 0.004 | 0.004 |
| **Health Service Utilization Intensity:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean number of ambulatory encounters | 19.2 | 14.8 | 19.2 | 19.8 | -0.002 | -0.000 |
| Mean number of emergency room encounters | 0.6 | 1.3 | 0.6 | 1.2 | -0.010 | -0.008 |
| Mean number of inpatient hospital encounters | 0.8 | 1.1 | 0.8 | 1.0 | 0.000 | 0.000 |
| Mean number of non-acute institutional encounters | 0.2 | 0.7 | 0.2 | 0.7 | -0.002 | -0.002 |
| Mean number of other ambulatory encounters | 8.1 | 11.6 | 8.1 | 11.0 | 0.006 | 0.001 |
| *Mean number of filled prescriptions* | *32.5* | *20.9* | *29.7* | *22.4* | *2.717* | *0.125* |
| *Mean number of generics* | *13.8* | *5.4* | *12.9* | *5.8* | *0.967* | *0.173* |
| Mean number of unique drug classes | 12.0 | 4.7 | 12.0 | 5.1 | -0.034 | -0.007 |

[1]Covariates in italics were not included in the propensity score logistic regression model

[2]Covariates in blue show a standardized difference greater than 0.1

[3]The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 1f. Weighted Baseline Characteristics of Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Propensity Score Stratified,**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ARBs | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Patients (Number) | 49,140 | 100.0% | 337,083 | 100.0% | - | - |
| **Demographics** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean age (years) | 73.6 | 11.1 | 73.7 | 12.0 | -0.109 | -0.009 |
| Age | **Number** | **Percent** | **Number** | **Percent** | | |
| 18-44 years | 1,100 | 2.2% | 8,414 | 2.5% | -0.258 | -0.017 |
| 45-54 years | 2,349 | 4.8% | 18,410 | 5.5% | -0.682 | -0.031 |
| 55-64 years | 5,573 | 11.3% | 40,943 | 12.1% | -0.806 | -0.026 |
| 65+ years | 40,119 | 81.6% | 269,315 | 79.9% | 1.746 | 0.047 |
| Sex | | | | | | |
| Female | 26,639 | 54.2% | 181,198 | 53.8% | 0.456 | 0.009 |
| Male | 22,501 | 45.8% | 155,885 | 46.2% | -0.456 | -0.009 |
| Race | | | | | | |
| American Indian or Alaska Native | 297 | 0.6% | 1,825 | 0.5% | 0.063 | 0.008 |
| Asian | 1,046 | 2.1% | 7,748 | 2.3% | -0.170 | -0.012 |
| Black or African American | 7,384 | 15.0% | 55,001 | 16.3% | -1.289 | -0.036 |
| Native Hawaiian or Other Pacific Islander | 66 | 0.1% | 475 | 0.1% | -0.007 | -0.002 |
| Unknown | 7,753 | 15.8% | 47,835 | 14.2% | 1.587 | 0.069 |
| White | 32,593 | 66.3% | 224,199 | 66.5% | -0.184 | -0.004 |
| Hispanic Origin | 1,061 | 2.2% | 8,949 | 2.7% | -0.495 | -0.032 |
| Year | | | | | | |
| 2015 | 3,730 | 7.6% | 28,917 | 8.6% | -0.988 | -0.036 |
| 2016 | 9,534 | 19.4% | 67,607 | 20.1% | -0.655 | -0.016 |
| 2017 | 10,600 | 21.6% | 74,244 | 22.0% | -0.455 | -0.011 |
| 2018 | 12,309 | 25.0% | 83,326 | 24.7% | 0.329 | 0.008 |
| 2019 | 12,738 | 25.9% | 81,807 | 24.3% | 1.653 | 0.038 |
| 2020 | 230 | 3.8% | 1,181 | 3.5% | 0.331 | 0.018 |
| **Recorded History of:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Charlson/Elixhauser Combined Comorbidity Score[3] | 5.7 | 3.0 | 5.7 | 2.9 | -0.003 | -0.001 |
| | **Number** | **Percent** | **Number** | **Percent** | | |
| *Ambulatory allergies or allergy treatment* | *25,269* | *51.4%* | *170,719* | *50.6%* | *0.777* | *0.016* |
| Angioedema (-183, -1) | 115 | 0.2% | 770 | 0.2% | 0.006 | 0.001 |
| *Angioedema (ever, -1)* | *775* | *1.6%* | *7,342* | *2.2%* | *-0.601* | *-0.044* |
| Diabetes | 24,847 | 50.6% | 174,248 | 51.7% | -1.128 | -0.023 |
| Ischemic heart disease | 31,038 | 63.2% | 211,390 | 62.7% | 0.451 | 0.009 |
| Renal disorders | 22,193 | 45.2% | 153,842 | 45.6% | -0.477 | -0.010 |
| Serious allergies | 7,717 | 15.7% | 53,278 | 15.8% | -0.101 | -0.003 |

**Table 1f. Weighted Baseline Characteristics of Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Propensity Score Stratified,**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ARBs | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Ambulatory allergies or treatment and not serious allergies | 20,111 | 40.9% | 136,253 | 40.4% | 0.505 | 0.010 |
| **History of Use:** | | | | | | |
| Diuretics (thiazides, potassium sparing, loop diuretics) | 34,636 | 70.5% | 231,958 | 68.8% | 1.671 | 0.036 |
| Everolimus | 14 | 0.0% | 98 | 0.0% | -0.000 | -0.000 |
| Nonsteroidal anti-inflammatory drugs (NSAIDs) | 6,349 | 12.9% | 43,543 | 12.9% | 0.003 | 0.000 |
| Sirolimus | 15 | 0.0% | 129 | 0.0% | -0.007 | -0.004 |
| **Health Service Utilization Intensity:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean number of ambulatory encounters | 19.9 | 17.4 | 20.3 | 22.2 | -0.439 | -0.022 |
| Mean number of emergency room encounters | 0.8 | 2.7 | 0.8 | 1.6 | 0.063 | 0.028 |
| Mean number of inpatient hospital encounters | 0.8 | 1.2 | 0.8 | 1.1 | 0.007 | 0.006 |
| Mean number of non-acute institutional encounters | 0.4 | 1.1 | 0.4 | 1.0 | 0.008 | 0.008 |
| Mean number of other ambulatory encounters | 11.3 | 18.2 | 11.3 | 16.8 | 0.017 | 0.001 |
| *Mean number of filled prescriptions* | *31.2* | *22.2* | *28.0* | *22.3* | *3.224* | *0.145* |
| *Mean number of generics* | *13.2* | *5.5* | *12.1* | *5.8* | *1.146* | *0.202* |
| Mean number of unique drug classes | 11.5 | 4.8 | 11.3 | 5.1 | 0.153 | 0.031 |

[1]Covariates in italics were not included in the propensity score logistic regression model

[2]Covariates in blue show a standardized difference greater than 0.1

[3]The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 1g. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Patients (Number) | 49,629 | 100.0% | 695,068 | 100.0% | - | - |
| **Demographics** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean age (years) | 70.4 | 11.1 | 72.7 | 12.5 | -2.309 | -0.196 |
| Age | **Number** | **Percent** | **Number** | **Percent** | | |
| 18-44 years | 1,592 | 3.2% | 21,593 | 3.1% | 0.101 | 0.006 |
| 45-54 years | 3,425 | 6.9% | 45,072 | 6.5% | 0.417 | 0.017 |
| 55-64 years | 8,067 | 16.3% | 97,279 | 14.0% | 2.259 | 0.063 |
| 65+ years | 36,545 | 73.6% | 531,124 | 76.4% | -2.777 | -0.064 |
| Sex | | | | | | |
| Female | 14,886 | 30.0% | 341,922 | 49.2% | -19.198 | -0.400 |
| Male | 34,743 | 70.0% | 353,146 | 50.8% | 19.198 | 0.400 |
| Race | | | | | | |
| American Indian or Alaska Native | 165 | 0.3% | 4,526 | 0.7% | -0.319 | -0.046 |
| Asian | 526 | 1.1% | 7,873 | 1.1% | -0.073 | -0.007 |
| Black or African American | 6,074 | 12.2% | 92,135 | 13.3% | -1.017 | -0.030 |
| Native Hawaiian or Other Pacific Islander | 46 | 0.1% | 741 | 0.1% | -0.014 | -0.004 |
| Unknown | 8,192 | 16.5% | 99,667 | 14.3% | 2.167 | 0.060 |
| White | 34,626 | 69.8% | 490,126 | 70.5% | -0.745 | -0.016 |
| Hispanic Origin | 990 | 2.0% | 15,590 | 2.2% | -0.248 | -0.017 |
| Year | | | | | | |
| 2015 | 951 | 1.9% | 87,092 | 12.5% | -10.614 | -0.419 |
| 2016 | 6,862 | 13.8% | 172,883 | 24.9% | -11.046 | -0.282 |
| 2017 | 11,714 | 23.6% | 156,612 | 22.5% | 1.071 | 0.025 |
| 2018 | 13,939 | 28.1% | 143,032 | 20.6% | 7.508 | 0.176 |
| 2019 | 15,918 | 32.1% | 133,697 | 19.2% | 12.839 | 0.297 |
| 2020 | 245 | 3.9% | 1,752 | 2.4% | 1.500 | 0.086 |
| **Recorded History of:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Charlson/Elixhauser Combined Comorbidity Score[3] | 5.1 | 2.6 | 5.8 | 3.0 | -0.734 | -0.262 |
| | **Number** | **Percent** | **Number** | **Percent** | | |
| *Ambulatory allergies or allergy treatment* | *23,931* | *48.2%* | *320,785* | *46.2%* | *2.068* | *0.041* |
| Angioedema (-183, -1) | 46 | 0.1% | 864 | 0.1% | -0.032 | -0.010 |
| *Angioedema (ever, -1)* | *333* | *0.7%* | *7,320* | *1.1%* | *-0.382* | *-0.041* |
| Diabetes | 24,859 | 50.1% | 326,119 | 46.9% | 3.171 | 0.063 |
| Ischemic heart disease | 39,138 | 78.9% | 433,124 | 62.3% | 16.547 | 0.369 |
| Renal disorders | 18,823 | 37.9% | 289,848 | 41.7% | -3.773 | -0.077 |
| Serious allergies | 5,370 | 10.8% | 110,996 | 16.0% | -5.149 | -0.152 |

**Table 1g. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Ambulatory allergies or treatment and not serious allergies | 20,361 | 41.0% | 253,046 | 36.4% | 4.620 | 0.095 |
| **History of Use:** | | | | | | |
| Diuretics (thiazides, potassium sparing, loop diuretics) | 42,882 | 86.4% | 458,271 | 65.9% | 20.473 | 0.495 |
| Everolimus | 11 | 0.0% | 183 | 0.0% | -0.004 | -0.003 |
| Nonsteroidal anti-inflammatory drugs (NSAIDs) | 5,678 | 11.4% | 88,974 | 12.8% | -1.360 | -0.042 |
| Sirolimus | ***** | ***** | 208 | 0.0% | -0.018 | -0.012 |
| **Health Service Utilization Intensity:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean number of ambulatory encounters | 17.5 | 13.4 | 17.4 | 19.7 | 0.193 | 0.011 |
| Mean number of emergency room encounters | 0.6 | 1.3 | 0.9 | 1.8 | -0.233 | -0.149 |
| Mean number of inpatient hospital encounters | 0.7 | 1.0 | 1.0 | 1.2 | -0.280 | -0.256 |
| Mean number of non-acute institutional encounters | 0.2 | 0.7 | 0.4 | 1.1 | -0.258 | -0.289 |
| Mean number of other ambulatory encounters | 7.3 | 10.6 | 12.8 | 18.0 | -5.565 | -0.377 |
| *Mean number of filled prescriptions* | *31.8* | *20.3* | *26.9* | *23.0* | *4.963* | *0.229* |
| *Mean number of generics* | *13.2* | *5.1* | *11.5* | *5.7* | *1.669* | *0.309* |
| Mean number of unique drug classes | 11.4 | 4.5 | 10.8 | 5.0 | 0.623 | 0.131 |

[1]Covariates in italics were not included in the propensity score logistic regression model

[2]Covariates in blue show a standardized difference greater than 0.1

[3]The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 1h. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedemain the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020, Fixed Ratio 1:1, Caliper: 0.05**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Patients (Number) | 49,628 | 100.0% | 49,628 | 7.1% | - | - |
| **Demographics** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean age (years) | 70.4 | 11.1 | 70.5 | 12.0 | -0.018 | -0.002 |
| Age | **Number** | **Percent** | **Number** | **Percent** | | |
| 18-44 years | 1,592 | 3.2% | 1,778 | 3.6% | -0.375 | -0.021 |
| 45-54 years | 3,425 | 6.9% | 3,879 | 7.8% | -0.915 | -0.036 |
| 55-64 years | 8,066 | 16.3% | 8,362 | 16.8% | -0.596 | -0.016 |
| 65+ years | 36,545 | 73.6% | 35,609 | 71.8% | 1.886 | 0.045 |
| Sex | | | | | | |
| Female | 14,886 | 30.0% | 15,194 | 30.6% | -0.621 | -0.014 |
| Male | 34,742 | 70.0% | 34,434 | 69.4% | 0.621 | 0.014 |
| Race | | | | | | |
| American Indian or Alaska Native | 165 | 0.3% | 157 | 0.3% | 0.016 | 0.003 |
| Asian | 526 | 1.1% | 498 | 1.0% | 0.056 | 0.006 |
| Black or African American | 6,073 | 12.2% | 6,128 | 12.3% | -0.111 | -0.003 |
| Native Hawaiian or Other Pacific Islander | 46 | 0.1% | 60 | 0.1% | -0.028 | -0.009 |
| Unknown | 8,192 | 16.5% | 8,156 | 16.4% | 0.073 | 0.003 |
| White | 34,626 | 69.8% | 34,629 | 69.8% | -0.006 | -0.000 |
| Hispanic Origin | 990 | 2.0% | 1,109 | 2.2% | -0.240 | -0.017 |
| Year | | | | | | |
| 2015 | 951 | 1.9% | 895 | 1.8% | 0.113 | 0.008 |
| 2016 | 6,862 | 13.8% | 6,855 | 13.8% | 0.014 | 0.000 |
| 2017 | 11,714 | 23.6% | 11,709 | 23.6% | 0.010 | 0.000 |
| 2018 | 13,939 | 28.1% | 14,045 | 28.3% | -0.214 | -0.005 |
| 2019 | 15,917 | 32.1% | 15,886 | 32.0% | 0.062 | 0.001 |
| 2020 | 245 | 3.9% | 238 | 3.8% | 0.112 | 0.006 |
| **Recorded History of:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Charlson/Elixhauser Combined Comorbidity Score[3] | 5.1 | 2.6 | 5.1 | 2.6 | -0.008 | -0.003 |
| | **Number** | **Percent** | **Number** | **Percent** | | |
| *Ambulatory allergies or allergy treatment* | *23,930* | *48.2%* | *23,912* | *48.2%* | *0.036* | *0.001* |
| Angioedema (-183, -1) | 46 | 0.1% | 54 | 0.1% | -0.016 | -0.005 |
| *Angioedema (ever, -1)* | *333* | *0.7%* | *539* | *1.1%* | *-0.415* | *-0.044* |
| Diabetes | 24,858 | 50.1% | 24,757 | 49.9% | 0.204 | 0.004 |
| Ischemic heart disease | 39,137 | 78.9% | 39,128 | 78.8% | 0.018 | 0.000 |
| Renal disorders | 18,823 | 37.9% | 18,881 | 38.0% | -0.117 | -0.002 |
| Serious allergies | 5,370 | 10.8% | 5,418 | 10.9% | -0.097 | -0.003 |

**Table 1h. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedemain the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020, Fixed Ratio 1:1, Caliper: 0.05**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Ambulatory allergies or treatment and not serious allergies | 20,360 | 41.0% | 20,491 | 41.3% | -0.264 | -0.005 |
| **History of Use:** | | | | | | |
| Diuretics (thiazides, potassium sparing, loop diuretics) | 42,881 | 86.4% | 43,054 | 86.8% | -0.349 | -0.010 |
| Everolimus | 11 | 0.0% | 14 | 0.0% | -0.006 | -0.004 |
| Nonsteroidal anti-inflammatory drugs (NSAIDs) | 5,678 | 11.4% | 5,746 | 11.6% | -0.137 | -0.004 |
| Sirolimus | ***** | ***** | ***** | ***** | -0.002 | -0.002 |
| **Health Service Utilization Intensity:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean number of ambulatory encounters | 17.5 | 13.4 | 17.6 | 20.0 | -0.048 | -0.003 |
| Mean number of emergency room encounters | 0.6 | 1.3 | 0.6 | 1.1 | -0.007 | -0.006 |
| Mean number of inpatient hospital encounters | 0.7 | 1.0 | 0.7 | 0.9 | -0.004 | -0.004 |
| Mean number of non-acute institutional encounters | 0.2 | 0.7 | 0.2 | 0.7 | -0.003 | -0.005 |
| Mean number of other ambulatory encounters | 7.3 | 10.6 | 7.3 | 9.7 | -0.004 | -0.000 |
| *Mean number of filled prescriptions* | *31.8* | *20.3* | *28.0* | *22.5* | *3.788* | *0.177* |
| *Mean number of generics* | *13.2* | *5.1* | *12.2* | *5.6* | *1.029* | *0.192* |
| Mean number of unique drug classes | 11.4 | 4.5 | 11.4 | 5.0 | -0.002 | -0.000 |

[1]Covariates in italics were not included in the propensity score logistic regression model

[2]Covariates in blue show a standardized difference greater than 0.1

[3]The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity sco re predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 1i. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)**

| Characteristic[1,2] | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ARBs | | | |
| | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Patients (Number) | 35,703 | 100.0% | 337,204 | 100.0% | - | - |
| **Demographics** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean age (years) | 72.8 | 10.6 | 73.8 | 12.0 | -1.042 | -0.092 |
| Age | **Number** | **Percent** | **Number** | **Percent** | | |
| 18-44 years | 774 | 2.2% | 8,505 | 2.5% | -0.354 | -0.023 |
| 45-54 years | 1,794 | 5.0% | 18,304 | 5.4% | -0.403 | -0.018 |
| 55-64 years | 4,275 | 12.0% | 40,567 | 12.0% | -0.057 | -0.002 |
| 65+ years | 28,860 | 80.8% | 269,828 | 80.0% | 0.814 | 0.021 |
| Sex | | | | | | |
| Female | 13,901 | 38.9% | 187,925 | 55.7% | -16.795 | -0.341 |
| Male | 21,802 | 61.1% | 149,279 | 44.3% | 16.795 | 0.341 |
| Race | | | | | | |
| American Indian or Alaska Native | 86 | 0.2% | 1,948 | 0.6% | -0.337 | -0.053 |
| Asian | 863 | 2.4% | 7,814 | 2.3% | 0.100 | 0.007 |
| Black or African American | 4,832 | 13.5% | 55,825 | 16.6% | -3.021 | -0.085 |
| Native Hawaiian or Other Pacific Islander | 46 | 0.1% | 478 | 0.1% | -0.013 | -0.004 |
| Unknown | 5,777 | 16.2% | 47,811 | 14.2% | 2.002 | 0.056 |
| White | 24,099 | 67.5% | 223,328 | 66.2% | 1.269 | 0.027 |
| Hispanic Origin | 887 | 2.5% | 9,034 | 2.7% | -0.195 | -0.012 |
| Year | | | | | | |
| 2015 | 615 | 1.7% | 32,231 | 9.6% | -7.836 | -0.345 |
| 2016 | 4,471 | 12.5% | 70,701 | 21.0% | -8.444 | -0.228 |
| 2017 | 7,825 | 21.9% | 73,818 | 21.9% | 0.026 | 0.001 |
| 2018 | 10,142 | 28.4% | 81,689 | 24.2% | 4.181 | 0.095 |
| 2019 | 12,431 | 34.8% | 77,659 | 23.0% | 11.788 | 0.262 |
| 2020 | 219 | 5.2% | 1,106 | 3.2% | 2.000 | 0.099 |
| **Recorded History of:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Charlson/Elixhauser Combined Comorbidity Score[3] | 5.3 | 2.6 | 5.8 | 3.0 | -0.460 | -0.165 |
| | **Number** | **Percent** | **Number** | **Percent** | | |
| *Ambulatory allergies or allergy treatment* | *19,158* | *53.7%* | *169,574* | *50.3%* | *3.371* | *0.068* |
| Angioedema (-183, -1) | 35 | 0.1% | 825 | 0.2% | -0.147 | -0.035 |
| *Angioedema (ever, -1)* | *541* | *1.5%* | *7,359* | *2.2%* | *-0.667* | *-0.050* |
| Diabetes | 19,018 | 53.3% | 173,568 | 51.5% | 1.795 | 0.036 |
| Ischemic heart disease | 27,797 | 77.9% | 204,033 | 60.5% | 17.349 | 0.383 |
| Renal disorders | 14,977 | 41.9% | 154,691 | 45.9% | -3.926 | -0.079 |
| Serious allergies | 4,472 | 12.5% | 54,454 | 16.1% | -3.623 | -0.104 |

**Table 1i. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)**

| Characteristic[1,2] | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ARBs | | | |
| | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Ambulatory allergies or treatment and not serious allergies | 16,113 | 45.1% | 134,493 | 39.9% | 5.246 | 0.106 |
| **History of Use:** | | | | | | |
| Diuretics (thiazides, potassium sparing, loop diuretics) | 31,138 | 87.2% | 222,966 | 66.1% | 21.092 | 0.515 |
| Everolimus | ***** | ***** | 98 | 0.0% | -0.001 | -0.001 |
| Nonsteroidal anti-inflammatory drugs (NSAIDs) | 4,177 | 11.7% | 44,193 | 13.1% | -1.406 | -0.043 |
| Sirolimus | ***** | ***** | 142 | 0.0% | -0.028 | -0.017 |
| **Health Service Utilization Intensity:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean number of ambulatory encounters | 19.0 | 14.7 | 20.4 | 22.5 | -1.447 | -0.076 |
| Mean number of emergency room encounters | 0.6 | 1.3 | 0.8 | 1.7 | -0.200 | -0.134 |
| Mean number of inpatient hospital encounters | 0.7 | 1.0 | 0.8 | 1.1 | -0.130 | -0.120 |
| Mean number of non-acute institutional encounters | 0.2 | 0.7 | 0.4 | 1.0 | -0.211 | -0.241 |
| Mean number of other ambulatory encounters | 7.4 | 10.4 | 11.7 | 17.4 | -4.289 | -0.299 |
| *Mean number of filled prescriptions* | *33.3* | *21.7* | *27.8* | *22.3* | *5.583* | *0.254* |
| *Mean number of generics* | *14.0* | *5.4* | *12.0* | *5.8* | *2.009* | *0.358* |
| Mean number of unique drug classes | 12.1 | 4.8 | 11.2 | 5.1 | 0.886 | 0.179 |

[1]Covariates in italics were not included in the propensity score logistic regression model

[2]Covariates in blue show a standardized difference greater than 0.1

[3]The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 1j. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Adjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ARBs | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Patients (Number) | 35,702 | 100.0% | 35,702 | 10.6% | - | - |
| **Demographics** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean age (years) | 72.8 | 10.6 | 72.8 | 11.4 | -0.050 | -0.005 |
| Age | **Number** | **Percent** | **Number** | **Percent** | | |
| 18-44 years | 774 | 2.2% | 796 | 2.2% | -0.062 | -0.004 |
| 45-54 years | 1,794 | 5.0% | 2,104 | 5.9% | -0.868 | -0.039 |
| 55-64 years | 4,275 | 12.0% | 4,789 | 13.4% | -1.440 | -0.045 |
| 65+ years | 28,859 | 80.8% | 28,013 | 78.5% | 2.370 | 0.063 |
| Sex | | | | | | |
| Female | 13,901 | 38.9% | 14,074 | 39.4% | -0.485 | -0.010 |
| Male | 21,801 | 61.1% | 21,628 | 60.6% | 0.485 | 0.010 |
| Race | | | | | | |
| American Indian or Alaska Native | 86 | 0.2% | 85 | 0.2% | 0.003 | 0.001 |
| Asian | 862 | 2.4% | 886 | 2.5% | -0.067 | -0.004 |
| Black or African American | 4,832 | 13.5% | 4,869 | 13.6% | -0.104 | -0.003 |
| Native Hawaiian or Other Pacific Islander | 46 | 0.1% | 43 | 0.1% | 0.008 | 0.002 |
| Unknown | 5,777 | 16.2% | 5,754 | 16.1% | 0.064 | 0.003 |
| White | 24,099 | 67.5% | 24,065 | 67.4% | 0.095 | 0.002 |
| Hispanic Origin | 887 | 2.5% | 899 | 2.5% | -0.034 | -0.002 |
| Year | | | | | | |
| 2015 | 615 | 1.7% | 586 | 1.6% | 0.081 | 0.006 |
| 2016 | 4,471 | 12.5% | 4,444 | 12.4% | 0.076 | 0.002 |
| 2017 | 7,824 | 21.9% | 7,801 | 21.9% | 0.064 | 0.002 |
| 2018 | 10,142 | 28.4% | 10,242 | 28.7% | -0.280 | -0.006 |
| 2019 | 12,431 | 34.8% | 12,429 | 34.8% | 0.006 | 0.000 |
| 2020 | 219 | 5.2% | 200 | 4.8% | 0.455 | 0.021 |
| **Recorded History of:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Charlson/Elixhauser Combined Comorbidity Score[3] | 5.3 | 2.6 | 5.3 | 2.6 | 0.016 | 0.006 |
| | **Number** | **Percent** | **Number** | **Percent** | | |
| *Ambulatory allergies or allergy treatment* | *19,157* | *53.7%* | *18,976* | *53.2%* | *0.507* | *0.010* |
| Angioedema (-183, -1) | 35 | 0.1% | 38 | 0.1% | -0.008 | -0.003 |
| *Angioedema (ever, -1)* | *541* | *1.5%* | *731* | *2.0%* | *-0.532* | *-0.040* |
| Diabetes | 19,017 | 53.3% | 19,134 | 53.6% | -0.328 | -0.007 |
| Ischemic heart disease | 27,796 | 77.9% | 27,790 | 77.8% | 0.017 | 0.000 |
| Renal disorders | 14,977 | 42.0% | 14,929 | 41.8% | 0.134 | 0.003 |
| Serious allergies | 4,472 | 12.5% | 4,463 | 12.5% | 0.025 | 0.001 |

**Table 1j. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Adjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05**

| Characteristic[1,2] | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ARBs | | | |
| | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Ambulatory allergies or treatment and not serious allergies | 16,112 | 45.1% | 16,023 | 44.9% | 0.249 | 0.005 |
| **History of Use:** | | | | | | |
| Diuretics (thiazides, potassium sparing, loop diuretics) | 31,137 | 87.2% | 31,197 | 87.4% | -0.168 | -0.005 |
| Everolimus | ***** | ***** | ***** | ***** | 0.003 | 0.002 |
| Nonsteroidal anti-inflammatory drugs (NSAIDs) | 4,177 | 11.7% | 4,171 | 11.7% | 0.017 | 0.001 |
| Sirolimus | ***** | ***** | ***** | ***** | -0.008 | -0.006 |
| **Health Service Utilization Intensity:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean number of ambulatory encounters | 19.0 | 14.7 | 18.8 | 19.1 | 0.195 | 0.011 |
| Mean number of emergency room encounters | 0.6 | 1.3 | 0.6 | 1.1 | -0.008 | -0.007 |
| Mean number of inpatient hospital encounters | 0.7 | 1.0 | 0.7 | 1.0 | 0.003 | 0.003 |
| Mean number of non-acute institutional encounters | 0.2 | 0.7 | 0.2 | 0.7 | -0.002 | -0.003 |
| Mean number of other ambulatory encounters | 7.4 | 10.4 | 7.4 | 10.0 | 0.032 | 0.003 |
| *Mean number of filled prescriptions* | *33.3* | *21.7* | *30.0* | *22.9* | *3.305* | *0.148* |
| *Mean number of generics* | *14.0* | *5.4* | *12.9* | *5.8* | *1.078* | *0.192* |
| Mean number of unique drug classes | 12.1 | 4.7 | 12.1 | 5.1 | -0.007 | -0.001 |

[1]Covariates in italics were not included in the propensity score logistic regression model

[2]Covariates in blue show a standardized difference greater than 0.1

[3]The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 1k. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Patients (Number) | 69,639 | 100.0% | 694,882 | 100.0% | - | - |
| **Demographics** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean age (years) | 70.2 | 11.2 | 72.7 | 12.5 | -2.563 | -0.216 |
| Age | **Number** | **Percent** | **Number** | **Percent** | | |
| 18-44 years | 2,412 | 3.5% | 21,587 | 3.1% | 0.357 | 0.020 |
| 45-54 years | 5,115 | 7.3% | 45,057 | 6.5% | 0.861 | 0.034 |
| 55-64 years | 11,494 | 16.5% | 97,244 | 14.0% | 2.511 | 0.070 |
| 65+ years | 50,618 | 72.7% | 530,994 | 76.4% | -3.729 | -0.086 |
| Sex | | | | | | |
| Female | 21,199 | 30.4% | 341,867 | 49.2% | -18.757 | -0.390 |
| Male | 48,440 | 69.6% | 353,015 | 50.8% | 18.757 | 0.390 |
| Race | | | | | | |
| American Indian or Alaska Native | 242 | 0.3% | 4,525 | 0.7% | -0.304 | -0.043 |
| Asian | 666 | 1.0% | 7,871 | 1.1% | -0.176 | -0.017 |
| Black or African American | 9,015 | 12.9% | 92,098 | 13.3% | -0.308 | -0.009 |
| Native Hawaiian or Other Pacific Islander | 66 | 0.1% | 741 | 0.1% | -0.012 | -0.004 |
| Unknown | 11,656 | 16.7% | 99,645 | 14.3% | 2.398 | 0.066 |
| White | 47,994 | 68.9% | 490,002 | 70.5% | -1.598 | -0.035 |
| Hispanic Origin | 1,351 | 1.9% | 15,586 | 2.2% | -0.303 | -0.021 |
| Year | | | | | | |
| 2015 | 1,349 | 1.9% | 87,092 | 12.5% | -10.596 | -0.418 |
| 2016 | 10,510 | 15.1% | 172,880 | 24.9% | -9.787 | -0.247 |
| 2017 | 16,864 | 24.2% | 156,573 | 22.5% | 1.684 | 0.040 |
| 2018 | 19,077 | 27.4% | 142,979 | 20.6% | 6.818 | 0.160 |
| 2019 | 21,511 | 30.9% | 133,608 | 19.2% | 11.662 | 0.272 |
| 2020 | 328 | 3.6% | 1,750 | 2.4% | 1.194 | 0.070 |
| **Recorded History of:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Charlson/Elixhauser Combined Comorbidity Score[3] | 5.2 | 2.7 | 5.8 | 3.0 | -0.610 | -0.214 |
| | **Number** | **Percent** | **Number** | **Percent** | | |
| *Ambulatory allergies or allergy treatment* | *33,754* | *48.5%* | *320,699* | *46.2%* | *2.318* | *0.046* |
| Angioedema (-183, -1) | 83 | 0.1% | 864 | 0.1% | -0.005 | -0.001 |
| *Angioedema (ever, -1)* | *494* | *0.7%* | *7,317* | *1.1%* | *-0.344* | *-0.037* |
| Diabetes | 35,071 | 50.4% | 326,005 | 46.9% | 3.446 | 0.069 |
| Ischemic heart disease | 55,067 | 79.1% | 432,968 | 62.3% | 16.767 | 0.375 |
| Renal disorders | 27,364 | 39.3% | 289,746 | 41.7% | -2.403 | -0.049 |
| Serious allergies | 8,047 | 11.6% | 110,960 | 16.0% | -4.413 | -0.128 |

**Table 1k. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Ambulatory allergies or treatment and not serious allergies | 28,444 | 40.8% | 252,983 | 36.4% | 4.438 | 0.091 |
| **History of Use:** | | | | | | |
| Diuretics (thiazides, potassium sparing, loop diuretics) | 60,338 | 86.6% | 458,102 | 65.9% | 20.719 | 0.502 |
| Everolimus | 11 | 0.0% | 183 | 0.0% | -0.011 | -0.007 |
| Nonsteroidal anti-inflammatory drugs (NSAIDs) | 7,793 | 11.2% | 88,957 | 12.8% | -1.611 | -0.050 |
| Sirolimus | ***** | ***** | 208 | 0.0% | -0.018 | -0.013 |
| **Health Service Utilization Intensity:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean number of ambulatory encounters | 17.9 | 13.7 | 17.4 | 19.7 | 0.531 | 0.031 |
| Mean number of emergency room encounters | 0.7 | 1.4 | 0.9 | 1.8 | -0.188 | -0.115 |
| Mean number of inpatient hospital encounters | 0.8 | 1.1 | 1.0 | 1.2 | -0.211 | -0.186 |
| Mean number of non-acute institutional encounters | 0.2 | 0.8 | 0.4 | 1.1 | -0.217 | -0.235 |
| Mean number of other ambulatory encounters | 8.1 | 12.2 | 12.8 | 18.0 | -4.732 | -0.308 |
| *Mean number of filled prescriptions* | *31.3* | *19.8* | *26.9* | *23.0* | *4.408* | *0.205* |
| *Mean number of generics* | *13.1* | *5.1* | *11.5* | *5.7* | *1.614* | *0.297* |
| Mean number of unique drug classes | 11.4 | 4.5 | 10.8 | 5.0 | 0.626 | 0.131 |

[1]Covariates in italics were not included in the propensity score logistic regression model

[2]Covariates in blue show a standardized difference greater than 0.1

[3]The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 1l. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Adjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Patients (Number) | 69,639 | 100.0% | 69,639 | 10.0% | - | - |
| **Demographics** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean age (years) | 70.2 | 11.2 | 70.2 | 12.2 | -0.019 | -0.002 |
| Age | **Number** | **Percent** | **Number** | **Percent** | | |
| 18-44 years | 2,412 | 3.5% | 2,717 | 3.9% | -0.438 | -0.024 |
| 45-54 years | 5,115 | 7.3% | 5,694 | 8.2% | -0.831 | -0.032 |
| 55-64 years | 11,494 | 16.5% | 11,900 | 17.1% | -0.583 | -0.016 |
| 65+ years | 50,618 | 72.7% | 49,328 | 70.8% | 1.852 | 0.044 |
| Sex | | | | | | |
| Female | 21,199 | 30.4% | 21,398 | 30.7% | -0.286 | -0.006 |
| Male | 48,440 | 69.6% | 48,241 | 69.3% | 0.286 | 0.006 |
| Race | | | | | | |
| American Indian or Alaska Native | 242 | 0.3% | 242 | 0.3% | 0.000 | 0.000 |
| Asian | 666 | 1.0% | 662 | 1.0% | 0.006 | 0.001 |
| Black or African American | 9,015 | 12.9% | 9,043 | 13.0% | -0.040 | -0.001 |
| Native Hawaiian or Other Pacific Islander | 66 | 0.1% | 75 | 0.1% | -0.013 | -0.004 |
| Unknown | 11,656 | 16.7% | 11,662 | 16.7% | -0.009 | -0.000 |
| White | 47,994 | 68.9% | 47,955 | 68.9% | 0.056 | 0.001 |
| Hispanic Origin | 1,351 | 1.9% | 1,521 | 2.2% | -0.244 | -0.017 |
| Year | | | | | | |
| 2015 | 1,349 | 1.9% | 1,255 | 1.8% | 0.135 | 0.010 |
| 2016 | 10,510 | 15.1% | 10,469 | 15.0% | 0.059 | 0.002 |
| 2017 | 16,864 | 24.2% | 16,928 | 24.3% | -0.092 | -0.002 |
| 2018 | 19,077 | 27.4% | 19,069 | 27.4% | 0.011 | 0.000 |
| 2019 | 21,511 | 30.9% | 21,555 | 31.0% | -0.063 | -0.001 |
| 2020 | 328 | 3.6% | 363 | 4.0% | -0.385 | -0.020 |
| **Recorded History of:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Charlson/Elixhauser Combined Comorbidity Score[3] | 5.2 | 2.7 | 5.2 | 2.6 | -0.017 | -0.006 |
| | **Number** | **Percent** | **Number** | **Percent** | | |
| *Ambulatory allergies or allergy treatment* | *33,754* | *48.5%* | *33,596* | *48.2%* | *0.227* | *0.005* |
| Angioedema (-183, -1) | 83 | 0.1% | 92 | 0.1% | -0.013 | -0.004 |
| *Angioedema (ever, -1)* | *494* | *0.7%* | *723* | *1.0%* | *-0.329* | *-0.035* |
| Diabetes | 35,071 | 50.4% | 34,906 | 50.1% | 0.237 | 0.005 |
| Ischemic heart disease | 55,067 | 79.1% | 55,153 | 79.2% | -0.123 | -0.003 |
| Renal disorders | 27,364 | 39.3% | 27,495 | 39.5% | -0.188 | -0.004 |
| Serious allergies | 8,047 | 11.6% | 8,038 | 11.5% | 0.013 | 0.000 |

**Table 1l. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Adjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Ambulatory allergies or treatment and not serious allergies | 28,444 | 40.8% | 28,475 | 40.9% | -0.045 | -0.001 |
| **History of Use:** | | | | | | |
| Diuretics (thiazides, potassium sparing, loop diuretics) | 60,338 | 86.6% | 60,422 | 86.8% | -0.121 | -0.004 |
| Everolimus | 11 | 0.0% | 12 | 0.0% | -0.001 | -0.001 |
| Nonsteroidal anti-inflammatory drugs (NSAIDs) | 7,793 | 11.2% | 7,766 | 11.2% | 0.039 | 0.001 |
| Sirolimus | ***** | ***** | 14 | 0.0% | -0.009 | -0.007 |
| **Health Service Utilization Intensity:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean number of ambulatory encounters | 17.9 | 13.7 | 17.9 | 20.5 | -0.041 | -0.002 |
| Mean number of emergency room encounters | 0.7 | 1.4 | 0.7 | 1.2 | -0.003 | -0.002 |
| Mean number of inpatient hospital encounters | 0.8 | 1.1 | 0.8 | 0.9 | -0.011 | -0.010 |
| Mean number of non-acute institutional encounters | 0.2 | 0.8 | 0.2 | 0.7 | -0.006 | -0.008 |
| Mean number of other ambulatory encounters | 8.1 | 12.2 | 8.2 | 11.0 | -0.062 | -0.005 |
| *Mean number of filled prescriptions* | *31.3* | *19.8* | *28.2* | *22.9* | *3.118* | *0.146* |
| *Mean number of generics* | *13.1* | *5.1* | *12.2* | *5.7* | *0.922* | *0.170* |
| Mean number of unique drug classes | 11.4 | 4.5 | 11.4 | 5.0 | -0.041 | -0.009 |

[1]Covariates in italics were not included in the propensity score logistic regression model

[2]Covariates in blue show a standardized difference greater than 0.1

[3]The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 1m. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)**

| Characteristic[1,2] | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Patients (Number) | 49,140 | 100.0% | 337,083 | 100.0% | - | - |
| **Demographics** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean age (years) | 72.6 | 10.7 | 73.8 | 12.0 | -1.241 | -0.109 |
| Age | **Number** | **Percent** | **Number** | **Percent** | | |
| 18-44 years | 1,164 | 2.4% | 8,502 | 2.5% | -0.153 | -0.010 |
| 45-54 years | 2,653 | 5.4% | 18,293 | 5.4% | -0.028 | -0.001 |
| 55-64 years | 5,990 | 12.2% | 40,547 | 12.0% | 0.161 | 0.005 |
| 65+ years | 39,333 | 80.0% | 269,741 | 80.0% | 0.021 | 0.001 |
| Sex | | | | | | |
| Female | 19,226 | 39.1% | 187,871 | 55.7% | -16.609 | -0.337 |
| Male | 29,914 | 60.9% | 149,212 | 44.3% | 16.609 | 0.337 |
| Race | | | | | | |
| American Indian or Alaska Native | 133 | 0.3% | 1,948 | 0.6% | -0.307 | -0.047 |
| Asian | 1,070 | 2.2% | 7,811 | 2.3% | -0.140 | -0.009 |
| Black or African American | 6,989 | 14.2% | 55,801 | 16.6% | -2.331 | -0.065 |
| Native Hawaiian or Other Pacific Islander | 61 | 0.1% | 478 | 0.1% | -0.018 | -0.005 |
| Unknown | 8,082 | 16.4% | 47,793 | 14.2% | 2.268 | 0.063 |
| White | 32,805 | 66.8% | 223,252 | 66.2% | 0.528 | 0.011 |
| Hispanic Origin | 1,135 | 2.3% | 9,032 | 2.7% | -0.370 | -0.024 |
| Year | | | | | | |
| 2015 | 878 | 1.8% | 32,231 | 9.6% | -7.775 | -0.341 |
| 2016 | 6,685 | 13.6% | 70,696 | 21.0% | -7.369 | -0.196 |
| 2017 | 11,072 | 22.5% | 73,800 | 21.9% | 0.638 | 0.015 |
| 2018 | 13,611 | 27.7% | 81,657 | 24.2% | 3.474 | 0.079 |
| 2019 | 16,598 | 33.8% | 77,594 | 23.0% | 10.758 | 0.240 |
| 2020 | 296 | 4.9% | 1,105 | 3.2% | 1.652 | 0.084 |
| **Recorded History of:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Charlson/Elixhauser Combined Comorbidity Score[3] | 5.4 | 2.7 | 5.8 | 3.0 | -0.374 | -0.133 |
| | **Number** | **Percent** | **Number** | **Percent** | | |
| *Ambulatory allergies or allergy treatment* | *26,106* | *53.1%* | *169,522* | *50.3%* | *2.835* | *0.057* |
| Angioedema (-183, -1) | 58 | 0.1% | 825 | 0.2% | -0.127 | -0.030 |
| *Angioedema (ever, -1)* | *750* | *1.5%* | *7,357* | *2.2%* | *-0.656* | *-0.049* |
| Diabetes | 26,110 | 53.1% | 173,497 | 51.5% | 1.664 | 0.033 |
| Ischemic heart disease | 38,297 | 77.9% | 203,944 | 60.5% | 17.432 | 0.385 |
| Renal disorders | 21,237 | 43.2% | 154,620 | 45.9% | -2.653 | -0.053 |
| Serious allergies | 6,466 | 13.2% | 54,435 | 16.1% | -2.991 | -0.085 |

**Table 1m. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Unadjusted, Aggregated)**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Ambulatory allergies or treatment and not serious allergies | 21,703 | 44.2% | 134,451 | 39.9% | 4.279 | 0.087 |
| **History of Use:** | | | | | | |
| Diuretics (thiazides, potassium sparing, loop diuretics) | 42,889 | 87.3% | 222,859 | 66.1% | 21.165 | 0.517 |
| Everolimus | 15 | 0.0% | 98 | 0.0% | 0.001 | 0.001 |
| Nonsteroidal anti-inflammatory drugs (NSAIDs) | 5,633 | 11.5% | 44,187 | 13.1% | -1.645 | -0.050 |
| Sirolimus | ***** | ***** | 142 | 0.0% | -0.030 | -0.018 |
| **Health Service Utilization Intensity:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean number of ambulatory encounters | 19.2 | 14.8 | 20.4 | 22.5 | -1.228 | -0.064 |
| Mean number of emergency room encounters | 0.6 | 1.3 | 0.8 | 1.7 | -0.169 | -0.112 |
| Mean number of inpatient hospital encounters | 0.8 | 1.1 | 0.8 | 1.1 | -0.079 | -0.071 |
| Mean number of non-acute institutional encounters | 0.2 | 0.7 | 0.4 | 1.0 | -0.174 | -0.192 |
| Mean number of other ambulatory encounters | 8.1 | 11.6 | 11.7 | 17.4 | -3.639 | -0.246 |
| *Mean number of filled prescriptions* | *32.5* | *20.9* | *27.8* | *22.3* | *4.697* | *0.217* |
| *Mean number of generics* | *13.8* | *5.4* | *12.0* | *5.8* | *1.857* | *0.331* |
| Mean number of unique drug classes | 12.0 | 4.7 | 11.2 | 5.1 | 0.812 | 0.164 |

[1]Covariates in italics were not included in the propensity score logistic regression model

[2]Covariates in blue show a standardized difference greater than 0.1

[3]The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity sc ore predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 1n. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Adjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Patients (Number) | 49,137 | 100.0% | 49,137 | 14.6% | - | - |
| **Demographics** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean age (years) | 72.6 | 10.7 | 72.6 | 11.5 | -0.016 | -0.001 |
| Age | **Number** | **Percent** | **Number** | **Percent** | | |
| 18-44 years | 1,164 | 2.4% | 1,231 | 2.5% | -0.136 | -0.009 |
| 45-54 years | 2,652 | 5.4% | 2,977 | 6.1% | -0.661 | -0.029 |
| 55-64 years | 5,988 | 12.2% | 6,682 | 13.6% | -1.412 | -0.043 |
| 65+ years | 39,333 | 80.0% | 38,247 | 77.8% | 2.210 | 0.058 |
| Sex | | | | | | |
| Female | 19,226 | 39.1% | 19,287 | 39.3% | -0.124 | -0.003 |
| Male | 29,911 | 60.9% | 29,850 | 60.7% | 0.124 | 0.003 |
| Race | | | | | | |
| American Indian or Alaska Native | 133 | 0.3% | 144 | 0.3% | -0.022 | -0.004 |
| Asian | 1,070 | 2.2% | 1,059 | 2.2% | 0.022 | 0.002 |
| Black or African American | 6,988 | 14.2% | 7,004 | 14.3% | -0.033 | -0.001 |
| Native Hawaiian or Other Pacific Islander | 61 | 0.1% | 53 | 0.1% | 0.016 | 0.005 |
| Unknown | 8,080 | 16.4% | 8,091 | 16.5% | -0.022 | -0.001 |
| White | 32,805 | 66.8% | 32,786 | 66.7% | 0.039 | 0.001 |
| Hispanic Origin | 1,135 | 2.3% | 1,221 | 2.5% | -0.175 | -0.011 |
| Year | | | | | | |
| 2015 | 878 | 1.8% | 822 | 1.7% | 0.114 | 0.009 |
| 2016 | 6,685 | 13.6% | 6,735 | 13.7% | -0.102 | -0.003 |
| 2017 | 11,072 | 22.5% | 11,079 | 22.5% | -0.014 | -0.000 |
| 2018 | 13,611 | 27.7% | 13,558 | 27.6% | 0.108 | 0.002 |
| 2019 | 16,595 | 33.8% | 16,643 | 33.9% | -0.098 | -0.002 |
| 2020 | 296 | 4.9% | 300 | 5.0% | -0.066 | -0.003 |
| **Recorded History of:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Charlson/Elixhauser Combined Comorbidity Score[3] | 5.4 | 2.7 | 5.4 | 2.7 | 0.001 | 0.000 |
| | **Number** | **Percent** | **Number** | **Percent** | | |
| *Ambulatory allergies or allergy treatment* | *26,103* | *53.1%* | *26,126* | *53.2%* | *-0.047* | *-0.001* |
| Angioedema (-183, -1) | 58 | 0.1% | 56 | 0.1% | 0.004 | 0.001 |
| *Angioedema (ever, -1)* | *750* | *1.5%* | *1,084* | *2.2%* | *-0.680* | *-0.050* |
| Diabetes | 26,109 | 53.1% | 25,978 | 52.9% | 0.267 | 0.005 |
| Ischemic heart disease | 38,294 | 77.9% | 38,161 | 77.7% | 0.271 | 0.007 |
| Renal disorders | 21,235 | 43.2% | 21,281 | 43.3% | -0.094 | -0.002 |
| Serious allergies | 6,466 | 13.2% | 6,500 | 13.2% | -0.069 | -0.002 |

**Table 1n. Cohort of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 (Adjusted, Aggregated), Fixed Ratio 1:1, Caliper: 0.05**

| | Medical Product | | | | Covariate Balance | |
|---|---|---|---|---|---|---|
| | SV | | ACEI | | | |
| Characteristic[1,2] | Number | Percent | Number | Percent | Absolute Difference | Standardized Difference |
| Ambulatory allergies or treatment and not serious allergies | 21,700 | 44.2% | 21,734 | 44.2% | -0.069 | -0.001 |
| **History of Use:** | | | | | | |
| Diuretics (thiazides, potassium sparing, loop diuretics) | 42,886 | 87.3% | 42,937 | 87.4% | -0.104 | -0.003 |
| Everolimus | 15 | 0.0% | 19 | 0.0% | -0.008 | -0.004 |
| Nonsteroidal anti-inflammatory drugs (NSAIDs) | 5,633 | 11.5% | 5,752 | 11.7% | -0.242 | -0.008 |
| Sirolimus | ***** | ***** | ***** | ***** | 0.004 | 0.004 |
| **Health Service Utilization Intensity:** | **Mean** | **Standard Deviation** | **Mean** | **Standard Deviation** | | |
| Mean number of ambulatory encounters | 19.2 | 14.8 | 19.2 | 19.8 | -0.002 | -0.000 |
| Mean number of emergency room encounters | 0.6 | 1.3 | 0.6 | 1.2 | -0.010 | -0.008 |
| Mean number of inpatient hospital encounters | 0.8 | 1.1 | 0.8 | 1.0 | 0.000 | 0.000 |
| Mean number of non-acute institutional encounters | 0.2 | 0.7 | 0.2 | 0.7 | -0.002 | -0.002 |
| Mean number of other ambulatory encounters | 8.1 | 11.6 | 8.1 | 11.0 | 0.006 | 0.001 |
| *Mean number of filled prescriptions* | *32.5* | *20.9* | *29.7* | *22.4* | *2.717* | *0.125* |
| *Mean number of generics* | *13.8* | *5.4* | *12.9* | *5.8* | *0.967* | *0.173* |
| Mean number of unique drug classes | 12.0 | 4.7 | 12.0 | 5.1 | -0.034 | -0.007 |

[1]Covariates in italics were not included in the propensity score logistic regression model

[2]Covariates in blue show a standardized difference greater than 0.1

[3]The Charlson/Elixhauser Combined Comorbidity Score is calculated based on comorbidities observed during a requester-defined window around the exposure episode start date. (Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759)

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 2. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,639 | ***** | ***** | ***** | ***** | 2.14 | ***** | -4.6 | ***** | 0.30 ( 0.23, 0.40) | <0.001 |
| ACEI (14-day gap) | 694,882 | ***** | ***** | ***** | ***** | 6.74 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,639 | ***** | ***** | ***** | ***** | 2.65 | ***** | -7.22 | ***** | 0.27 ( 0.19, 0.39) | <0.001 |
| ACEI (14-day gap) | 69,639 | ***** | ***** | ***** | ***** | 9.87 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,639 | ***** | ***** | ***** | ***** | 2.14 | ***** | -4.33 | ***** | 0.31 ( 0.23, 0.43) | <0.001 |
| ACEI (14-day gap) | 69,639 | ***** | ***** | ***** | ***** | 6.47 | ***** | | | | |
| **Propensity Score Adjusted Stratified Analysis; Percentiles= 10[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,639 | ***** | ***** | ***** | ***** | 2.14 | ***** | -4.6 | ***** | 0.32 ( 0.24, 0.42) | <0.001 |
| ACEI (14-day gap) | 694,882 | ***** | ***** | ***** | ***** | 6.74 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 3. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 69,639 | ***** | ***** | ***** | ***** | 2.14 | ***** | -4.6 | ***** | 0.30 ( 0.23, 0.40) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 694,882 | ***** | ***** | ***** | ***** | 6.74 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 69,639 | ***** | ***** | ***** | ***** | 2.65 | ***** | -7.22 | ***** | 0.27 ( 0.19, 0.39) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 69,639 | ***** | ***** | ***** | ***** | 9.87 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 69,639 | ***** | ***** | ***** | ***** | 2.14 | ***** | -4.33 | ***** | 0.31 ( 0.23, 0.43) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 69,639 | ***** | ***** | ***** | ***** | 6.47 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 69,639 | ***** | ***** | ***** | ***** | 3.49 | ***** | -11.86 | ***** | 0.22 ( 0.14, 0.36) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 694,882 | ***** | ***** | ***** | ***** | 15.35 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 69,639 | ***** | ***** | ***** | ***** | 3.61 | ***** | -15.66 | ***** | 0.19 ( 0.11, 0.31) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 69,639 | ***** | ***** | ***** | ***** | 19.27 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 69,639 | ***** | ***** | ***** | ***** | 3.49 | ***** | -14.63 | ***** | 0.19 ( 0.12, 0.32) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 69,639 | ***** | ***** | ***** | ***** | 18.12 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 55,796 | ***** | ***** | ***** | ***** | 3.17 | ***** | -2.88 | ***** | 0.53 ( 0.29, 0.94) | 0.029 |
| ACEI (183-day prior, 14-day gap) | 638,366 | ***** | ***** | ***** | ***** | 6.05 | ***** | | | | |

**Table 3. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-daygap) | 51,126 | ***** | ***** | ***** | ***** | 3.59 | ***** | -1.3 | ***** | 0.73 ( 0.34, 1.60) | 0.435 |
| ACEI (183-day prior, 14-daygap) | 51,126 | ***** | ***** | ***** | ***** | 4.89 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-daygap) | 55,796 | ***** | ***** | ***** | ***** | 3.17 | ***** | -2.13 | ***** | 0.59 ( 0.30, 1.18) | 0.137 |
| ACEI (183-day prior, 14-daygap) | 63,837 | ***** | ***** | ***** | ***** | 5.3 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-daygap) | 37,655 | ***** | ***** | ***** | ***** | 2.5 | ***** | -3.29 | ***** | 0.43 ( 0.20, 0.92) | 0.029 |
| ACEI (183-day prior, 14-daygap) | 462,969 | ***** | ***** | ***** | ***** | 5.78 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-daygap) | 25,679 | ***** | ***** | ***** | ***** | 2.23 | ***** | -3.35 | ***** | 0.40 ( 0.13, 1.28) | 0.121 |
| ACEI (183-day prior, 14-daygap) | 25,679 | ***** | ***** | ***** | ***** | 5.58 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-daygap) | 37,655 | ***** | ***** | ***** | ***** | 2.5 | ***** | -3.02 | ***** | 0.45 ( 0.19, 1.07) | 0.07 |
| ACEI (183-day prior, 14-daygap) | 47,340 | ***** | ***** | ***** | ***** | 5.52 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-daygap) | 30,271 | ***** | ***** | ***** | ***** | 0.52 | ***** | -3.87 | ***** | 0.12 ( 0.04, 0.37) | <0.001 |
| ACEI (183-day prior, 14-daygap) | 397,712 | ***** | ***** | ***** | ***** | 4.39 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-daygap) | 17,788 | ***** | ***** | ***** | ***** | 0.4 | ***** | -3.98 | ***** | 0.09 ( 0.01, 0.70) | 0.022 |
| ACEI (183-day prior, 14-daygap) | 17,788 | ***** | ***** | ***** | ***** | 4.37 | ***** | | | | |

**Table 3. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-daygap) | 30,271 | ***** | ***** | ***** | ***** | 0.52 | ***** | -2.91 | ***** | 0.15 ( 0.05, 0.49) | 0.002 |
| ACEI (183-day prior, 14-daygap) | 40,739 | ***** | ***** | ***** | ***** | 3.43 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-daygap) | 18,853 | ***** | ***** | ***** | ***** | 1.81 | ***** | -2.31 | ***** | 0.44 ( 0.21, 0.93) | 0.033 |
| ACEI (183-day prior, 14-daygap) | 235,524 | ***** | ***** | ***** | ***** | 4.12 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-daygap) | 6,391 | ***** | ***** | ***** | ***** | 1.87 | ***** | -1.87 | ***** | 0.50 ( 0.09, 2.73) | 0.423 |
| ACEI (183-day prior, 14-daygap) | 6,391 | ***** | ***** | ***** | ***** | 3.73 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-daygap) | 18,853 | ***** | ***** | ***** | ***** | 1.81 | ***** | -1.18 | ***** | 0.60 ( 0.24, 1.49) | 0.272 |
| ACEI (183-day prior, 14-daygap) | 23,569 | ***** | ***** | ***** | ***** | 2.99 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-daygap) | 13,182 | ***** | ***** | ***** | ***** | 1.72 | ***** | -1.83 | ***** | 0.48 ( 0.19, 1.16) | 0.104 |
| ACEI (183-day prior, 14-daygap) | 164,756 | ***** | ***** | ***** | ***** | 3.54 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-daygap) | 3,020 | ***** | ***** | ***** | ***** | 1.78 | ***** | -1.78 | ***** | 0.50 ( 0.05, 5.51) | 0.571 |
| ACEI (183-day prior, 14-daygap) | 3,020 | ***** | ***** | ***** | ***** | 3.55 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-daygap) | 13,182 | ***** | ***** | ***** | ***** | 1.72 | ***** | 0.25 | ***** | 1.16 ( 0.33, 3.99) | 0.82 |
| ACEI (183-day prior, 14-daygap) | 15,799 | ***** | ***** | ***** | ***** | 1.47 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 4. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (-183,-1)**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Angioedema (-183, -1)** | | | | | | | | | | | |
| Site-Adjusted Analysis | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,556 | ***** | ***** | ***** | ***** | 2.06 | ***** | -4.42 | ***** | 0.30 ( 0.23, 0.40) | <0.001 |
| ACEI (14-day gap) | 694,018 | ***** | ***** | ***** | ***** | 6.48 | ***** | | | | |
| Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1] | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,556 | ***** | ***** | ***** | ***** | 2.51 | ***** | -6.87 | ***** | 0.27 ( 0.18, 0.39) | <0.001 |
| ACEI (14-day gap) | 69,556 | ***** | ***** | ***** | ***** | 9.38 | ***** | | | | |
| Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,556 | ***** | ***** | ***** | ***** | 2.06 | ***** | -4.14 | ***** | 0.32 ( 0.23, 0.43) | <0.001 |
| ACEI (14-day gap) | 69,556 | ***** | ***** | ***** | ***** | 6.2 | ***** | | | | |
| **Angioedema (-183, -1)** | | | | | | | | | | | |
| Site-Adjusted Analysis | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 83 | ***** | ***** | ***** | ***** | 72.23 | ***** | -195.97 | ***** | 0.28 ( 0.07, 1.13) | 0.074 |
| ACEI (14-day gap) | 864 | ***** | ***** | ***** | ***** | 268.2 | ***** | | | | |
| Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1] | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 68 | ***** | ***** | ***** | ***** | 204.5 | ***** | -511.25 | ***** | 0.29 ( 0.06, 1.38) | 0.118 |
| ACEI (14-day gap) | 68 | ***** | ***** | ***** | ***** | 715.75 | ***** | | | | |
| Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 68 | ***** | ***** | ***** | ***** | 90.13 | ***** | -293.22 | ***** | 0.30 ( 0.06, 1.44) | 0.131 |
| ACEI (14-day gap) | 68 | ***** | ***** | ***** | ***** | 383.35 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 5. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183,-1) and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Angioedema (-183, -1)** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 69,556 | ***** | ***** | ***** | ***** | 2.06 | ***** | -4.42 | ***** | 0.30 ( 0.23, 0.40) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 694,018 | ***** | ***** | ***** | ***** | 6.48 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 69,556 | ***** | ***** | ***** | ***** | 2.51 | ***** | -6.87 | ***** | 0.27 ( 0.18, 0.39) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 69,556 | ***** | ***** | ***** | ***** | 9.38 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 69,556 | ***** | ***** | ***** | ***** | 2.06 | ***** | -4.14 | ***** | 0.32 ( 0.23, 0.43) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 69,556 | ***** | ***** | ***** | ***** | 6.2 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 69,556 | ***** | ***** | ***** | ***** | 3.3 | ***** | -11.18 | ***** | 0.22 ( 0.14, 0.36) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 694,018 | ***** | ***** | ***** | ***** | 14.48 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 69,556 | ***** | ***** | ***** | ***** | 3.42 | ***** | -14.47 | ***** | 0.19 ( 0.11, 0.32) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 69,556 | ***** | ***** | ***** | ***** | 17.89 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 69,556 | ***** | ***** | ***** | ***** | 3.3 | ***** | -13.57 | ***** | 0.19 ( 0.12, 0.33) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 69,556 | ***** | ***** | ***** | ***** | 16.87 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 55,726 | ***** | ***** | ***** | ***** | 2.91 | ***** | -2.83 | ***** | 0.51 ( 0.28, 0.93) | 0.028 |
| ACEI (183-day prior, 14-day gap) | 637,620 | ***** | ***** | ***** | ***** | 5.74 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 51,069 | ***** | ***** | ***** | ***** | 3.26 | ***** | -1.63 | ***** | 0.67 ( 0.30, 1.48) | 0.321 |
| ACEI (183-day prior, 14-day gap) | 51,069 | ***** | ***** | ***** | ***** | 4.89 | ***** | | | | |

**Table 5. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183,-1) and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 55,726 | ***** | ***** | ***** | ***** | 2.91 | ***** | -2.18 | ***** | 0.57 ( 0.28, 1.16) | 0.12 |
| ACEI (183-day prior, 14-day gap) | 63,770 | ***** | ***** | ***** | ***** | 5.08 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 37,612 | ***** | ***** | ***** | ***** | 2.5 | ***** | -3.15 | ***** | 0.44 ( 0.21, 0.94) | 0.034 |
| ACEI (183-day prior, 14-day gap) | 462,481 | ***** | ***** | ***** | ***** | 5.65 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 25,660 | ***** | ***** | ***** | ***** | 2.23 | ***** | -3.35 | ***** | 0.40 ( 0.13, 1.28) | 0.121 |
| ACEI (183-day prior, 14-day gap) | 25,660 | ***** | ***** | ***** | ***** | 5.59 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 37,612 | ***** | ***** | ***** | ***** | 2.5 | ***** | -3.02 | ***** | 0.45 ( 0.19, 1.07) | 0.07 |
| ACEI (183-day prior, 14-day gap) | 47,301 | ***** | ***** | ***** | ***** | 5.52 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 30,241 | ***** | ***** | ***** | ***** | 0.52 | ***** | -3.8 | ***** | 0.12 ( 0.04, 0.38) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 397,313 | ***** | ***** | ***** | ***** | 4.33 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 17,775 | ***** | ***** | ***** | ***** | 0.4 | ***** | -3.98 | ***** | 0.09 ( 0.01, 0.70) | 0.022 |
| ACEI (183-day prior, 14-day gap) | 17,775 | ***** | ***** | ***** | ***** | 4.38 | ***** | | | | |

**Table 5. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183,-1) and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 30,241 | ***** | ***** | ***** | ***** | 0.52 | ***** | -2.91 | ***** | 0.15 ( 0.05, 0.49) | 0.002 |
| ACEI (183-day prior, 14-day gap) | 40,704 | ***** | ***** | ***** | ***** | 3.43 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 18,831 | ***** | ***** | ***** | ***** | 1.81 | ***** | -2.27 | ***** | 0.44 ( 0.21, 0.94) | 0.035 |
| ACEI (183-day prior, 14-day gap) | 235,324 | ***** | ***** | ***** | ***** | 4.08 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 6,379 | ***** | ***** | ***** | ***** | 1.87 | ***** | -1.87 | ***** | 0.50 ( 0.09, 2.73) | 0.423 |
| ACEI (183-day prior, 14-day gap) | 6,379 | ***** | ***** | ***** | ***** | 3.74 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 18,831 | ***** | ***** | ***** | ***** | 1.81 | ***** | -1.18 | ***** | 0.60 ( 0.24, 1.49) | 0.272 |
| ACEI (183-day prior, 14-day gap) | 23,552 | ***** | ***** | ***** | ***** | 2.99 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 13,165 | ***** | ***** | ***** | ***** | 1.72 | ***** | -1.75 | ***** | 0.49 ( 0.20, 1.19) | 0.115 |
| ACEI (183-day prior, 14-day gap) | 164,613 | ***** | ***** | ***** | ***** | 3.47 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 3,013 | ***** | ***** | ***** | ***** | 1.78 | ***** | -1.78 | ***** | 0.50 ( 0.05, 5.51) | 0.571 |
| ACEI (183-day prior, 14-day gap) | 3,013 | ***** | ***** | ***** | ***** | 3.55 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 13,165 | ***** | ***** | ***** | ***** | 1.72 | ***** | 0.25 | ***** | 1.15 ( 0.33, 3.99) | 0.82 |
| ACEI (183-day prior, 14-day gap) | 15,786 | ***** | ***** | ***** | ***** | 1.47 | ***** | | | | |

**Table 5. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183,-1) and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Angioedema (-183, -1)** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 83 | ***** | ***** | ***** | ***** | 72.23 | ***** | -195.97 | ***** | 0.28 ( 0.07, 1.13) | 0.074 |
| ACEI (183-day prior, 14-day gap) | 864 | ***** | ***** | ***** | ***** | 268.2 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 68 | ***** | ***** | ***** | ***** | 204.5 | ***** | -511.25 | ***** | 0.29 ( 0.06, 1.38) | 0.118 |
| ACEI (183-day prior, 14-day gap) | 68 | ***** | ***** | ***** | ***** | 715.75 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 68 | ***** | ***** | ***** | ***** | 90.13 | ***** | -293.22 | ***** | 0.30 ( 0.06, 1.44) | 0.131 |
| ACEI (183-day prior, 14-day gap) | 68 | ***** | ***** | ***** | ***** | 383.35 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 83 | ***** | ***** | ***** | ***** | 158.98 | ***** | -582.21 | ***** | 0.21 ( 0.03, 1.49) | 0.118 |
| ACEI (183-day prior, 14-day gap) | 864 | ***** | ***** | ***** | ***** | 741.19 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 68 | ***** | ***** | ***** | ***** | 203.25 | ***** | -1016.26 | ***** | 0.17 ( 0.02, 1.38) | 0.097 |
| ACEI (183-day prior, 14-day gap) | 68 | ***** | ***** | ***** | ***** | 1,219.51 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 68 | ***** | ***** | ***** | ***** | 191.94 | ***** | -940.14 | ***** | 0.17 ( 0.02, 1.42) | 0.102 |
| ACEI (183-day prior, 14-day gap) | 68 | ***** | ***** | ***** | ***** | 1,132.08 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 70 | ***** | ***** | ***** | ***** | 215.98 | ***** | -60.81 | ***** | 0.85 ( 0.11, 6.49) | 0.876 |
| ACEI (183-day prior, 14-day gap) | 749 | ***** | ***** | ***** | ***** | 276.79 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 50 | ***** | ***** | ***** | ***** | 347.22 | ***** | 0 | ***** | 1.00 ( 0.06, 15.99) | 1 |
| ACEI (183-day prior, 14-day gap) | 50 | ***** | ***** | ***** | ***** | 347.22 | ***** | | | | |

**Table 5. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183,-1) and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 57 | ***** | ***** | ***** | ***** | 261.78 | ***** | 16.08 | ***** | 1.11 ( 0.07, 17.85) | 0.939 |
| ACEI (183-day prior, 14-day gap) | 61 | ***** | ***** | ***** | ***** | 245.7 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 45 | ***** | ***** | ***** | ***** | 0 | ***** | -136.2 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 490 | ***** | ***** | ***** | ***** | 136.2 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 22 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 22 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 35 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 38 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 32 | ***** | ***** | ***** | ***** | 0 | ***** | -73.62 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 402 | ***** | ***** | ***** | ***** | 73.62 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 14 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 14 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 5. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183,-1) and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 28 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 33 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 22 | ***** | ***** | ***** | ***** | 0 | ***** | -47.33 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 205 | ***** | ***** | ***** | ***** | 47.33 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 20 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 11 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 18 | ***** | ***** | ***** | ***** | 0 | ***** | -92.65 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 148 | ***** | ***** | ***** | ***** | 92.65 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 16 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 6. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (ever, -1)**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Angioedema (ever, -1)** | | | | | | | | | | | |
| Site-Adjusted Analysis | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,145 | ***** | ***** | ***** | ***** | 1.99 | ***** | -3.89 | ***** | 0.32 ( 0.24, 0.43) | <0.001 |
| ACEI (14-day gap) | 687,565 | ***** | ***** | ***** | ***** | 5.88 | ***** | | | | |
| Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1] | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,144 | ***** | ***** | ***** | ***** | 2.38 | ***** | -6.12 | ***** | 0.28 ( 0.19, 0.41) | <0.001 |
| ACEI (14-day gap) | 69,144 | ***** | ***** | ***** | ***** | 8.5 | ***** | | | | |
| Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,144 | ***** | ***** | ***** | ***** | 1.99 | ***** | -3.59 | ***** | 0.34 ( 0.25, 0.47) | <0.001 |
| ACEI (14-day gap) | 69,144 | ***** | ***** | ***** | ***** | 5.58 | ***** | | | | |
| **Angioedema (ever, -1)** | | | | | | | | | | | |
| Site-Adjusted Analysis | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 494 | ***** | ***** | ***** | ***** | 25.6 | ***** | -71.51 | ***** | 0.25 ( 0.09, 0.67) | 0.006 |
| ACEI (14-day gap) | 7,317 | ***** | ***** | ***** | ***** | 97.12 | ***** | | | | |
| Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1] | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 487 | ***** | ***** | ***** | ***** | 24.08 | ***** | -120.42 | ***** | 0.17 ( 0.04, 0.74) | 0.019 |
| ACEI (14-day gap) | 487 | ***** | ***** | ***** | ***** | 144.51 | ***** | | | | |
| Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 487 | ***** | ***** | ***** | ***** | 25.94 | ***** | -86.94 | ***** | 0.23 ( 0.08, 0.68) | 0.008 |
| ACEI (14-day gap) | 487 | ***** | ***** | ***** | ***** | 112.88 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 7. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Serious Allergies**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Serious allergies** | | | | | | | | | | | |
| Site-Adjusted Analysis | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 61,592 | ***** | ***** | ***** | ***** | 2.08 | ***** | -4.4 | ***** | 0.31 ( 0.23, 0.41) | <0.001 |
| ACEI (14-day gap) | 583,922 | ***** | ***** | ***** | ***** | 6.47 | ***** | | | | |
| Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1] | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 61,582 | ***** | ***** | ***** | ***** | 2.4 | ***** | -6.08 | ***** | 0.28 ( 0.19, 0.42) | <0.001 |
| ACEI (14-day gap) | 61,582 | ***** | ***** | ***** | ***** | 8.47 | ***** | | | | |
| Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 61,582 | ***** | ***** | ***** | ***** | 2.08 | ***** | -3.7 | ***** | 0.34 ( 0.25, 0.48) | <0.001 |
| ACEI (14-day gap) | 61,582 | ***** | ***** | ***** | ***** | 5.77 | ***** | | | | |
| **Serious allergies** | | | | | | | | | | | |
| Site-Adjusted Analysis | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 8,047 | ***** | ***** | ***** | ***** | 2.69 | ***** | -5.63 | ***** | 0.31 ( 0.15, 0.66) | 0.002 |
| ACEI (14-day gap) | 110,960 | ***** | ***** | ***** | ***** | 8.32 | ***** | | | | |
| Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1] | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 8,038 | ***** | ***** | ***** | ***** | 3.46 | ***** | -7.61 | ***** | 0.31 ( 0.11, 0.85) | 0.023 |
| ACEI (14-day gap) | 8,038 | ***** | ***** | ***** | ***** | 11.07 | ***** | | | | |
| Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05 | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 8,038 | ***** | ***** | ***** | ***** | 2.69 | ***** | -4.38 | ***** | 0.36 ( 0.15, 0.85) | 0.02 |
| ACEI (14-day gap) | 8,038 | ***** | ***** | ***** | ***** | 7.07 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 8. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin-Converting Enzyme Inhibitors (ACEI) 183-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Sex: Male** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 48,440 | ***** | ***** | ***** | ***** | 2.4 | ***** | -3.58 | ***** | 0.38 ( 0.28, 0.52) | <0.001 |
| ACEI (14-day gap) | 353,015 | ***** | ***** | ***** | ***** | 5.98 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 48,398 | ***** | ***** | ***** | ***** | 2.67 | ***** | -5.84 | ***** | 0.31 ( 0.20, 0.49) | <0.001 |
| ACEI (14-day gap) | 48,398 | ***** | ***** | ***** | ***** | 8.51 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 48,398 | ***** | ***** | ***** | ***** | 2.4 | ***** | -2.99 | ***** | 0.43 ( 0.30, 0.61) | <0.001 |
| ACEI (14-day gap) | 48,398 | ***** | ***** | ***** | ***** | 5.39 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 48,440 | ***** | ***** | ***** | ***** | 3.06 | ***** | -11.55 | ***** | 0.21 ( 0.11, 0.38) | <0.001 |
| ACEI (14-day gap) | 353,015 | ***** | ***** | ***** | ***** | 14.61 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 48,398 | ***** | ***** | ***** | ***** | 2.88 | ***** | -12.96 | ***** | 0.18 ( 0.09, 0.36) | <0.001 |
| ACEI (14-day gap) | 48,398 | ***** | ***** | ***** | ***** | 15.85 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 48,398 | ***** | ***** | ***** | ***** | 3.06 | ***** | -12.32 | ***** | 0.20 ( 0.10, 0.38) | <0.001 |
| ACEI (14-day gap) | 48,398 | ***** | ***** | ***** | ***** | 15.38 | ***** | | | | |

**Table 8. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin-Converting Enzyme Inhibitors (ACEI) 183-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 39,001 | ***** | ***** | ***** | ***** | 3.76 | ***** | -1.83 | ***** | 0.67 ( 0.35, 1.27) | 0.22 |
| ACEI (14-day gap) | 325,549 | ***** | ***** | ***** | ***** | 5.59 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 35,714 | ***** | ***** | ***** | ***** | 4.19 | ***** | -0.93 | ***** | 0.82 ( 0.34, 1.97) | 0.655 |
| ACEI (14-day gap) | 35,714 | ***** | ***** | ***** | ***** | 5.12 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 38,972 | ***** | ***** | ***** | ***** | 3.77 | ***** | -0.03 | ***** | 0.97 ( 0.42, 2.25) | 0.948 |
| ACEI (14-day gap) | 44,405 | ***** | ***** | ***** | ***** | 3.8 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 26,480 | ***** | ***** | ***** | ***** | 3.54 | ***** | -1.19 | ***** | 0.75 ( 0.35, 1.63) | 0.47 |
| ACEI (14-day gap) | 236,720 | ***** | ***** | ***** | ***** | 4.74 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 18,101 | ***** | ***** | ***** | ***** | 3.95 | ***** | -3.95 | ***** | 0.50 ( 0.17, 1.46) | 0.206 |
| ACEI (14-day gap) | 18,101 | ***** | ***** | ***** | ***** | 7.91 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 26,460 | ***** | ***** | ***** | ***** | 3.55 | ***** | -2.76 | ***** | 0.56 ( 0.23, 1.37) | 0.205 |
| ACEI (14-day gap) | 33,143 | ***** | ***** | ***** | ***** | 6.31 | ***** | | | | |

**Table 8. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin-Converting Enzyme Inhibitors (ACEI) 183-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 21,352 | ***** | ***** | ***** | ***** | 0.25 | ***** | -3.26 | ***** | 0.07 ( 0.01, 0.50) | 0.008 |
| ACEI (14-day gap) | 203,872 | ***** | ***** | ***** | ***** | 3.5 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 12,542 | ***** | ***** | ***** | ***** | 0 | ***** | -2.84 | ***** | - | - |
| ACEI (14-day gap) | 12,542 | ***** | ***** | ***** | ***** | 2.84 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 21,337 | ***** | ***** | ***** | ***** | 0.25 | ***** | -2.51 | ***** | 0.09 ( 0.01, 0.66) | 0.018 |
| ACEI (14-day gap) | 28,497 | ***** | ***** | ***** | ***** | 2.75 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 13,288 | ***** | ***** | ***** | ***** | 2.57 | ***** | -0.83 | ***** | 0.75 ( 0.35, 1.63) | 0.469 |
| ACEI (14-day gap) | 120,238 | ***** | ***** | ***** | ***** | 3.41 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 4,429 | ***** | ***** | ***** | ***** | 1.37 | ***** | -1.37 | ***** | 0.50 ( 0.05, 5.51) | 0.571 |
| ACEI (14-day gap) | 4,429 | ***** | ***** | ***** | ***** | 2.74 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 13,277 | ***** | ***** | ***** | ***** | 2.58 | ***** | 1.04 | ***** | 1.64 ( 0.52, 5.16) | 0.399 |
| ACEI (14-day gap) | 16,416 | ***** | ***** | ***** | ***** | 1.54 | ***** | | | | |

**Table 8. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin-Converting Enzyme Inhibitors (ACEI) 183-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 9,303 | ***** | ***** | ***** | ***** | 2.43 | ***** | -0.48 | ***** | 0.81 ( 0.33, 2.03) | 0.658 |
| ACEI (14-day gap) | 84,117 | ***** | ***** | ***** | ***** | 2.91 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 2,042 | ***** | ***** | ***** | ***** | 2.65 | ***** | 2.65 | ***** | - | - |
| ACEI (14-day gap) | 2,042 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 9,299 | ***** | ***** | ***** | ***** | 2.43 | ***** | 1.16 | ***** | 1.87 ( 0.45, 7.84) | 0.39 |
| ACEI (14-day gap) | 10,933 | ***** | ***** | ***** | ***** | 1.27 | ***** | | | | |
| **Sex: Female** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 21,199 | ***** | ***** | ***** | ***** | 1.52 | ***** | -6 | ***** | 0.19 ( 0.11, 0.35) | <0.001 |
| ACEI (14-day gap) | 341,867 | ***** | ***** | ***** | ***** | 7.53 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 21,198 | ***** | ***** | ***** | ***** | 2.47 | ***** | -9.38 | ***** | 0.21 ( 0.11, 0.41) | <0.001 |
| ACEI (14-day gap) | 21,198 | ***** | ***** | ***** | ***** | 11.84 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 21,198 | ***** | ***** | ***** | ***** | 1.52 | ***** | -6.1 | ***** | 0.19 ( 0.10, 0.36) | <0.001 |
| ACEI (14-day gap) | 21,198 | ***** | ***** | ***** | ***** | 7.62 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 21,199 | ***** | ***** | ***** | ***** | 4.49 | ***** | -11.64 | ***** | 0.27 ( 0.13, 0.58) | <0.001 |
| ACEI (14-day gap) | 341,867 | ***** | ***** | ***** | ***** | 16.13 | ***** | | | | |

**Table 8. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin-Converting Enzyme Inhibitors (ACEI) 183-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 21,198 | ***** | ***** | ***** | ***** | 4.65 | ***** | -17.95 | ***** | 0.21 ( 0.09, 0.46) | <0.001 |
| ACEI (14-day gap) | 21,198 | ***** | ***** | ***** | ***** | 22.6 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 21,198 | ***** | ***** | ***** | ***** | 4.49 | ***** | -16.99 | ***** | 0.21 ( 0.09, 0.46) | <0.001 |
| ACEI (14-day gap) | 21,198 | ***** | ***** | ***** | ***** | 21.48 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 16,795 | ***** | ***** | ***** | ***** | 1.77 | ***** | -4.76 | ***** | 0.27 ( 0.07, 1.11) | 0.069 |
| ACEI (14-day gap) | 312,817 | ***** | ***** | ***** | ***** | 6.52 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 15,272 | ***** | ***** | ***** | ***** | 2.23 | ***** | -3.34 | ***** | 0.40 ( 0.08, 2.06) | 0.273 |
| ACEI (14-day gap) | 15,272 | ***** | ***** | ***** | ***** | 5.57 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 16,794 | ***** | ***** | ***** | ***** | 1.77 | ***** | -4.9 | ***** | 0.27 ( 0.06, 1.23) | 0.09 |
| ACEI (14-day gap) | 19,286 | ***** | ***** | ***** | ***** | 6.66 | ***** | | | | |

**Table 8. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin-Converting Enzyme Inhibitors (ACEI) 183-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 11,175 | ***** | ***** | ***** | ***** | 0 | ***** | -6.88 | ***** | - | - |
| ACEI (14-day gap) | 226,249 | ***** | ***** | ***** | ***** | 6.88 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 7,313 | ***** | ***** | ***** | ***** | 0 | ***** | -3.97 | ***** | - | - |
| ACEI (14-day gap) | 7,313 | ***** | ***** | ***** | ***** | 3.97 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 11,174 | ***** | ***** | ***** | ***** | 0 | ***** | -2.83 | ***** | - | - |
| ACEI (14-day gap) | 13,934 | ***** | ***** | ***** | ***** | 2.83 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 8,919 | ***** | ***** | ***** | ***** | 1.18 | ***** | -4.13 | ***** | 0.22 ( 0.05, 0.89) | 0.034 |
| ACEI (14-day gap) | 193,840 | ***** | ***** | ***** | ***** | 5.31 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 4,920 | ***** | ***** | ***** | ***** | 1.43 | ***** | -5.74 | ***** | 0.20 ( 0.02, 1.71) | 0.142 |
| ACEI (14-day gap) | 4,920 | ***** | ***** | ***** | ***** | 7.17 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 8,918 | ***** | ***** | ***** | ***** | 1.18 | ***** | -3.07 | ***** | 0.28 ( 0.06, 1.28) | 0.101 |
| ACEI (14-day gap) | 11,847 | ***** | ***** | ***** | ***** | 4.25 | ***** | | | | |

**Table 8. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin-Converting Enzyme Inhibitors (ACEI) 183-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 5,565 | ***** | ***** | ***** | ***** | 0 | ***** | -4.87 | ***** | - | - |
| ACEI (14-day gap) | 115,286 | ***** | ***** | ***** | ***** | 4.87 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 1,759 | ***** | ***** | ***** | ***** | 0 | ***** | -6.82 | ***** | - | - |
| ACEI (14-day gap) | 1,759 | ***** | ***** | ***** | ***** | 6.82 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 5,565 | ***** | ***** | ***** | ***** | 0 | ***** | -5.21 | ***** | - | - |
| ACEI (14-day gap) | 6,776 | ***** | ***** | ***** | ***** | 5.21 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 3,879 | ***** | ***** | ***** | ***** | 0 | ***** | -4.21 | ***** | - | - |
| ACEI (14-day gap) | 80,639 | ***** | ***** | ***** | ***** | 4.21 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 834 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 834 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 3,882 | ***** | ***** | ***** | ***** | 0 | ***** | -1.02 | ***** | - | - |
| ACEI (14-day gap) | 4,528 | ***** | ***** | ***** | ***** | 1.02 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2] Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 9. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 18-44 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 2,412 | ***** | ***** | ***** | ***** | 1.3 | ***** | -7.86 | ***** | 0.14 ( 0.02, 1.03) | 0.053 |
| ACEI (14-day gap) | 21,587 | ***** | ***** | ***** | ***** | 9.15 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 2,385 | ***** | ***** | ***** | ***** | 2.49 | ***** | -4.99 | ***** | 0.33 ( 0.03, 3.20) | 0.341 |
| ACEI (14-day gap) | 2,385 | ***** | ***** | ***** | ***** | 7.48 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 2,385 | ***** | ***** | ***** | ***** | 1.31 | ***** | -3.65 | ***** | 0.25 ( 0.03, 2.28) | 0.221 |
| ACEI (14-day gap) | 2,385 | ***** | ***** | ***** | ***** | 4.96 | ***** | | | | |
| **Age Group: 45-54 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 5,115 | ***** | ***** | ***** | ***** | 2.92 | ***** | -7.36 | ***** | 0.28 ( 0.12, 0.69) | 0.006 |
| ACEI (14-day gap) | 45,057 | ***** | ***** | ***** | ***** | 10.28 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 5,075 | ***** | ***** | ***** | ***** | 3.26 | ***** | -9.79 | ***** | 0.25 ( 0.07, 0.89) | 0.032 |
| ACEI (14-day gap) | 5,075 | ***** | ***** | ***** | ***** | 13.05 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 5,075 | ***** | ***** | ***** | ***** | 2.94 | ***** | -6.18 | ***** | 0.31 ( 0.11, 0.84) | 0.022 |
| ACEI (14-day gap) | 5,075 | ***** | ***** | ***** | ***** | 9.12 | ***** | | | | |

**Table 9. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 55-64 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 11,494 | ***** | ***** | ***** | ***** | 2.62 | ***** | -6.32 | ***** | 0.29 ( 0.15, 0.54) | <0.001 |
| ACEI (14-day gap) | 97,244 | ***** | ***** | ***** | ***** | 8.94 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 11,435 | ***** | ***** | ***** | ***** | 3.76 | ***** | -7.98 | ***** | 0.32 ( 0.14, 0.71) | 0.005 |
| ACEI (14-day gap) | 11,435 | ***** | ***** | ***** | ***** | 11.74 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 11,435 | ***** | ***** | ***** | ***** | 2.63 | ***** | -5.81 | ***** | 0.30 ( 0.15, 0.61) | <0.001 |
| ACEI (14-day gap) | 11,435 | ***** | ***** | ***** | ***** | 8.44 | ***** | | | | |
| **Age Group: 65+ Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 50,618 | ***** | ***** | ***** | ***** | 2 | ***** | -4.03 | ***** | 0.32 ( 0.23, 0.44) | <0.001 |
| ACEI (14-day gap) | 530,994 | ***** | ***** | ***** | ***** | 6.03 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 50,470 | ***** | ***** | ***** | ***** | 2.2 | ***** | -5.56 | ***** | 0.28 ( 0.18, 0.45) | <0.001 |
| ACEI (14-day gap) | 50,470 | ***** | ***** | ***** | ***** | 7.76 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 50,470 | ***** | ***** | ***** | ***** | 2.01 | ***** | -3.06 | ***** | 0.38 ( 0.26, 0.55) | <0.001 |
| ACEI (14-day gap) | 50,470 | ***** | ***** | ***** | ***** | 5.07 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 18-44** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,412 | ***** | ***** | ***** | ***** | 1.3 | ***** | -7.86 | ***** | 0.14 ( 0.02, 1.03) | 0.053 |
| ACEI (183-day prior, 14-day gap) | 21,587 | ***** | ***** | ***** | ***** | 9.15 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,385 | ***** | ***** | ***** | ***** | 2.49 | ***** | -4.99 | ***** | 0.33 ( 0.03, 3.20) | 0.341 |
| ACEI (183-day prior, 14-day gap) | 2,385 | ***** | ***** | ***** | ***** | 7.48 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,385 | ***** | ***** | ***** | ***** | 1.31 | ***** | -3.65 | ***** | 0.25 ( 0.03, 2.28) | 0.221 |
| ACEI (183-day prior, 14-day gap) | 2,385 | ***** | ***** | ***** | ***** | 4.96 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,412 | ***** | ***** | ***** | ***** | 0 | ***** | -18.03 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 21,587 | ***** | ***** | ***** | ***** | 18.03 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,385 | ***** | ***** | ***** | ***** | 0 | ***** | -17.89 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 2,385 | ***** | ***** | ***** | ***** | 17.89 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,385 | ***** | ***** | ***** | ***** | 0 | ***** | -15.97 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 2,385 | ***** | ***** | ***** | ***** | 15.97 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,896 | ***** | ***** | ***** | ***** | 7.93 | ***** | -0.4 | ***** | 1.00 ( 0.13, 7.77) | 0.998 |
| ACEI (183-day prior, 14-day gap) | 19,995 | ***** | ***** | ***** | ***** | 8.33 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,698 | ***** | ***** | ***** | ***** | 10.46 | ***** | 10.46 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 1,698 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,880 | ***** | ***** | ***** | ***** | 8 | ***** | 8 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 2,154 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,216 | ***** | ***** | ***** | ***** | 0 | ***** | -7.42 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 12,614 | ***** | ***** | ***** | ***** | 7.42 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 719 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 719 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,204 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 1,414 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 966 | ***** | ***** | ***** | ***** | 0 | ***** | -5.85 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 10,169 | ***** | ***** | ***** | ***** | 5.85 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 441 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 441 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 956 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 1,139 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 562 | ***** | ***** | ***** | ***** | 0 | ***** | -7.89 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 5,183 | ***** | ***** | ***** | ***** | 7.89 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 141 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 141 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 555 | ***** | ***** | ***** | ***** | 0 | ***** | -9.27 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 573 | ***** | ***** | ***** | ***** | 9.27 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 383 | ***** | ***** | ***** | ***** | 0 | ***** | -1.38 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 3,344 | ***** | ***** | ***** | ***** | 1.38 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 378 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 353 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 45-54** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,115 | ***** | ***** | ***** | ***** | 2.92 | ***** | -7.36 | ***** | 0.28 ( 0.12, 0.69) | 0.006 |
| ACEI (183-day prior, 14-day gap) | 45,057 | ***** | ***** | ***** | ***** | 10.28 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,075 | ***** | ***** | ***** | ***** | 3.26 | ***** | -9.79 | ***** | 0.25 ( 0.07, 0.89) | 0.032 |
| ACEI (183-day prior, 14-day gap) | 5,075 | ***** | ***** | ***** | ***** | 13.05 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,075 | ***** | ***** | ***** | ***** | 2.94 | ***** | -6.18 | ***** | 0.31 ( 0.11, 0.84) | 0.022 |
| ACEI (183-day prior, 14-day gap) | 5,075 | ***** | ***** | ***** | ***** | 9.12 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,115 | ***** | ***** | ***** | ***** | 5.27 | ***** | -18.42 | ***** | 0.22 ( 0.05, 0.89) | 0.033 |
| ACEI (183-day prior, 14-day gap) | 45,057 | ***** | ***** | ***** | ***** | 23.69 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,075 | ***** | ***** | ***** | ***** | 5.52 | ***** | -24.82 | ***** | 0.18 ( 0.04, 0.82) | 0.027 |
| ACEI (183-day prior, 14-day gap) | 5,075 | ***** | ***** | ***** | ***** | 30.34 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,075 | ***** | ***** | ***** | ***** | 5.31 | ***** | -27.1 | ***** | 0.16 ( 0.04, 0.72) | 0.017 |
| ACEI (183-day prior, 14-day gap) | 5,075 | ***** | ***** | ***** | ***** | 32.41 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,098 | ***** | ***** | ***** | ***** | 7.33 | ***** | -1.87 | ***** | 0.82 ( 0.20, 3.47) | 0.791 |
| ACEI (183-day prior, 14-day gap) | 41,763 | ***** | ***** | ***** | ***** | 9.21 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 3,697 | ***** | ***** | ***** | ***** | 4.72 | ***** | 4.72 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 3,697 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,069 | ***** | ***** | ***** | ***** | 7.38 | ***** | 7.38 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 4,617 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,644 | ***** | ***** | ***** | ***** | 0 | ***** | -9.51 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 27,857 | ***** | ***** | ***** | ***** | 9.51 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,646 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 1,646 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,629 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 3,190 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,067 | ***** | ***** | ***** | ***** | 0 | ***** | -5.25 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 22,987 | ***** | ***** | ***** | ***** | 5.25 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,055 | ***** | ***** | ***** | ***** | 0 | ***** | -6.84 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 1,055 | ***** | ***** | ***** | ***** | 6.84 | ***** | | | | |

**Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,055 | ***** | ***** | ***** | ***** | 0 | ***** | -4.46 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 2,606 | ***** | ***** | ***** | ***** | 4.46 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,282 | ***** | ***** | ***** | ***** | 0 | ***** | -4.42 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 12,534 | ***** | ***** | ***** | ***** | 4.42 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 358 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 358 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,276 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 1,388 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 910 | ***** | ***** | ***** | ***** | 4.91 | ***** | -0.56 | ***** | 0.91 ( 0.12, 7.11) | 0.926 |
| ACEI (183-day prior, 14-day gap) | 8,409 | ***** | ***** | ***** | ***** | 5.47 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 173 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 173 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 905 | ***** | ***** | ***** | ***** | 4.93 | ***** | -5.63 | ***** | 0.48 ( 0.04, 5.33) | 0.553 |
| ACEI (183-day prior, 14-day gap) | 896 | ***** | ***** | ***** | ***** | 10.57 | ***** | | | | |

**Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 55-64** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 11,494 | ***** | ***** | ***** | ***** | 2.62 | ***** | -6.32 | ***** | 0.29 ( 0.15, 0.54) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 97,244 | ***** | ***** | ***** | ***** | 8.94 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 11,435 | ***** | ***** | ***** | ***** | 3.76 | ***** | -7.98 | ***** | 0.32 ( 0.14, 0.71) | 0.005 |
| ACEI (183-day prior, 14-day gap) | 11,435 | ***** | ***** | ***** | ***** | 11.74 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 11,435 | ***** | ***** | ***** | ***** | 2.63 | ***** | -5.81 | ***** | 0.30 ( 0.15, 0.61) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 11,435 | ***** | ***** | ***** | ***** | 8.44 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 11,494 | ***** | ***** | ***** | ***** | 2.38 | ***** | -14.94 | ***** | 0.14 ( 0.03, 0.55) | 0.005 |
| ACEI (183-day prior, 14-day gap) | 97,244 | ***** | ***** | ***** | ***** | 17.32 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 11,435 | ***** | ***** | ***** | ***** | 2.48 | ***** | -19.85 | ***** | 0.11 ( 0.03, 0.48) | 0.003 |
| ACEI (183-day prior, 14-day gap) | 11,435 | ***** | ***** | ***** | ***** | 22.33 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 11,435 | ***** | ***** | ***** | ***** | 2.4 | ***** | -17.47 | ***** | 0.12 ( 0.03, 0.51) | 0.004 |
| ACEI (183-day prior, 14-day gap) | 11,435 | ***** | ***** | ***** | ***** | 19.86 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,991 | ***** | ***** | ***** | ***** | 6.63 | ***** | -1.11 | ***** | 0.86 ( 0.31, 2.40) | 0.78 |
| ACEI (183-day prior, 14-day gap) | 89,848 | ***** | ***** | ***** | ***** | 7.74 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,175 | ***** | ***** | ***** | ***** | 8.35 | ***** | 4.18 | ***** | 2.00 ( 0.37, 10.92) | 0.423 |
| ACEI (183-day prior, 14-day gap) | 8,175 | ***** | ***** | ***** | ***** | 4.18 | ***** | | | | |

**Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,947 | ***** | ***** | ***** | ***** | 6.66 | ***** | 1.19 | ***** | 1.21 ( 0.30, 4.83) | 0.791 |
| ACEI (183-day prior, 14-day gap) | 10,478 | ***** | ***** | ***** | ***** | 5.47 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | **5,921** | ***** | ***** | ***** | ***** | **4.56** | ***** | **-2.77** | ***** | **0.63 ( 0.15, 2.64)** | **0.532** |
| ACEI (183-day prior, 14-day gap) | **62,798** | ***** | ***** | ***** | ***** | **7.33** | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 3,863 | ***** | ***** | ***** | ***** | 3.76 | ***** | -7.52 | ***** | 0.33 ( 0.03, 3.20) | 0.341 |
| ACEI (183-day prior, 14-day gap) | 3,863 | ***** | ***** | ***** | ***** | 11.28 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,890 | ***** | ***** | ***** | ***** | 4.59 | ***** | -5.96 | ***** | 0.44 ( 0.09, 2.19) | 0.318 |
| ACEI (183-day prior, 14-day gap) | 7,492 | ***** | ***** | ***** | ***** | 10.54 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,693 | ***** | ***** | ***** | ***** | 0 | ***** | -6.39 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 52,858 | ***** | ***** | ***** | ***** | 6.39 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,597 | ***** | ***** | ***** | ***** | 0 | ***** | -2.75 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 2,597 | ***** | ***** | ***** | ***** | 2.75 | ***** | | | | |

**Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,666 | ***** | ***** | ***** | ***** | 0 | ***** | -4.48 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 6,324 | ***** | ***** | ***** | ***** | 4.48 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,889 | ***** | ***** | ***** | ***** | 1.68 | ***** | -4.87 | ***** | 0.26 ( 0.04, 1.88) | 0.182 |
| ACEI (183-day prior, 14-day gap) | 29,789 | ***** | ***** | ***** | ***** | 6.55 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 857 | ***** | ***** | ***** | ***** | 0 | ***** | -6.89 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 857 | ***** | ***** | ***** | ***** | 6.89 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,875 | ***** | ***** | ***** | ***** | 1.68 | ***** | -4.1 | ***** | 0.29 ( 0.03, 2.61) | 0.27 |
| ACEI (183-day prior, 14-day gap) | 3,516 | ***** | ***** | ***** | ***** | 5.79 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,036 | ***** | ***** | ***** | ***** | 2.25 | ***** | -4.07 | ***** | 0.35 ( 0.05, 2.60) | 0.307 |
| ACEI (183-day prior, 14-day gap) | 20,218 | ***** | ***** | ***** | ***** | 6.32 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 407 | ***** | ***** | ***** | ***** | 13.8 | ***** | 13.8 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 407 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,028 | ***** | ***** | ***** | ***** | 2.26 | ***** | 0.2 | ***** | 0.96 ( 0.06, 15.62) | 0.98 |
| ACEI (183-day prior, 14-day gap) | 2,286 | ***** | ***** | ***** | ***** | 2.06 | ***** | | | | |

**Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 65+** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 50,618 | ***** | ***** | ***** | ***** | 2 | ***** | -4.03 | ***** | 0.32 ( 0.23, 0.44) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 530,994 | ***** | ***** | ***** | ***** | 6.03 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 50,470 | ***** | ***** | ***** | ***** | 2.2 | ***** | -5.56 | ***** | 0.28 ( 0.18, 0.45) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 50,470 | ***** | ***** | ***** | ***** | 7.76 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 50,470 | ***** | ***** | ***** | ***** | 2.01 | ***** | -3.06 | ***** | 0.38 ( 0.26, 0.55) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 50,470 | ***** | ***** | ***** | ***** | 5.07 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 50,618 | ***** | ***** | ***** | ***** | 3.72 | ***** | -10.45 | ***** | 0.26 ( 0.15, 0.44) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 530,994 | ***** | ***** | ***** | ***** | 14.17 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 50,470 | ***** | ***** | ***** | ***** | 3.59 | ***** | -11.32 | ***** | 0.24 ( 0.13, 0.44) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 50,470 | ***** | ***** | ***** | ***** | 14.91 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 50,470 | ***** | ***** | ***** | ***** | 3.73 | ***** | -10.03 | ***** | 0.27 ( 0.15, 0.48) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 50,470 | ***** | ***** | ***** | ***** | 13.76 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 40,811 | ***** | ***** | ***** | ***** | 1.79 | ***** | -3.6 | ***** | 0.33 ( 0.14, 0.81) | 0.015 |
| ACEI (183-day prior, 14-day gap) | 486,760 | ***** | ***** | ***** | ***** | 5.4 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 37,246 | ***** | ***** | ***** | ***** | 2.21 | ***** | -2.65 | ***** | 0.45 ( 0.16, 1.31) | 0.144 |
| ACEI (183-day prior, 14-day gap) | 37,246 | ***** | ***** | ***** | ***** | 4.86 | ***** | | | | |

**Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 40,696 | ***** | ***** | ***** | ***** | 1.8 | ***** | -3.65 | ***** | 0.33 ( 0.12, 0.88) | 0.027 |
| ACEI (183-day prior, 14-day gap) | 46,185 | ***** | ***** | ***** | ***** | 5.45 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 27,874 | ***** | ***** | ***** | ***** | 2.4 | ***** | -2.77 | ***** | 0.47 ( 0.19, 1.14) | 0.093 |
| ACEI (183-day prior, 14-day gap) | 359,705 | ***** | ***** | ***** | ***** | 5.18 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 19,364 | ***** | ***** | ***** | ***** | 1.47 | ***** | -1.47 | ***** | 0.50 ( 0.09, 2.73) | 0.423 |
| ACEI (183-day prior, 14-day gap) | 19,364 | ***** | ***** | ***** | ***** | 2.95 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 27,793 | ***** | ***** | ***** | ***** | 2.41 | ***** | -1.32 | ***** | 0.65 ( 0.22, 1.90) | 0.433 |
| ACEI (183-day prior, 14-day gap) | 34,914 | ***** | ***** | ***** | ***** | 3.73 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 22,545 | ***** | ***** | ***** | ***** | 0.7 | ***** | -3.26 | ***** | 0.18 ( 0.06, 0.56) | 0.003 |
| ACEI (183-day prior, 14-day gap) | 311,698 | ***** | ***** | ***** | ***** | 3.96 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 13,620 | ***** | ***** | ***** | ***** | 0 | ***** | -3.1 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 13,620 | ***** | ***** | ***** | ***** | 3.1 | ***** | | | | |

**Table 10. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 22,479 | ***** | ***** | ***** | ***** | 0.7 | ***** | -1.87 | ***** | 0.27 ( 0.08, 0.94) | 0.039 |
| ACEI (183-day prior, 14-day gap) | 30,209 | ***** | ***** | ***** | ***** | 2.57 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 14,120 | ***** | ***** | ***** | ***** | 2.08 | ***** | -1.55 | ***** | 0.57 ( 0.25, 1.30) | 0.181 |
| ACEI (183-day prior, 14-day gap) | 188,019 | ***** | ***** | ***** | ***** | 3.63 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,956 | ***** | ***** | ***** | ***** | 2.41 | ***** | -2.41 | ***** | 0.50 ( 0.09, 2.73) | 0.423 |
| ACEI (183-day prior, 14-day gap) | 4,956 | ***** | ***** | ***** | ***** | 4.83 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 14,084 | ***** | ***** | ***** | ***** | 2.08 | ***** | -0.76 | ***** | 0.72 ( 0.26, 1.98) | 0.527 |
| ACEI (183-day prior, 14-day gap) | 17,695 | ***** | ***** | ***** | ***** | 2.84 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 9,854 | ***** | ***** | ***** | ***** | 1.38 | ***** | -1.68 | ***** | 0.45 ( 0.14, 1.42) | 0.173 |
| ACEI (183-day prior, 14-day gap) | 132,787 | ***** | ***** | ***** | ***** | 3.06 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,346 | ***** | ***** | ***** | ***** | 2.29 | ***** | -2.29 | ***** | 0.50 ( 0.05, 5.51) | 0.571 |
| ACEI (183-day prior, 14-day gap) | 2,346 | ***** | ***** | ***** | ***** | 4.59 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 9,839 | ***** | ***** | ***** | ***** | 1.38 | ***** | 0.6 | ***** | 1.76 ( 0.29, 10.51) | 0.537 |
| ACEI (183-day prior, 14-day gap) | 11,906 | ***** | ***** | ***** | ***** | 0.78 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2] Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 11. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Unknown** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 11,656 | ***** | ***** | ***** | ***** | 1.26 | ***** | -5.51 | ***** | 0.18 ( 0.07, 0.43) | <0.001 |
| ACEI (14-day gap) | 99,645 | ***** | ***** | ***** | ***** | 6.77 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 11,647 | ***** | ***** | ***** | ***** | 1.82 | ***** | -7.28 | ***** | 0.20 ( 0.07, 0.59) | 0.003 |
| ACEI (14-day gap) | 11,647 | ***** | ***** | ***** | ***** | 9.09 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 11,647 | ***** | ***** | ***** | ***** | 1.26 | ***** | -5.1 | ***** | 0.20 ( 0.08, 0.51) | <0.001 |
| ACEI (14-day gap) | 11,647 | ***** | ***** | ***** | ***** | 6.36 | ***** | | | | |
| **Race: American Indian** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 242 | ***** | ***** | ***** | ***** | 0 | ***** | -2.38 | ***** | - | - |
| ACEI (14-day gap) | 4,525 | ***** | ***** | ***** | ***** | 2.38 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 11. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Asian** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 666 | ***** | ***** | ***** | ***** | 0 | ***** | -2.63 | ***** | - | - |
| ACEI (14-day gap) | 7,871 | ***** | ***** | ***** | ***** | 2.63 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 656 | ***** | ***** | ***** | ***** | 0 | ***** | -8.2 | ***** | - | - |
| ACEI (14-day gap) | 656 | ***** | ***** | ***** | ***** | 8.2 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 656 | ***** | ***** | ***** | ***** | 0 | ***** | -3.98 | ***** | - | - |
| ACEI (14-day gap) | 656 | ***** | ***** | ***** | ***** | 3.98 | ***** | | | | |
| **Race: Black** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 9,015 | ***** | ***** | ***** | ***** | 5.6 | ***** | -16.98 | ***** | 0.24 ( 0.14, 0.39) | <0.001 |
| ACEI (14-day gap) | 92,098 | ***** | ***** | ***** | ***** | 22.58 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 8,997 | ***** | ***** | ***** | ***** | 8.01 | ***** | -14.02 | ***** | 0.36 ( 0.19, 0.70) | 0.003 |
| ACEI (14-day gap) | 8,997 | ***** | ***** | ***** | ***** | 22.03 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 8,997 | ***** | ***** | ***** | ***** | 5.62 | ***** | -11.34 | ***** | 0.32 ( 0.18, 0.56) | <0.001 |
| ACEI (14-day gap) | 8,997 | ***** | ***** | ***** | ***** | 16.96 | ***** | | | | |

**Table 11. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Pacific Islander** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 66 | ***** | ***** | ***** | ***** | 53.19 | ***** | 38.83 | ***** | 1.89 ( 0.19, 18.82) | 0.588 |
| ACEI (14-day gap) | 741 | ***** | ***** | ***** | ***** | 14.36 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Race: White** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 47,994 | ***** | ***** | ***** | ***** | 1.79 | ***** | -2.56 | ***** | 0.40 ( 0.28, 0.57) | <0.001 |
| ACEI (14-day gap) | 490,002 | ***** | ***** | ***** | ***** | 4.35 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 47,950 | ***** | ***** | ***** | ***** | 1.69 | ***** | -4.07 | ***** | 0.29 ( 0.17, 0.50) | <0.001 |
| ACEI (14-day gap) | 47,950 | ***** | ***** | ***** | ***** | 5.76 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 47,950 | ***** | ***** | ***** | ***** | 1.79 | ***** | -2.28 | ***** | 0.42 ( 0.28, 0.63) | <0.001 |
| ACEI (14-day gap) | 47,950 | ***** | ***** | ***** | ***** | 4.08 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Unknown** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 11,656 | ***** | ***** | ***** | ***** | 1.26 | ***** | -5.51 | ***** | 0.18 ( 0.07, 0.43) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 99,645 | ***** | ***** | ***** | ***** | 6.77 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 11,647 | ***** | ***** | ***** | ***** | 1.82 | ***** | -7.28 | ***** | 0.20 ( 0.07, 0.59) | 0.003 |
| ACEI (183-day prior, 14-day gap) | 11,647 | ***** | ***** | ***** | ***** | 9.09 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 11,647 | ***** | ***** | ***** | ***** | 1.26 | ***** | -5.1 | ***** | 0.20 ( 0.08, 0.51) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 11,647 | ***** | ***** | ***** | ***** | 6.36 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 11,656 | ***** | ***** | ***** | ***** | 1.19 | ***** | -14.8 | ***** | 0.07 ( 0.01, 0.51) | 0.009 |
| ACEI (183-day prior, 14-day gap) | 99,645 | ***** | ***** | ***** | ***** | 15.99 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 11,647 | ***** | ***** | ***** | ***** | 1.24 | ***** | -13.6 | ***** | 0.08 ( 0.01, 0.64) | 0.017 |
| ACEI (183-day prior, 14-day gap) | 11,647 | ***** | ***** | ***** | ***** | 14.84 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 11,647 | ***** | ***** | ***** | ***** | 1.19 | ***** | -13 | ***** | 0.08 ( 0.01, 0.63) | 0.016 |
| ACEI (183-day prior, 14-day gap) | 11,647 | ***** | ***** | ***** | ***** | 14.19 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,924 | ***** | ***** | ***** | ***** | 3.27 | ***** | -1.79 | ***** | 0.65 ( 0.16, 2.72) | 0.557 |
| ACEI (183-day prior, 14-day gap) | 91,186 | ***** | ***** | ***** | ***** | 5.05 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,088 | ***** | ***** | ***** | ***** | 4.12 | ***** | 0 | ***** | 1.00 ( 0.14, 7.10) | 1 |
| ACEI (183-day prior, 14-day gap) | 8,088 | ***** | ***** | ***** | ***** | 4.12 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,917 | ***** | ***** | ***** | ***** | 3.27 | ***** | -0.79 | ***** | 0.80 ( 0.13, 4.82) | 0.812 |
| ACEI (183-day prior, 14-day gap) | 10,535 | ***** | ***** | ***** | ***** | 4.06 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 6,151 | ***** | ***** | ***** | ***** | 2.19 | ***** | -3.13 | ***** | 0.42 ( 0.06, 3.07) | 0.391 |
| ACEI (183-day prior, 14-day gap) | 64,648 | ***** | ***** | ***** | ***** | 5.32 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,017 | ***** | ***** | ***** | ***** | 0 | ***** | -10.88 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 4,017 | ***** | ***** | ***** | ***** | 10.88 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 6,145 | ***** | ***** | ***** | ***** | 2.19 | ***** | -6.54 | ***** | 0.25 ( 0.03, 2.15) | 0.207 |
| ACEI (183-day prior, 14-day gap) | 7,599 | ***** | ***** | ***** | ***** | 8.73 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,905 | ***** | ***** | ***** | ***** | 0 | ***** | -4.5 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 53,827 | ***** | ***** | ***** | ***** | 4.5 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,674 | ***** | ***** | ***** | ***** | 0 | ***** | -7.74 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 2,674 | ***** | ***** | ***** | ***** | 7.74 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,899 | ***** | ***** | ***** | ***** | 0 | ***** | -4.41 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 6,304 | ***** | ***** | ***** | ***** | 4.41 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 3,093 | ***** | ***** | ***** | ***** | 0 | ***** | -3.81 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 31,199 | ***** | ***** | ***** | ***** | 3.81 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 950 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 950 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 3,092 | ***** | ***** | ***** | ***** | 0 | ***** | -4.27 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 3,546 | ***** | ***** | ***** | ***** | 4.27 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,169 | ***** | ***** | ***** | ***** | 2.09 | ***** | -1.71 | ***** | 0.52 ( 0.07, 3.92) | 0.528 |
| ACEI (183-day prior, 14-day gap) | 21,466 | ***** | ***** | ***** | ***** | 3.8 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 443 | ***** | ***** | ***** | ***** | 12.22 | ***** | 12.22 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 443 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,168 | ***** | ***** | ***** | ***** | 2.09 | ***** | 2.09 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 2,331 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Race: American Indian** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 242 | ***** | ***** | ***** | ***** | 0 | ***** | -2.38 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 4,525 | ***** | ***** | ***** | ***** | 2.38 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 242 | ***** | ***** | ***** | ***** | 0 | ***** | -5.54 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 4,525 | ***** | ***** | ***** | ***** | 5.54 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 187 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 4,184 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 168 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 168 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 182 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 218 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 117 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 2,739 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 78 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 78 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 114 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 153 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 97 | ***** | ***** | ***** | ***** | 0 | ***** | -5.01 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 2,252 | ***** | ***** | ***** | ***** | 5.01 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 51 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 51 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 94 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 121 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 54 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 1,257 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 15 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 15 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 54 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 65 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 36 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 837 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 37 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 47 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Race: Asian** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 666 | ***** | ***** | ***** | ***** | 0 | ***** | -2.63 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 7,871 | ***** | ***** | ***** | ***** | 2.63 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 656 | ***** | ***** | ***** | ***** | 0 | ***** | -8.2 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 656 | ***** | ***** | ***** | ***** | 8.2 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 656 | ***** | ***** | ***** | ***** | 0 | ***** | -3.98 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 656 | ***** | ***** | ***** | ***** | 3.98 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 666 | ***** | ***** | ***** | ***** | 0 | ***** | -4.83 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 7,871 | ***** | ***** | ***** | ***** | 4.83 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 656 | ***** | ***** | ***** | ***** | 0 | ***** | -21.84 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 656 | ***** | ***** | ***** | ***** | 21.84 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 656 | ***** | ***** | ***** | ***** | 0 | ***** | -19.49 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 656 | ***** | ***** | ***** | ***** | 19.49 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 507 | ***** | ***** | ***** | ***** | 0 | ***** | -6.02 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 7,147 | ***** | ***** | ***** | ***** | 6.02 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 454 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 454 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 501 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 590 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 350 | ***** | ***** | ***** | ***** | 0 | ***** | -5.15 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 5,095 | ***** | ***** | ***** | ***** | 5.15 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 345 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 429 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 266 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 4,335 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 147 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 147 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 264 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 362 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 176 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 2,368 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 56 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 56 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 177 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 202 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 124 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 1,546 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 26 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 26 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 128 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 127 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Race: Black** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 9,015 | ***** | ***** | ***** | ***** | 5.6 | ***** | -16.98 | ***** | 0.24 ( 0.14, 0.39) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 92,098 | ***** | ***** | ***** | ***** | 22.58 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,997 | ***** | ***** | ***** | ***** | 8.01 | ***** | -14.02 | ***** | 0.36 ( 0.19, 0.70) | 0.003 |
| ACEI (183-day prior, 14-day gap) | 8,997 | ***** | ***** | ***** | ***** | 22.03 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,997 | ***** | ***** | ***** | ***** | 5.62 | ***** | -11.34 | ***** | 0.32 ( 0.18, 0.56) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 8,997 | ***** | ***** | ***** | ***** | 16.96 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 9,015 | ***** | ***** | ***** | ***** | 12.05 | ***** | -36.7 | ***** | 0.24 ( 0.12, 0.49) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 92,098 | ***** | ***** | ***** | ***** | 48.75 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,997 | ***** | ***** | ***** | ***** | 12.49 | ***** | -29.66 | ***** | 0.30 ( 0.13, 0.65) | 0.003 |
| ACEI (183-day prior, 14-day gap) | 8,997 | ***** | ***** | ***** | ***** | 42.15 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,997 | ***** | ***** | ***** | ***** | 12.07 | ***** | -28.57 | ***** | 0.30 ( 0.13, 0.65) | 0.002 |
| ACEI (183-day prior, 14-day gap) | 8,997 | ***** | ***** | ***** | ***** | 40.64 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 7,146 | ***** | ***** | ***** | ***** | 10.79 | ***** | -7.19 | ***** | 0.59 ( 0.24, 1.46) | 0.257 |
| ACEI (183-day prior, 14-day gap) | 84,673 | ***** | ***** | ***** | ***** | 17.98 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 6,522 | ***** | ***** | ***** | ***** | 11 | ***** | 2.75 | ***** | 1.33 ( 0.30, 5.96) | 0.706 |
| ACEI (183-day prior, 14-day gap) | 6,522 | ***** | ***** | ***** | ***** | 8.25 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 7,131 | ***** | ***** | ***** | ***** | 10.82 | ***** | -1.65 | ***** | 0.86 ( 0.27, 2.70) | 0.792 |
| ACEI (183-day prior, 14-day gap) | 8,247 | ***** | ***** | ***** | ***** | 12.47 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,325 | ***** | ***** | ***** | ***** | 0 | ***** | -18.68 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 56,518 | ***** | ***** | ***** | ***** | 18.68 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,673 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 2,673 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,312 | ***** | ***** | ***** | ***** | 0 | ***** | -9.48 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 5,589 | ***** | ***** | ***** | ***** | 9.48 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 3,268 | ***** | ***** | ***** | ***** | 1.69 | ***** | -12.92 | ***** | 0.12 ( 0.02, 0.83) | 0.032 |
| ACEI (183-day prior, 14-day gap) | 47,205 | ***** | ***** | ***** | ***** | 14.6 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,643 | ***** | ***** | ***** | ***** | 0 | ***** | -4.82 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 1,643 | ***** | ***** | ***** | ***** | 4.82 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 3,254 | ***** | ***** | ***** | ***** | 1.69 | ***** | -12.76 | ***** | 0.11 ( 0.01, 0.88) | 0.037 |
| ACEI (183-day prior, 14-day gap) | 4,644 | ***** | ***** | ***** | ***** | 14.45 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,852 | ***** | ***** | ***** | ***** | 2.69 | ***** | -9.47 | ***** | 0.22 ( 0.03, 1.58) | 0.131 |
| ACEI (183-day prior, 14-day gap) | 24,182 | ***** | ***** | ***** | ***** | 12.16 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 485 | ***** | ***** | ***** | ***** | 0 | ***** | -26.5 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 485 | ***** | ***** | ***** | ***** | 26.5 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,845 | ***** | ***** | ***** | ***** | 2.7 | ***** | -4.24 | ***** | 0.39 ( 0.04, 3.74) | 0.413 |
| ACEI (183-day prior, 14-day gap) | 2,323 | ***** | ***** | ***** | ***** | 6.94 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,245 | ***** | ***** | ***** | ***** | 0 | ***** | -11.59 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 15,670 | ***** | ***** | ***** | ***** | 11.59 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 192 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 192 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,240 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 1,386 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Race: Pacific Islander** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 66 | ***** | ***** | ***** | ***** | 53.19 | ***** | 38.83 | ***** | 1.89 ( 0.19, 18.82) | 0.588 |
| ACEI (183-day prior, 14-day gap) | 741 | ***** | ***** | ***** | ***** | 14.36 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 66 | ***** | ***** | ***** | ***** | 0 | ***** | -34.75 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 741 | ***** | ***** | ***** | ***** | 34.75 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 52 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 654 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 42 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 42 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 49 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 49 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 35 | ***** | ***** | ***** | ***** | 383.14 | ***** | 356.7 | ***** | 7.85 ( 0.38, 161.1) | 0.182 |
| ACEI (183-day prior, 14-day gap) | 496 | ***** | ***** | ***** | ***** | 26.44 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 22 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 22 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 32 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 41 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 28 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 424 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 15 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 15 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 26 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 32 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 15 | ***** | ***** | ***** | ***** | 0 | ***** | -24.5 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 208 | ***** | ***** | ***** | ***** | 24.5 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 16 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 17 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 138 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 12 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Race: White** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 47,994 | ***** | ***** | ***** | ***** | 1.79 | ***** | -2.56 | ***** | 0.40 ( 0.28, 0.57) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 490,002 | ***** | ***** | ***** | ***** | 4.35 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 47,950 | ***** | ***** | ***** | ***** | 1.69 | ***** | -4.07 | ***** | 0.29 ( 0.17, 0.50) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 47,950 | ***** | ***** | ***** | ***** | 5.76 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 47,950 | ***** | ***** | ***** | ***** | 1.79 | ***** | -2.28 | ***** | 0.42 ( 0.28, 0.63) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 47,950 | ***** | ***** | ***** | ***** | 4.08 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 47,994 | ***** | ***** | ***** | ***** | 2.52 | ***** | -6.66 | ***** | 0.27 ( 0.14, 0.53) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 490,002 | ***** | ***** | ***** | ***** | 9.17 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 47,950 | ***** | ***** | ***** | ***** | 2.6 | ***** | -8.97 | ***** | 0.23 ( 0.11, 0.46) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 47,950 | ***** | ***** | ***** | ***** | 11.57 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 47,950 | ***** | ***** | ***** | ***** | 2.52 | ***** | -8.79 | ***** | 0.22 ( 0.11, 0.45) | <0.001 |
| ACEI (183-day prior, 14-day gap) | 47,950 | ***** | ***** | ***** | ***** | 11.3 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 38,981 | ***** | ***** | ***** | ***** | 1.88 | ***** | -2.29 | ***** | 0.45 ( 0.19, 1.11) | 0.083 |
| ACEI (183-day prior, 14-day gap) | 450,526 | ***** | ***** | ***** | ***** | 4.17 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 35,736 | ***** | ***** | ***** | ***** | 1.84 | ***** | -1.84 | ***** | 0.50 ( 0.15, 1.66) | 0.258 |
| ACEI (183-day prior, 14-day gap) | 35,736 | ***** | ***** | ***** | ***** | 3.68 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 38,945 | ***** | ***** | ***** | ***** | 1.88 | ***** | -1.62 | ***** | 0.53 ( 0.19, 1.53) | 0.243 |
| ACEI (183-day prior, 14-day gap) | 43,997 | ***** | ***** | ***** | ***** | 3.5 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 26,678 | ***** | ***** | ***** | ***** | 2.51 | ***** | -1.24 | ***** | 0.67 ( 0.27, 1.64) | 0.379 |
| ACEI (183-day prior, 14-day gap) | 333,484 | ***** | ***** | ***** | ***** | 3.74 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 18,611 | ***** | ***** | ***** | ***** | 2.29 | ***** | -0.76 | ***** | 0.75 ( 0.17, 3.35) | 0.706 |
| ACEI (183-day prior, 14-day gap) | 18,611 | ***** | ***** | ***** | ***** | 3.06 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 26,652 | ***** | ***** | ***** | ***** | 2.51 | ***** | -0.63 | ***** | 0.80 ( 0.26, 2.46) | 0.702 |
| ACEI (183-day prior, 14-day gap) | 33,227 | ***** | ***** | ***** | ***** | 3.13 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 21,709 | ***** | ***** | ***** | ***** | 0.48 | ***** | -2.44 | ***** | 0.17 ( 0.04, 0.67) | 0.012 |
| ACEI (183-day prior, 14-day gap) | 289,671 | ***** | ***** | ***** | ***** | 2.93 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 13,175 | ***** | ***** | ***** | ***** | 0 | ***** | -1.06 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 13,175 | ***** | ***** | ***** | ***** | 1.06 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 21,689 | ***** | ***** | ***** | ***** | 0.48 | ***** | -1.24 | ***** | 0.28 ( 0.06, 1.30) | 0.103 |
| ACEI (183-day prior, 14-day gap) | 28,845 | ***** | ***** | ***** | ***** | 1.73 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 13,664 | ***** | ***** | ***** | ***** | 2.14 | ***** | -1.05 | ***** | 0.67 ( 0.29, 1.52) | 0.339 |
| ACEI (183-day prior, 14-day gap) | 176,322 | ***** | ***** | ***** | ***** | 3.19 | ***** | | | | |

**Table 12. Effect Estimates of New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,841 | ***** | ***** | ***** | ***** | 1.24 | ***** | -2.48 | ***** | 0.33 ( 0.03, 3.20) | 0.341 |
| ACEI (183-day prior, 14-day gap) | 4,841 | ***** | ***** | ***** | ***** | 3.72 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 13,654 | ***** | ***** | ***** | ***** | 2.14 | ***** | -0.5 | ***** | 0.80 ( 0.28, 2.23) | 0.664 |
| ACEI (183-day prior, 14-day gap) | 17,028 | ***** | ***** | ***** | ***** | 2.65 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 9,601 | ***** | ***** | ***** | ***** | 1.88 | ***** | -0.71 | ***** | 0.72 ( 0.26, 1.98) | 0.53 |
| ACEI (183-day prior, 14-day gap) | 125,105 | ***** | ***** | ***** | ***** | 2.59 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,298 | ***** | ***** | ***** | ***** | 0 | ***** | -2.29 | ***** | - | - |
| ACEI (183-day prior, 14-day gap) | 2,298 | ***** | ***** | ***** | ***** | 2.29 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 9,595 | ***** | ***** | ***** | ***** | 1.88 | ***** | 0.28 | ***** | 1.16 ( 0.29, 4.63) | 0.837 |
| ACEI (183-day prior, 14-day gap) | 11,538 | ***** | ***** | ***** | ***** | 1.6 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 13. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type**

| Medical Product | Number of New Users | Years at Risk | Person Days at | Person Years at | Number of Events | per 1,000 Person Years | 1,000 New | Difference per 1,000 Person | in Risk per 1,000 | (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 49,140 | ***** | ***** | ***** | ***** | 2.55 | ***** | -0.47 | ***** | 0.80 ( 0.58, 1.09) | 0.161 |
| ARBs (14-day gap) | 337,083 | ***** | ***** | ***** | ***** | 3.02 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 49,137 | ***** | ***** | ***** | ***** | 3.3 | ***** | -0.1 | ***** | 0.97 ( 0.61, 1.56) | 0.904 |
| ARBs (14-day gap) | 49,137 | ***** | ***** | ***** | ***** | 3.4 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 49,137 | ***** | ***** | ***** | ***** | 2.55 | ***** | -0.31 | ***** | 0.85 ( 0.58, 1.26) | 0.417 |
| ARBs (14-day gap) | 49,137 | ***** | ***** | ***** | ***** | 2.85 | ***** | | | | |
| **Propensity Score Adjusted Stratified Analysis; Percentiles= 10[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 49,140 | ***** | ***** | ***** | ***** | 2.55 | ***** | -0.47 | ***** | 0.94 ( 0.68, 1.29) | 0.685 |
| ARBs (14-day gap) | 337,083 | ***** | ***** | ***** | ***** | 3.02 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 14. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 49,140 | ***** | ***** | ***** | ***** | 2.55 | ***** | -0.47 | ***** | 0.80 ( 0.58, 1.09) | 0.161 |
| ARBs (183-day prior, 14-day gap) | 337,083 | ***** | ***** | ***** | ***** | 3.02 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 49,137 | ***** | ***** | ***** | ***** | 3.3 | ***** | -0.1 | ***** | 0.97 ( 0.61, 1.56) | 0.904 |
| ARBs (183-day prior, 14-day gap) | 49,137 | ***** | ***** | ***** | ***** | 3.4 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 49,137 | ***** | ***** | ***** | ***** | 2.55 | ***** | -0.31 | ***** | 0.85 ( 0.58, 1.26) | 0.417 |
| ARBs (183-day prior, 14-day gap) | 49,137 | ***** | ***** | ***** | ***** | 2.85 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 49,140 | ***** | ***** | ***** | ***** | 3.86 | ***** | -2.1 | ***** | 0.64 ( 0.37, 1.10) | 0.104 |
| ARBs (183-day prior, 14-day gap) | 337,083 | ***** | ***** | ***** | ***** | 5.96 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 49,137 | ***** | ***** | ***** | ***** | 3.69 | ***** | -1.42 | ***** | 0.72 ( 0.35, 1.47) | 0.371 |
| ARBs (183-day prior, 14-day gap) | 49,137 | ***** | ***** | ***** | ***** | 5.1 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 49,137 | ***** | ***** | ***** | ***** | 3.86 | ***** | -1.74 | ***** | 0.68 ( 0.35, 1.33) | 0.259 |
| ARBs (183-day prior, 14-day gap) | 49,137 | ***** | ***** | ***** | ***** | 5.61 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 39,111 | ***** | ***** | ***** | ***** | 3.01 | ***** | -0.41 | ***** | 0.89 ( 0.43, 1.84) | 0.748 |
| ARBs (183-day prior, 14-day gap) | 316,224 | ***** | ***** | ***** | ***** | 3.42 | ***** | | | | |

**Table 14. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 36,512 | ***** | ***** | ***** | ***** | 3.57 | ***** | -1.34 | ***** | 0.73 ( 0.29, 1.81) | 0.493 |
| ARBs (183-day prior, 14-day gap) | 36,512 | ***** | ***** | ***** | ***** | 4.91 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 39,110 | ***** | ***** | ***** | ***** | 3.01 | ***** | -1.49 | ***** | 0.67 ( 0.28, 1.58) | 0.362 |
| ARBs (183-day prior, 14-day gap) | 45,890 | ***** | ***** | ***** | ***** | 4.5 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 26,476 | ***** | ***** | ***** | ***** | 3.55 | ***** | 0.74 | ***** | 1.30 ( 0.59, 2.86) | 0.513 |
| ARBs (183-day prior, 14-day gap) | 243,445 | ***** | ***** | ***** | ***** | 2.81 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 19,243 | ***** | ***** | ***** | ***** | 2.97 | ***** | 2.97 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 19,243 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 26,476 | ***** | ***** | ***** | ***** | 3.55 | ***** | 3.55 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 35,682 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 21,374 | ***** | ***** | ***** | ***** | 2.23 | ***** | -0.02 | ***** | 0.99 ( 0.50, 1.96) | 0.966 |
| ARBs (183-day prior, 14-day gap) | 214,230 | ***** | ***** | ***** | ***** | 2.25 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 13,557 | ***** | ***** | ***** | ***** | 2.61 | ***** | 0 | ***** | 1.00 ( 0.29, 3.45) | 1 |
| ARBs (183-day prior, 14-day gap) | 13,557 | ***** | ***** | ***** | ***** | 2.61 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 21,374 | ***** | ***** | ***** | ***** | 2.23 | ***** | -0.61 | ***** | 0.78 ( 0.34, 1.77) | 0.552 |
| ARBs (183-day prior, 14-day gap) | 31,191 | ***** | ***** | ***** | ***** | 2.84 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 13,101 | ***** | ***** | ***** | ***** | 1.13 | ***** | -0.94 | ***** | 0.56 ( 0.17, 1.78) | 0.324 |
| ARBs (183-day prior, 14-day gap) | 130,069 | ***** | ***** | ***** | ***** | 2.07 | ***** | | | | |

**Table 14. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,935 | ***** | ***** | ***** | ***** | 3.62 | ***** | 2.41 | ***** | 3.00 ( 0.31, 28.84) | 0.341 |
| ARBs (183-day prior, 14-day gap) | 4,935 | ***** | ***** | ***** | ***** | 1.21 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 13,101 | ***** | ***** | ***** | ***** | 1.13 | ***** | -0.22 | ***** | 0.84 ( 0.20, 3.54) | 0.817 |
| ARBs (183-day prior, 14-day gap) | 18,451 | ***** | ***** | ***** | ***** | 1.35 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,995 | ***** | ***** | ***** | ***** | 1.02 | ***** | -0.53 | ***** | 0.68 ( 0.16, 2.82) | 0.592 |
| ARBs (183-day prior, 14-day gap) | 92,640 | ***** | ***** | ***** | ***** | 1.56 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,357 | ***** | ***** | ***** | ***** | 2.26 | ***** | 2.26 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 2,357 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,995 | ***** | ***** | ***** | ***** | 1.02 | ***** | -0.79 | ***** | 0.58 ( 0.11, 3.02) | 0.521 |
| ARBs (183-day prior, 14-day gap) | 12,667 | ***** | ***** | ***** | ***** | 1.81 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 15. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (-183, -1)**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Angioedema (-183, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 49,082 | ***** | ***** | ***** | ***** | 2.19 | ***** | -0.24 | ***** | 0.87 ( 0.62, 1.22) | 0.421 |
| ARBs (14-day gap) | 336,258 | ***** | ***** | ***** | ***** | 2.43 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 49,079 | ***** | ***** | ***** | ***** | 2.82 | ***** | 0.19 | ***** | 1.07 ( 0.64, 1.81) | 0.789 |
| ARBs (14-day gap) | 49,079 | ***** | ***** | ***** | ***** | 2.62 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 49,079 | ***** | ***** | ***** | ***** | 2.19 | ***** | -0.25 | ***** | 0.87 ( 0.57, 1.32) | 0.501 |
| ARBs (14-day gap) | 49,079 | ***** | ***** | ***** | ***** | 2.45 | ***** | | | | |
| **Angioedema (-183, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 58 | ***** | ***** | ***** | ***** | 333.15 | ***** | 61.51 | ***** | 1.13 ( 0.49, 2.58) | 0.778 |
| ARBs (14-day gap) | 825 | ***** | ***** | ***** | ***** | 271.63 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 55 | ***** | ***** | ***** | ***** | 304.57 | ***** | -203.05 | ***** | 0.60 ( 0.14, 2.51) | 0.484 |
| ARBs (14-day gap) | 55 | ***** | ***** | ***** | ***** | 507.61 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 55 | ***** | ***** | ***** | ***** | 296.21 | ***** | 13.27 | ***** | 0.76 ( 0.21, 2.70) | 0.672 |
| ARBs (14-day gap) | 55 | ***** | ***** | ***** | ***** | 282.94 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183, -1) and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Angioedema (-183, -1)** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 49,082 | ***** | ***** | ***** | ***** | 2.19 | ***** | -0.24 | ***** | 0.87 ( 0.62, 1.22) | 0.421 |
| ARBs (183-day prior,14-day gap) | 336,258 | ***** | ***** | ***** | ***** | 2.43 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 49,079 | ***** | ***** | ***** | ***** | 2.82 | ***** | 0.19 | ***** | 1.07 ( 0.64, 1.81) | 0.789 |
| ARBs (183-day prior,14-day gap) | 49,079 | ***** | ***** | ***** | ***** | 2.62 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 49,079 | ***** | ***** | ***** | ***** | 2.19 | ***** | -0.25 | ***** | 0.87 ( 0.57, 1.32) | 0.501 |
| ARBs (183-day prior,14-day gap) | 49,079 | ***** | ***** | ***** | ***** | 2.45 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 49,082 | ***** | ***** | ***** | ***** | 2.49 | ***** | -1.6 | ***** | 0.60 ( 0.31, 1.19) | 0.146 |
| ARBs (183-day prior,14-day gap) | 336,258 | ***** | ***** | ***** | ***** | 4.08 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 49,079 | ***** | ***** | ***** | ***** | 2.27 | ***** | -1.13 | ***** | 0.67 ( 0.27, 1.63) | 0.374 |
| ARBs (183-day prior,14-day gap) | 49,079 | ***** | ***** | ***** | ***** | 3.4 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 49,079 | ***** | ***** | ***** | ***** | 2.49 | ***** | -1.6 | ***** | 0.61 ( 0.27, 1.37) | 0.229 |
| ARBs (183-day prior,14-day gap) | 49,079 | ***** | ***** | ***** | ***** | 4.08 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 39,070 | ***** | ***** | ***** | ***** | 3.01 | ***** | 0.02 | ***** | 1.01 ( 0.49, 2.11) | 0.969 |
| ARBs (183-day prior,14-day gap) | 315,501 | ***** | ***** | ***** | ***** | 2.99 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 36,476 | ***** | ***** | ***** | ***** | 3.58 | ***** | -1.34 | ***** | 0.73 ( 0.29, 1.81) | 0.493 |
| ARBs (183-day prior,14-day gap) | 36,476 | ***** | ***** | ***** | ***** | 4.92 | ***** | | | | |

**Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183, -1) and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 39,069 | ***** | ***** | ***** | ***** | 3.01 | ***** | -1.5 | ***** | 0.67 ( 0.28, 1.58) | 0.362 |
| ARBs (183-day prior,14-day gap) | 45,840 | ***** | ***** | ***** | ***** | 4.51 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 26,448 | ***** | ***** | ***** | ***** | 3.05 | ***** | 0.82 | ***** | 1.42 ( 0.60, 3.33) | 0.424 |
| ARBs (183-day prior,14-day gap) | 242,928 | ***** | ***** | ***** | ***** | 2.23 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 19,220 | ***** | ***** | ***** | ***** | 2.97 | ***** | 2.97 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | 19,220 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 26,448 | ***** | ***** | ***** | ***** | 3.05 | ***** | 3.05 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | 35,641 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 21,350 | ***** | ***** | ***** | ***** | 2.24 | ***** | 0.24 | ***** | 1.11 ( 0.56, 2.22) | 0.759 |
| ARBs (183-day prior,14-day gap) | 213,786 | ***** | ***** | ***** | ***** | 2 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 13,539 | ***** | ***** | ***** | ***** | 2.61 | ***** | 0.52 | ***** | 1.25 ( 0.34, 4.65) | 0.739 |
| ARBs (183-day prior,14-day gap) | 13,539 | ***** | ***** | ***** | ***** | 2.09 | ***** | | | | |

**Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183, -1) and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 21,350 | ***** | ***** | ***** | ***** | 2.24 | ***** | -0.43 | ***** | 0.83 ( 0.36, 1.90) | 0.663 |
| ARBs (183-day prior,14-day gap) | 31,152 | ***** | ***** | ***** | ***** | 2.67 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 13,089 | ***** | ***** | ***** | ***** | 1.13 | ***** | -0.72 | ***** | 0.62 ( 0.19, 2.00) | 0.425 |
| ARBs (183-day prior,14-day gap) | 129,786 | ***** | ***** | ***** | ***** | 1.85 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,924 | ***** | ***** | ***** | ***** | 3.63 | ***** | 3.63 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | 4,924 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 13,089 | ***** | ***** | ***** | ***** | 1.13 | ***** | 0.05 | ***** | 1.05 ( 0.24, 4.72) | 0.946 |
| ARBs (183-day prior,14-day gap) | 18,422 | ***** | ***** | ***** | ***** | 1.08 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,986 | ***** | ***** | ***** | ***** | 1.02 | ***** | -0.39 | ***** | 0.75 ( 0.18, 3.13) | 0.69 |
| ARBs (183-day prior,14-day gap) | 92,446 | ***** | ***** | ***** | ***** | 1.41 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,353 | ***** | ***** | ***** | ***** | 2.26 | ***** | 2.26 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | 2,353 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,986 | ***** | ***** | ***** | ***** | 1.02 | ***** | -0.43 | ***** | 0.71 ( 0.13, 3.88) | 0.694 |
| ARBs (183-day prior,14-day gap) | 12,645 | ***** | ***** | ***** | ***** | 1.45 | ***** | | | | |

**Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183, -1) and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Angioedema (-183, -1)** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 58 | ***** | ***** | ***** | ***** | 333.15 | ***** | 61.51 | ***** | 1.13 ( 0.49, 2.58) | 0.778 |
| ARBs (183-day prior,14-day gap) | 825 | ***** | ***** | ***** | ***** | 271.63 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 55 | ***** | ***** | ***** | ***** | 304.57 | ***** | -203.05 | ***** | 0.60 ( 0.14, 2.51) | 0.484 |
| ARBs (183-day prior,14-day gap) | 55 | ***** | ***** | ***** | ***** | 507.61 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 55 | ***** | ***** | ***** | ***** | 296.21 | ***** | 13.27 | ***** | 0.76 ( 0.21, 2.70) | 0.672 |
| ARBs (183-day prior,14-day gap) | 55 | ***** | ***** | ***** | ***** | 282.94 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 58 | ***** | ***** | ***** | ***** | 1,295.34 | ***** | 491.05 | ***** | 1.51 ( 0.60, 3.80) | 0.378 |
| ARBs (183-day prior,14-day gap) | 825 | ***** | ***** | ***** | ***** | 804.29 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 55 | ***** | ***** | ***** | ***** | 847.46 | ***** | -282.49 | ***** | 0.75 ( 0.17, 3.35) | 0.706 |
| ARBs (183-day prior,14-day gap) | 55 | ***** | ***** | ***** | ***** | 1,129.94 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 55 | ***** | ***** | ***** | ***** | 1,061.01 | ***** | 110.89 | ***** | 1.07 ( 0.27, 4.30) | 0.919 |
| ARBs (183-day prior,14-day gap) | 55 | ***** | ***** | ***** | ***** | 950.12 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 41 | ***** | ***** | ***** | ***** | 0 | ***** | -194.97 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | 725 | ***** | ***** | ***** | ***** | 194.97 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 36 | ***** | ***** | ***** | ***** | 0 | ***** | -390.63 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | 36 | ***** | ***** | ***** | ***** | 390.63 | ***** | | | | |

**Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183, -1) and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 39 | ***** | ***** | ***** | ***** | 0 | ***** | -262.47 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | 50 | ***** | ***** | ***** | ***** | 262.47 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 28 | ***** | ***** | ***** | ***** | 460.83 | ***** | 184.79 | ***** | 1.52 ( 0.20, 11.78) | 0.69 |
| ARBs (183-day prior,14-day gap) | 522 | ***** | ***** | ***** | ***** | 276.04 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 22 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | 22 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 29 | ***** | ***** | ***** | ***** | 432.9 | ***** | 432.9 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | 42 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 24 | ***** | ***** | ***** | ***** | 0 | ***** | -118.47 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | 449 | ***** | ***** | ***** | ***** | 118.47 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 21 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | 21 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 16. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Prior Angioedema (-183, -1) and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 26 | ***** | ***** | ***** | ***** | 0 | ***** | -145.56 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | 36 | ***** | ***** | ***** | ***** | 145.56 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 13 | ***** | ***** | ***** | ***** | 0 | ***** | -106.48 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | 286 | ***** | ***** | ***** | ***** | 106.48 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 16 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | 23 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | -66.89 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | 197 | ***** | ***** | ***** | ***** | 66.89 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 11 | ***** | ***** | ***** | ***** | 0 | ***** | -243.31 | ***** | - | - |
| ARBs (183-day prior,14-day gap) | 17 | ***** | ***** | ***** | ***** | 243.31 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 17. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (ever, -1)**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Angioedema (ever, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 48,390 | ***** | ***** | ***** | ***** | 1.92 | ***** | -0.11 | ***** | 0.91 ( 0.63, 1.32) | 0.627 |
| ARBs (14-day gap) | 329,726 | ***** | ***** | ***** | ***** | 2.03 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 48,383 | ***** | ***** | ***** | ***** | 2.47 | ***** | 0.49 | ***** | 1.25 ( 0.69, 2.25) | 0.457 |
| ARBs (14-day gap) | 48,383 | ***** | ***** | ***** | ***** | 1.97 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 48,383 | ***** | ***** | ***** | ***** | 1.92 | ***** | -0.02 | ***** | 0.96 ( 0.60, 1.51) | 0.845 |
| ARBs (14-day gap) | 48,383 | ***** | ***** | ***** | ***** | 1.94 | ***** | | | | |
| **Angioedema (ever, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 750 | ***** | ***** | ***** | ***** | 45.4 | ***** | -2.55 | ***** | 0.83 ( 0.45, 1.54) | 0.558 |
| ARBs (14-day gap) | 7,357 | ***** | ***** | ***** | ***** | 47.94 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 744 | ***** | ***** | ***** | ***** | 64.88 | ***** | 12.98 | ***** | 1.25 ( 0.49, 3.17) | 0.638 |
| ARBs (14-day gap) | 744 | ***** | ***** | ***** | ***** | 51.9 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 744 | ***** | ***** | ***** | ***** | 41.87 | ***** | 9.65 | ***** | 1.16 ( 0.49, 2.74) | 0.739 |
| ARBs (14-day gap) | 744 | ***** | ***** | ***** | ***** | 32.22 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 18. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Serious Allergies**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Serious allergies** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 42,674 | ***** | ***** | ***** | ***** | 2.28 | ***** | -0.3 | ***** | 0.84 ( 0.59, 1.20) | 0.332 |
| ARBs (14-day gap) | 282,648 | ***** | ***** | ***** | ***** | 2.59 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 42,666 | ***** | ***** | ***** | ***** | 2.76 | ***** | 0 | ***** | 1.00 ( 0.57, 1.74) | 1 |
| ARBs (14-day gap) | 42,666 | ***** | ***** | ***** | ***** | 2.76 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 42,666 | ***** | ***** | ***** | ***** | 2.28 | ***** | -0.21 | ***** | 0.88 ( 0.57, 1.37) | 0.57 |
| ARBs (14-day gap) | 42,666 | ***** | ***** | ***** | ***** | 2.49 | ***** | | | | |
| **Serious allergies** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 6,466 | ***** | ***** | ***** | ***** | 4.48 | ***** | -1.01 | ***** | 0.76 ( 0.39, 1.50) | 0.427 |
| ARBs (14-day gap) | 54,435 | ***** | ***** | ***** | ***** | 5.5 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 6,436 | ***** | ***** | ***** | ***** | 4.22 | ***** | -0.84 | ***** | 0.83 ( 0.25, 2.73) | 0.763 |
| ARBs (14-day gap) | 6,436 | ***** | ***** | ***** | ***** | 5.06 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 6,436 | ***** | ***** | ***** | ***** | 4.51 | ***** | 1.05 | ***** | 1.25 ( 0.49, 3.15) | 0.64 |
| ARBs (14-day gap) | 6,436 | ***** | ***** | ***** | ***** | 3.46 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 19. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin II Receptor Blockers (ARB) 183-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Sex: Male** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 29,914 | ***** | ***** | ***** | ***** | 1.92 | ***** | -0.98 | ***** | 0.63 ( 0.40, 1.00) | 0.05 |
| ARBs (14-day gap) | 149,212 | ***** | ***** | ***** | ***** | 2.9 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 29,883 | ***** | ***** | ***** | ***** | 2.72 | ***** | -0.32 | ***** | 0.89 ( 0.47, 1.72) | 0.739 |
| ARBs (14-day gap) | 29,883 | ***** | ***** | ***** | ***** | 3.04 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 29,883 | ***** | ***** | ***** | ***** | 1.92 | ***** | -0.81 | ***** | 0.67 ( 0.39, 1.16) | 0.154 |
| ARBs (14-day gap) | 29,883 | ***** | ***** | ***** | ***** | 2.73 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 29,914 | ***** | ***** | ***** | ***** | 4.07 | ***** | -0.96 | ***** | 0.79 ( 0.39, 1.58) | 0.501 |
| ARBs (14-day gap) | 149,212 | ***** | ***** | ***** | ***** | 5.02 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 29,883 | ***** | ***** | ***** | ***** | 4.19 | ***** | 0 | ***** | 1.00 ( 0.40, 2.52) | 1 |
| ARBs (14-day gap) | 29,883 | ***** | ***** | ***** | ***** | 4.19 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 29,883 | ***** | ***** | ***** | ***** | 4.07 | ***** | -0.13 | ***** | 0.96 ( 0.39, 2.35) | 0.922 |
| ARBs (14-day gap) | 29,883 | ***** | ***** | ***** | ***** | 4.2 | ***** | | | | |

**Table 19. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin II Receptor Blockers (ARB) 183-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 23,979 | ***** | ***** | ***** | ***** | 1.22 | ***** | -1.66 | ***** | 0.42 ( 0.10, 1.77) | 0.239 |
| ARBs (14-day gap) | 139,746 | ***** | ***** | ***** | ***** | 2.88 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 22,255 | ***** | ***** | ***** | ***** | 1.46 | ***** | -2.2 | ***** | 0.40 ( 0.08, 2.06) | 0.273 |
| ARBs (14-day gap) | 22,255 | ***** | ***** | ***** | ***** | 3.66 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 23,959 | ***** | ***** | ***** | ***** | 1.22 | ***** | -2.75 | ***** | 0.31 ( 0.07, 1.47) | 0.142 |
| ARBs (14-day gap) | 27,741 | ***** | ***** | ***** | ***** | 3.97 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 16,323 | ***** | ***** | ***** | ***** | 3.29 | ***** | 0.88 | ***** | 1.42 ( 0.48, 4.15) | 0.526 |
| ARBs (14-day gap) | 107,317 | ***** | ***** | ***** | ***** | 2.41 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 11,742 | ***** | ***** | ***** | ***** | 2.44 | ***** | 2.44 | ***** | - | - |
| ARBs (14-day gap) | 11,742 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 16,314 | ***** | ***** | ***** | ***** | 3.29 | ***** | 3.29 | ***** | - | - |
| ARBs (14-day gap) | 21,548 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 19. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin II Receptor Blockers (ARB) 183-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 13,186 | ***** | ***** | ***** | ***** | 1.61 | ***** | -1.16 | ***** | 0.57 ( 0.20, 1.57) | 0.275 |
| ARBs (14-day gap) | 94,188 | ***** | ***** | ***** | ***** | 2.77 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 8,232 | ***** | ***** | ***** | ***** | 2.61 | ***** | -0.87 | ***** | 0.75 ( 0.17, 3.35) | 0.706 |
| ARBs (14-day gap) | 8,232 | ***** | ***** | ***** | ***** | 3.47 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 13,178 | ***** | ***** | ***** | ***** | 1.61 | ***** | -2.28 | ***** | 0.40 ( 0.13, 1.23) | 0.11 |
| ARBs (14-day gap) | 18,720 | ***** | ***** | ***** | ***** | 3.89 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 8,155 | ***** | ***** | ***** | ***** | 0.6 | ***** | -1.23 | ***** | 0.34 ( 0.05, 2.55) | 0.296 |
| ARBs (14-day gap) | 56,397 | ***** | ***** | ***** | ***** | 1.83 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 2,967 | ***** | ***** | ***** | ***** | 2 | ***** | 0 | ***** | 1.00 ( 0.06, 15.99) | 1 |
| ARBs (14-day gap) | 2,967 | ***** | ***** | ***** | ***** | 2 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 8,149 | ***** | ***** | ***** | ***** | 0.6 | ***** | -0.77 | ***** | 0.42 ( 0.04, 4.08) | 0.458 |
| ARBs (14-day gap) | 10,875 | ***** | ***** | ***** | ***** | 1.38 | ***** | | | | |

**Table 19. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin II Receptor Blockers (ARB) 183-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 5,618 | ***** | ***** | ***** | ***** | 0 | ***** | -2.15 | ***** | - | - |
| ARBs (14-day gap) | 39,949 | ***** | ***** | ***** | ***** | 2.15 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 1,428 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 1,428 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 5,616 | ***** | ***** | ***** | ***** | 0 | ***** | -1.24 | ***** | - | - |
| ARBs (14-day gap) | 7,452 | ***** | ***** | ***** | ***** | 1.24 | ***** | | | | |
| **Sex: Female** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 19,226 | ***** | ***** | ***** | ***** | 3.56 | ***** | 0.45 | ***** | 1.07 ( 0.70, 1.64) | 0.749 |
| ARBs (14-day gap) | 187,871 | ***** | ***** | ***** | ***** | 3.11 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 19,218 | ***** | ***** | ***** | ***** | 4.52 | ***** | 0.25 | ***** | 1.06 ( 0.55, 2.05) | 0.866 |
| ARBs (14-day gap) | 19,218 | ***** | ***** | ***** | ***** | 4.27 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 19,218 | ***** | ***** | ***** | ***** | 3.56 | ***** | 0.88 | ***** | 1.27 ( 0.71, 2.27) | 0.413 |
| ARBs (14-day gap) | 19,218 | ***** | ***** | ***** | ***** | 2.68 | ***** | | | | |

**Table 19. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin II Receptor Blockers (ARB) 183-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 19,226 | ***** | ***** | ***** | ***** | 3.54 | ***** | -3.17 | ***** | 0.52 ( 0.21, 1.28) | 0.156 |
| ARBs (14-day gap) | 187,871 | ***** | ***** | ***** | ***** | 6.71 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 19,218 | ***** | ***** | ***** | ***** | 2.91 | ***** | -3.64 | ***** | 0.44 ( 0.14, 1.44) | 0.177 |
| ARBs (14-day gap) | 19,218 | ***** | ***** | ***** | ***** | 6.55 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 19,218 | ***** | ***** | ***** | ***** | 3.54 | ***** | -2.97 | ***** | 0.54 ( 0.18, 1.57) | 0.256 |
| ARBs (14-day gap) | 19,218 | ***** | ***** | ***** | ***** | 6.51 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 15,132 | ***** | ***** | ***** | ***** | 5.85 | ***** | 2.01 | ***** | 1.53 ( 0.65, 3.57) | 0.328 |
| ARBs (14-day gap) | 176,478 | ***** | ***** | ***** | ***** | 3.84 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 14,102 | ***** | ***** | ***** | ***** | 7 | ***** | 1.17 | ***** | 1.20 ( 0.37, 3.93) | 0.763 |
| ARBs (14-day gap) | 14,102 | ***** | ***** | ***** | ***** | 5.83 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 15,128 | ***** | ***** | ***** | ***** | 5.86 | ***** | 1.22 | ***** | 1.26 ( 0.41, 3.91) | 0.688 |
| ARBs (14-day gap) | 17,918 | ***** | ***** | ***** | ***** | 4.63 | ***** | | | | |

**Table 19. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin II Receptor Blockers (ARB) 183-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 10,153 | ***** | ***** | ***** | ***** | 3.97 | ***** | 0.85 | ***** | 1.31 ( 0.40, 4.26) | 0.658 |
| ARBs (14-day gap) | 136,128 | ***** | ***** | ***** | ***** | 3.13 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 7,322 | ***** | ***** | ***** | ***** | 5.83 | ***** | 5.83 | ***** | - | - |
| ARBs (14-day gap) | 7,322 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 10,151 | ***** | ***** | ***** | ***** | 3.97 | ***** | 3.97 | ***** | - | - |
| ARBs (14-day gap) | 13,812 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 8,188 | ***** | ***** | ***** | ***** | 3.25 | ***** | 1.39 | ***** | 1.78 ( 0.70, 4.52) | 0.222 |
| ARBs (14-day gap) | 120,042 | ***** | ***** | ***** | ***** | 1.86 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 5,187 | ***** | ***** | ***** | ***** | 4.04 | ***** | 1.35 | ***** | 1.50 ( 0.25, 8.98) | 0.657 |
| ARBs (14-day gap) | 5,187 | ***** | ***** | ***** | ***** | 2.69 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 8,186 | ***** | ***** | ***** | ***** | 3.25 | ***** | 1.88 | ***** | 2.34 ( 0.56, 9.82) | 0.244 |
| ARBs (14-day gap) | 12,064 | ***** | ***** | ***** | ***** | 1.37 | ***** | | | | |

**Table 19. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin II Receptor Blockers (ARB) 183-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 4,946 | ***** | ***** | ***** | ***** | 2 | ***** | -0.25 | ***** | 0.90 ( 0.22, 3.76) | 0.887 |
| ARBs (14-day gap) | 73,672 | ***** | ***** | ***** | ***** | 2.25 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 1,909 | ***** | ***** | ***** | ***** | 3.11 | ***** | 0 | ***** | 1.00 ( 0.06, 15.99) | 1 |
| ARBs (14-day gap) | 1,909 | ***** | ***** | ***** | ***** | 3.11 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 4,945 | ***** | ***** | ***** | ***** | 2 | ***** | 0.61 | ***** | 1.53 ( 0.22, 10.90) | 0.67 |
| ARBs (14-day gap) | 7,169 | ***** | ***** | ***** | ***** | 1.39 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 3,377 | ***** | ***** | ***** | ***** | 2.73 | ***** | 1.62 | ***** | 2.69 ( 0.61, 11.92) | 0.194 |
| ARBs (14-day gap) | 52,691 | ***** | ***** | ***** | ***** | 1.11 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 920 | ***** | ***** | ***** | ***** | 5.82 | ***** | 5.82 | ***** | - | - |
| ARBs (14-day gap) | 920 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 3,377 | ***** | ***** | ***** | ***** | 2.72 | ***** | 0.87 | ***** | 1.58 ( 0.22, 11.22) | 0.649 |
| ARBs (14-day gap) | 4,919 | ***** | ***** | ***** | ***** | 1.86 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 20. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 18-44 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 1,164 | ***** | ***** | ***** | ***** | 0 | ***** | -7.89 | ***** | - | - |
| ARBs (14-day gap) | 8,502 | ***** | ***** | ***** | ***** | 7.89 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 1,154 | ***** | ***** | ***** | ***** | 0 | ***** | -5.39 | ***** | - | - |
| ARBs (14-day gap) | 1,154 | ***** | ***** | ***** | ***** | 5.39 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 1,154 | ***** | ***** | ***** | ***** | 0 | ***** | -2.66 | ***** | - | - |
| ARBs (14-day gap) | 1,154 | ***** | ***** | ***** | ***** | 2.66 | ***** | | | | |
| **Age Group: 45-54 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 2,653 | ***** | ***** | ***** | ***** | 3.55 | ***** | -0.77 | ***** | 0.86 ( 0.26, 2.82) | 0.799 |
| ARBs (14-day gap) | 18,293 | ***** | ***** | ***** | ***** | 4.32 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 2,641 | ***** | ***** | ***** | ***** | 4.24 | ***** | -4.24 | ***** | 0.50 ( 0.09, 2.73) | 0.423 |
| ARBs (14-day gap) | 2,641 | ***** | ***** | ***** | ***** | 8.49 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 2,641 | ***** | ***** | ***** | ***** | 3.56 | ***** | -2.53 | ***** | 0.61 ( 0.15, 2.42) | 0.479 |
| ARBs (14-day gap) | 2,641 | ***** | ***** | ***** | ***** | 6.09 | ***** | | | | |

**Table 20. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 55-64 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 5,990 | ***** | ***** | ***** | ***** | 5.14 | ***** | 1.14 | ***** | 1.25 ( 0.64, 2.45) | 0.506 |
| ARBs (14-day gap) | 40,547 | ***** | ***** | ***** | ***** | 4 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 5,945 | ***** | ***** | ***** | ***** | 7.18 | ***** | 3.59 | ***** | 2.00 ( 0.60, 6.64) | 0.258 |
| ARBs (14-day gap) | 5,945 | ***** | ***** | ***** | ***** | 3.59 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 5,945 | ***** | ***** | ***** | ***** | 5.17 | ***** | 3.47 | ***** | 2.89 ( 0.91, 9.25) | 0.073 |
| ARBs (14-day gap) | 5,945 | ***** | ***** | ***** | ***** | 1.69 | ***** | | | | |
| **Age Group: 65+ Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 39,333 | ***** | ***** | ***** | ***** | 2.18 | ***** | -0.52 | ***** | 0.76 ( 0.52, 1.10) | 0.146 |
| ARBs (14-day gap) | 269,741 | ***** | ***** | ***** | ***** | 2.71 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 39,269 | ***** | ***** | ***** | ***** | 2.94 | ***** | 0 | ***** | 1.00 ( 0.57, 1.74) | 1 |
| ARBs (14-day gap) | 39,269 | ***** | ***** | ***** | ***** | 2.94 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 39,269 | ***** | ***** | ***** | ***** | 2.19 | ***** | -0.47 | ***** | 0.78 ( 0.49, 1.23) | 0.29 |
| ARBs (14-day gap) | 39,269 | ***** | ***** | ***** | ***** | 2.65 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 18-44** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,164 | ***** | ***** | ***** | ***** | 0 | ***** | -7.89 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 8,502 | ***** | ***** | ***** | ***** | 7.89 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,154 | ***** | ***** | ***** | ***** | 0 | ***** | -5.39 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,154 | ***** | ***** | ***** | ***** | 5.39 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,154 | ***** | ***** | ***** | ***** | 0 | ***** | -2.66 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,154 | ***** | ***** | ***** | ***** | 2.66 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,164 | ***** | ***** | ***** | ***** | 0 | ***** | -5.9 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 8,502 | ***** | ***** | ***** | ***** | 5.9 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,154 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,154 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,154 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,154 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 904 | ***** | ***** | ***** | ***** | 0 | ***** | -7.65 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 7,923 | ***** | ***** | ***** | ***** | 7.65 | ***** | | | | |

**Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 811 | ***** | ***** | ***** | ***** | 0 | ***** | -21.5 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 811 | ***** | ***** | ***** | ***** | 21.5 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 899 | ***** | ***** | ***** | ***** | 0 | ***** | -14.46 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,034 | ***** | ***** | ***** | ***** | 14.46 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 570 | ***** | ***** | ***** | ***** | 0 | ***** | -5.33 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 5,003 | ***** | ***** | ***** | ***** | 5.33 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 327 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 327 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 567 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 654 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 446 | ***** | ***** | ***** | ***** | 0 | ***** | -16.53 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 4,048 | ***** | ***** | ***** | ***** | 16.53 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 197 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 197 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 446 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 499 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 264 | ***** | ***** | ***** | ***** | 0 | ***** | -5.1 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,994 | ***** | ***** | ***** | ***** | 5.1 | ***** | | | | |

**Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 58 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 58 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 267 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 256 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 192 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,316 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 33 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 33 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 193 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 170 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Age Group: 45-54** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,653 | ***** | ***** | ***** | ***** | 3.55 | ***** | -0.77 | ***** | 0.86 ( 0.26, 2.82) | 0.799 |
| ARBs (183-day prior, 14-day gap) | 18,293 | ***** | ***** | ***** | ***** | 4.32 | ***** | | | | |

**Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

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|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,641 | ***** | ***** | ***** | ***** | 4.24 | ***** | -4.24 | ***** | 0.50 ( 0.09, 2.73) | 0.423 |
| ARBs (183-day prior, 14-day gap) | 2,641 | ***** | ***** | ***** | ***** | 8.49 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,641 | ***** | ***** | ***** | ***** | 3.56 | ***** | -2.53 | ***** | 0.61 ( 0.15, 2.42) | 0.479 |
| ARBs (183-day prior, 14-day gap) | 2,641 | ***** | ***** | ***** | ***** | 6.09 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,653 | ***** | ***** | ***** | ***** | 0 | ***** | -10.27 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 18,293 | ***** | ***** | ***** | ***** | 10.27 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,641 | ***** | ***** | ***** | ***** | 0 | ***** | -10.78 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 2,641 | ***** | ***** | ***** | ***** | 10.78 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,641 | ***** | ***** | ***** | ***** | 0 | ***** | -9.53 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 2,641 | ***** | ***** | ***** | ***** | 9.53 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,051 | ***** | ***** | ***** | ***** | 0 | ***** | -4.29 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 17,081 | ***** | ***** | ***** | ***** | 4.29 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,882 | ***** | ***** | ***** | ***** | 0 | ***** | -18.36 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,882 | ***** | ***** | ***** | ***** | 18.36 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,042 | ***** | ***** | ***** | ***** | 0 | ***** | -11.86 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 2,436 | ***** | ***** | ***** | ***** | 11.86 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,326 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 11,640 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 848 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 848 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,321 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,705 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,040 | ***** | ***** | ***** | ***** | 10.1 | ***** | 6.5 | ***** | 2.90 ( 0.58, 14.51) | 0.196 |
| ARBs (183-day prior, 14-day gap) | 9,733 | ***** | ***** | ***** | ***** | 3.6 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 549 | ***** | ***** | ***** | ***** | 13.32 | ***** | 13.32 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 549 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,039 | ***** | ***** | ***** | ***** | 10.11 | ***** | 5.88 | ***** | 2.46 ( 0.22, 27.20) | 0.463 |
| ARBs (183-day prior, 14-day gap) | 1,398 | ***** | ***** | ***** | ***** | 4.23 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 637 | ***** | ***** | ***** | ***** | 7.75 | ***** | 5.81 | ***** | 4.09 ( 0.36, 46.23) | 0.255 |
| ARBs (183-day prior, 14-day gap) | 5,198 | ***** | ***** | ***** | ***** | 1.94 | ***** | | | | |

**Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 184 | ***** | ***** | ***** | ***** | 31.69 | ***** | 31.69 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 184 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 638 | ***** | ***** | ***** | ***** | 7.74 | ***** | 7.74 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 723 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 435 | ***** | ***** | ***** | ***** | 0 | ***** | -2.69 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 3,436 | ***** | ***** | ***** | ***** | 2.69 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 88 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 88 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 435 | ***** | ***** | ***** | ***** | 0 | ***** | -9.96 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 477 | ***** | ***** | ***** | ***** | 9.96 | ***** | | | | |
| **Age Group: 55-64** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,990 | ***** | ***** | ***** | ***** | 5.14 | ***** | 1.14 | ***** | 1.25 ( 0.64, 2.45) | 0.506 |
| ARBs (183-day prior, 14-day gap) | 40,547 | ***** | ***** | ***** | ***** | 4 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,945 | ***** | ***** | ***** | ***** | 7.18 | ***** | 3.59 | ***** | 2.00 ( 0.60, 6.64) | 0.258 |
| ARBs (183-day prior, 14-day gap) | 5,945 | ***** | ***** | ***** | ***** | 3.59 | ***** | | | | |

**Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,945 | ***** | ***** | ***** | ***** | 5.17 | ***** | 3.47 | ***** | 2.89 ( 0.91, 9.25) | 0.073 |
| ARBs (183-day prior, 14-day gap) | 5,945 | ***** | ***** | ***** | ***** | 1.69 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,990 | ***** | ***** | ***** | ***** | 9.23 | ***** | 1.22 | ***** | 1.07 ( 0.37, 3.08) | 0.901 |
| ARBs (183-day prior, 14-day gap) | 40,547 | ***** | ***** | ***** | ***** | 8.02 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,945 | ***** | ***** | ***** | ***** | 9.61 | ***** | 4.81 | ***** | 2.00 ( 0.37, 10.92) | 0.423 |
| ARBs (183-day prior, 14-day gap) | 5,945 | ***** | ***** | ***** | ***** | 4.81 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,945 | ***** | ***** | ***** | ***** | 9.3 | ***** | 5.05 | ***** | 2.10 ( 0.38, 11.44) | 0.393 |
| ARBs (183-day prior, 14-day gap) | 5,945 | ***** | ***** | ***** | ***** | 4.24 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,618 | ***** | ***** | ***** | ***** | 6.43 | ***** | 4.18 | ***** | 2.92 ( 0.58, 14.60) | 0.193 |
| ARBs (183-day prior, 14-day gap) | 37,952 | ***** | ***** | ***** | ***** | 2.25 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,220 | ***** | ***** | ***** | ***** | 8.01 | ***** | 4.01 | ***** | 2.00 ( 0.18, 22.06) | 0.571 |
| ARBs (183-day prior, 14-day gap) | 4,220 | ***** | ***** | ***** | ***** | 4.01 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,594 | ***** | ***** | ***** | ***** | 6.47 | ***** | 3.87 | ***** | 2.34 ( 0.21, 25.82) | 0.487 |
| ARBs (183-day prior, 14-day gap) | 5,466 | ***** | ***** | ***** | ***** | 2.6 | ***** | | | | |

**Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 3,044 | ***** | ***** | ***** | ***** | 8.87 | ***** | 6.48 | ***** | 3.86 ( 0.74, 20.09) | 0.109 |
| ARBs (183-day prior, 14-day gap) | 27,412 | ***** | ***** | ***** | ***** | 2.39 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,036 | ***** | ***** | ***** | ***** | 7.12 | ***** | 7.12 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 2,036 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 3,028 | ***** | ***** | ***** | ***** | 8.91 | ***** | 8.91 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 3,974 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,406 | ***** | ***** | ***** | ***** | 2.2 | ***** | -1.19 | ***** | 0.65 ( 0.09, 5.00) | 0.682 |
| ARBs (183-day prior, 14-day gap) | 23,326 | ***** | ***** | ***** | ***** | 3.39 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,367 | ***** | ***** | ***** | ***** | 5.16 | ***** | 0 | ***** | 1.00 ( 0.06, 15.99) | 1 |
| ARBs (183-day prior, 14-day gap) | 1,367 | ***** | ***** | ***** | ***** | 5.16 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,394 | ***** | ***** | ***** | ***** | 2.21 | ***** | 0.5 | ***** | 1.15 ( 0.07, 18.54) | 0.922 |
| ARBs (183-day prior, 14-day gap) | 3,331 | ***** | ***** | ***** | ***** | 1.71 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,482 | ***** | ***** | ***** | ***** | 0 | ***** | -3.39 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 13,307 | ***** | ***** | ***** | ***** | 3.39 | ***** | | | | |

**Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 482 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 482 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,479 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,832 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,012 | ***** | ***** | ***** | ***** | 4.54 | ***** | 1 | ***** | 1.57 ( 0.19, 12.73) | 0.675 |
| ARBs (183-day prior, 14-day gap) | 9,049 | ***** | ***** | ***** | ***** | 3.54 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 214 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 214 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,010 | ***** | ***** | ***** | ***** | 4.56 | ***** | 4.56 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,204 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Age Group: 65+** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 39,333 | ***** | ***** | ***** | ***** | 2.18 | ***** | -0.52 | ***** | 0.76 ( 0.52, 1.10) | 0.146 |
| ARBs (183-day prior, 14-day gap) | 269,741 | ***** | ***** | ***** | ***** | 2.71 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 39,269 | ***** | ***** | ***** | ***** | 2.94 | ***** | 0 | ***** | 1.00 ( 0.57, 1.74) | 1 |
| ARBs (183-day prior, 14-day gap) | 39,269 | ***** | ***** | ***** | ***** | 2.94 | ***** | | | | |

**Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 39,269 | ***** | ***** | ***** | ***** | 2.19 | ***** | -0.47 | ***** | 0.78 ( 0.49, 1.23) | 0.29 |
| ARBs (183-day prior, 14-day gap) | 39,269 | ***** | ***** | ***** | ***** | 2.65 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 39,333 | ***** | ***** | ***** | ***** | 3.43 | ***** | -1.93 | ***** | 0.63 ( 0.33, 1.20) | 0.161 |
| ARBs (183-day prior, 14-day gap) | 269,741 | ***** | ***** | ***** | ***** | 5.37 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 39,269 | ***** | ***** | ***** | ***** | 3.18 | ***** | -1.77 | ***** | 0.64 ( 0.28, 1.49) | 0.301 |
| ARBs (183-day prior, 14-day gap) | 39,269 | ***** | ***** | ***** | ***** | 4.95 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 39,269 | ***** | ***** | ***** | ***** | 3.44 | ***** | -1.99 | ***** | 0.63 ( 0.29, 1.38) | 0.246 |
| ARBs (183-day prior, 14-day gap) | 39,269 | ***** | ***** | ***** | ***** | 5.42 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 31,540 | ***** | ***** | ***** | ***** | 2.78 | ***** | -0.62 | ***** | 0.82 ( 0.35, 1.89) | 0.639 |
| ARBs (183-day prior, 14-day gap) | 253,270 | ***** | ***** | ***** | ***** | 3.41 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 29,335 | ***** | ***** | ***** | ***** | 3.29 | ***** | -0.55 | ***** | 0.86 ( 0.29, 2.55) | 0.782 |
| ARBs (183-day prior, 14-day gap) | 29,335 | ***** | ***** | ***** | ***** | 3.84 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 31,491 | ***** | ***** | ***** | ***** | 2.79 | ***** | -1.68 | ***** | 0.64 ( 0.24, 1.70) | 0.367 |
| ARBs (183-day prior, 14-day gap) | 36,608 | ***** | ***** | ***** | ***** | 4.47 | ***** | | | | |

**Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 21,538 | ***** | ***** | ***** | ***** | 3.11 | ***** | 0.15 | ***** | 1.07 ( 0.43, 2.70) | 0.882 |
| ARBs (183-day prior, 14-day gap) | 199,393 | ***** | ***** | ***** | ***** | 2.97 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 15,962 | ***** | ***** | ***** | ***** | 2.67 | ***** | 2.67 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 15,962 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 21,507 | ***** | ***** | ***** | ***** | 3.12 | ***** | 3.12 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 28,996 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 17,483 | ***** | ***** | ***** | ***** | 1.82 | ***** | 0.07 | ***** | 1.05 ( 0.45, 2.43) | 0.911 |
| ARBs (183-day prior, 14-day gap) | 177,131 | ***** | ***** | ***** | ***** | 1.75 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 11,400 | ***** | ***** | ***** | ***** | 2.46 | ***** | 0.61 | ***** | 1.33 ( 0.30, 5.96) | 0.706 |
| ARBs (183-day prior, 14-day gap) | 11,400 | ***** | ***** | ***** | ***** | 1.84 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 17,460 | ***** | ***** | ***** | ***** | 1.83 | ***** | -0.33 | ***** | 0.84 ( 0.30, 2.31) | 0.733 |
| ARBs (183-day prior, 14-day gap) | 25,575 | ***** | ***** | ***** | ***** | 2.16 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 10,720 | ***** | ***** | ***** | ***** | 0.92 | ***** | -0.95 | ***** | 0.51 ( 0.12, 2.09) | 0.346 |
| ARBs (183-day prior, 14-day gap) | 109,576 | ***** | ***** | ***** | ***** | 1.87 | ***** | | | | |

**Table 21. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Age Group, and Follow-up Time**

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|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,259 | ***** | ***** | ***** | ***** | 2.79 | ***** | 1.39 | ***** | 2.00 ( 0.18, 22.06) | 0.571 |
| ARBs (183-day prior, 14-day gap) | 4,259 | ***** | ***** | ***** | ***** | 1.39 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 10,705 | ***** | ***** | ***** | ***** | 0.92 | ***** | -0.71 | ***** | 0.57 ( 0.11, 2.93) | 0.499 |
| ARBs (183-day prior, 14-day gap) | 15,297 | ***** | ***** | ***** | ***** | 1.63 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 7,356 | ***** | ***** | ***** | ***** | 0.62 | ***** | -0.69 | ***** | 0.48 ( 0.07, 3.58) | 0.477 |
| ARBs (183-day prior, 14-day gap) | 78,843 | ***** | ***** | ***** | ***** | 1.31 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,066 | ***** | ***** | ***** | ***** | 2.58 | ***** | 2.58 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 2,066 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 7,349 | ***** | ***** | ***** | ***** | 0.62 | ***** | -1.11 | ***** | 0.37 ( 0.04, 3.32) | 0.375 |
| ARBs (183-day prior, 14-day gap) | 10,577 | ***** | ***** | ***** | ***** | 1.73 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 22. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Unknown** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 8,082 | ***** | ***** | ***** | ***** | 1.84 | ***** | -0.67 | ***** | 0.71 ( 0.28, 1.78) | 0.468 |
| ARBs (14-day gap) | 47,793 | ***** | ***** | ***** | ***** | 2.52 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 8,026 | ***** | ***** | ***** | ***** | 1.92 | ***** | 0.64 | ***** | 1.50 ( 0.25, 8.98) | 0.657 |
| ARBs (14-day gap) | 8,026 | ***** | ***** | ***** | ***** | 1.28 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 8,026 | ***** | ***** | ***** | ***** | 1.85 | ***** | -0.21 | ***** | 0.87 ( 0.27, 2.74) | 0.807 |
| ARBs (14-day gap) | 8,026 | ***** | ***** | ***** | ***** | 2.07 | ***** | | | | |
| **Race: American Indian** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 133 | ***** | ***** | ***** | ***** | 0 | ***** | -1.36 | ***** | - | - |
| ARBs (14-day gap) | 1,948 | ***** | ***** | ***** | ***** | 1.36 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 131 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 131 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 131 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 131 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 22. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Asian** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 1,070 | ***** | ***** | ***** | ***** | 0 | ***** | -0.81 | ***** | - | - |
| ARBs (14-day gap) | 7,811 | ***** | ***** | ***** | ***** | 0.81 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 1,026 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 1,026 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 1,026 | ***** | ***** | ***** | ***** | 0 | ***** | -2.15 | ***** | - | - |
| ARBs (14-day gap) | 1,026 | ***** | ***** | ***** | ***** | 2.15 | ***** | | | | |
| **Race: Black** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 6,989 | ***** | ***** | ***** | ***** | 4.36 | ***** | -2.45 | ***** | 0.60 ( 0.31, 1.18) | 0.139 |
| ARBs (14-day gap) | 55,801 | ***** | ***** | ***** | ***** | 6.8 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 6,967 | ***** | ***** | ***** | ***** | 4.11 | ***** | -4.11 | ***** | 0.50 ( 0.17, 1.46) | 0.206 |
| ARBs (14-day gap) | 6,967 | ***** | ***** | ***** | ***** | 8.21 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 6,967 | ***** | ***** | ***** | ***** | 4.36 | ***** | -1.17 | ***** | 0.74 ( 0.32, 1.70) | 0.482 |
| ARBs (14-day gap) | 6,967 | ***** | ***** | ***** | ***** | 5.53 | ***** | | | | |

**Table 22. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Pacific Islander** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 61 | ***** | ***** | ***** | ***** | 0 | ***** | -8.97 | ***** | - | - |
| ARBs (14-day gap) | 478 | ***** | ***** | ***** | ***** | 8.97 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 50 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 50 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 50 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 50 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Race: White** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 32,805 | ***** | ***** | ***** | ***** | 2.48 | ***** | 0.07 | ***** | 0.97 ( 0.66, 1.42) | 0.858 |
| ARBs (14-day gap) | 223,252 | ***** | ***** | ***** | ***** | 2.4 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 32,796 | ***** | ***** | ***** | ***** | 3.61 | ***** | 0 | ***** | 1.00 ( 0.58, 1.72) | 1 |
| ARBs (14-day gap) | 32,796 | ***** | ***** | ***** | ***** | 3.61 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 32,796 | ***** | ***** | ***** | ***** | 2.48 | ***** | -0.16 | ***** | 0.89 ( 0.55, 1.44) | 0.647 |
| ARBs (14-day gap) | 32,796 | ***** | ***** | ***** | ***** | 2.63 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Unknown** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,082 | ***** | ***** | ***** | ***** | 1.84 | ***** | -0.67 | ***** | 0.71 ( 0.28, 1.78) | 0.468 |
| ARBs (183-day prior, 14-day gap) | 47,793 | ***** | ***** | ***** | ***** | 2.52 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,026 | ***** | ***** | ***** | ***** | 1.92 | ***** | 0.64 | ***** | 1.50 ( 0.25, 8.98) | 0.657 |
| ARBs (183-day prior, 14-day gap) | 8,026 | ***** | ***** | ***** | ***** | 1.28 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,026 | ***** | ***** | ***** | ***** | 1.85 | ***** | -0.21 | ***** | 0.87 ( 0.27, 2.74) | 0.807 |
| ARBs (183-day prior, 14-day gap) | 8,026 | ***** | ***** | ***** | ***** | 2.07 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,082 | ***** | ***** | ***** | ***** | 5.14 | ***** | 1.73 | ***** | 1.43 ( 0.41, 5.01) | 0.579 |
| ARBs (183-day prior, 14-day gap) | 47,793 | ***** | ***** | ***** | ***** | 3.41 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,026 | ***** | ***** | ***** | ***** | 5.35 | ***** | 5.35 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 8,026 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 8,026 | ***** | ***** | ***** | ***** | 5.17 | ***** | 5.17 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 8,026 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 6,161 | ***** | ***** | ***** | ***** | 0 | ***** | -2.52 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 44,551 | ***** | ***** | ***** | ***** | 2.52 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,627 | ***** | ***** | ***** | ***** | 0 | ***** | -2.93 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 5,627 | ***** | ***** | ***** | ***** | 2.93 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 6,121 | ***** | ***** | ***** | ***** | 0 | ***** | -5.66 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 7,377 | ***** | ***** | ***** | ***** | 5.66 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,181 | ***** | ***** | ***** | ***** | 3.22 | ***** | 1.65 | ***** | 2.18 ( 0.24, 19.59) | 0.488 |
| ARBs (183-day prior, 14-day gap) | 33,264 | ***** | ***** | ***** | ***** | 1.57 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,880 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 2,880 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 4,154 | ***** | ***** | ***** | ***** | 3.24 | ***** | 3.24 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 5,599 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 3,352 | ***** | ***** | ***** | ***** | 1.54 | ***** | -1.75 | ***** | 0.46 ( 0.06, 3.47) | 0.453 |
| ARBs (183-day prior, 14-day gap) | 28,534 | ***** | ***** | ***** | ***** | 3.29 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,957 | ***** | ***** | ***** | ***** | 0 | ***** | -3.59 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,957 | ***** | ***** | ***** | ***** | 3.59 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 3,332 | ***** | ***** | ***** | ***** | 1.55 | ***** | -1.98 | ***** | 0.43 ( 0.05, 4.18) | 0.47 |
| ARBs (183-day prior, 14-day gap) | 4,741 | ***** | ***** | ***** | ***** | 3.52 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,124 | ***** | ***** | ***** | ***** | 0 | ***** | -2.06 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 16,765 | ***** | ***** | ***** | ***** | 2.06 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 719 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 719 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,117 | ***** | ***** | ***** | ***** | 0 | ***** | -1.85 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 2,716 | ***** | ***** | ***** | ***** | 1.85 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,453 | ***** | ***** | ***** | ***** | 0 | ***** | -1.16 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 11,720 | ***** | ***** | ***** | ***** | 1.16 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 333 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 333 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,449 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,839 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Race: American Indian** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 133 | ***** | ***** | ***** | ***** | 0 | ***** | -1.36 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,948 | ***** | ***** | ***** | ***** | 1.36 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 131 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 131 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 131 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 131 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 133 | ***** | ***** | ***** | ***** | 0 | ***** | -6.38 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,948 | ***** | ***** | ***** | ***** | 6.38 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 131 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 131 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 131 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 131 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 101 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,839 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 97 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 97 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 101 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 122 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 62 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,233 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 49 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 49 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 63 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 91 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 55 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,023 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 41 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 41 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 55 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 85 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 32 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 550 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 15 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 15 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 33 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 44 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 19 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 369 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 23 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 27 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Race: Asian** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,070 | ***** | ***** | ***** | ***** | 0 | ***** | -0.81 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 7,811 | ***** | ***** | ***** | ***** | 0.81 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,026 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,026 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,026 | ***** | ***** | ***** | ***** | 0 | ***** | -2.15 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,026 | ***** | ***** | ***** | ***** | 2.15 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,070 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 7,811 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,026 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,026 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,026 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,026 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 775 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 7,366 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 698 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 698 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 743 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 957 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 515 | ***** | ***** | ***** | ***** | 0 | ***** | -2.16 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 5,969 | ***** | ***** | ***** | ***** | 2.16 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 385 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 385 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 499 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 769 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 410 | ***** | ***** | ***** | ***** | 0 | ***** | -1.04 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 5,294 | ***** | ***** | ***** | ***** | 1.04 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 264 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 264 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 397 | ***** | ***** | ***** | ***** | 0 | ***** | -8.23 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 678 | ***** | ***** | ***** | ***** | 8.23 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 269 | ***** | ***** | ***** | ***** | 0 | ***** | -1.55 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 3,215 | ***** | ***** | ***** | ***** | 1.55 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 100 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 100 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 262 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 401 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 184 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 2,248 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 55 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 55 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 179 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 261 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Race: Black** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 6,989 | ***** | ***** | ***** | ***** | 4.36 | ***** | -2.45 | ***** | 0.60 ( 0.31, 1.18) | 0.139 |
| ARBs (183-day prior, 14-day gap) | 55,801 | ***** | ***** | ***** | ***** | 6.8 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 6,967 | ***** | ***** | ***** | ***** | 4.11 | ***** | -4.11 | ***** | 0.50 ( 0.17, 1.46) | 0.206 |
| ARBs (183-day prior, 14-day gap) | 6,967 | ***** | ***** | ***** | ***** | 8.21 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 6,967 | ***** | ***** | ***** | ***** | 4.36 | ***** | -1.17 | ***** | 0.74 ( 0.32, 1.70) | 0.482 |
| ARBs (183-day prior, 14-day gap) | 6,967 | ***** | ***** | ***** | ***** | 5.53 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 6,989 | ***** | ***** | ***** | ***** | 3.9 | ***** | -9.75 | ***** | 0.28 ( 0.07, 1.14) | 0.075 |
| ARBs (183-day prior, 14-day gap) | 55,801 | ***** | ***** | ***** | ***** | 13.65 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 6,967 | ***** | ***** | ***** | ***** | 4.04 | ***** | -8.08 | ***** | 0.33 ( 0.07, 1.65) | 0.178 |
| ARBs (183-day prior, 14-day gap) | 6,967 | ***** | ***** | ***** | ***** | 12.12 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 6,967 | ***** | ***** | ***** | ***** | 3.91 | ***** | -10.53 | ***** | 0.27 ( 0.06, 1.26) | 0.095 |
| ARBs (183-day prior, 14-day gap) | 6,967 | ***** | ***** | ***** | ***** | 14.44 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,495 | ***** | ***** | ***** | ***** | 5.59 | ***** | -1.82 | ***** | 0.76 ( 0.18, 3.21) | 0.711 |
| ARBs (183-day prior, 14-day gap) | 52,264 | ***** | ***** | ***** | ***** | 7.4 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,052 | ***** | ***** | ***** | ***** | 6.92 | ***** | 0 | ***** | 1.00 ( 0.14, 7.10) | 1 |
| ARBs (183-day prior, 14-day gap) | 5,052 | ***** | ***** | ***** | ***** | 6.92 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 5,480 | ***** | ***** | ***** | ***** | 5.6 | ***** | 1.19 | ***** | 1.29 ( 0.18, 9.14) | 0.801 |
| ARBs (183-day prior, 14-day gap) | 6,431 | ***** | ***** | ***** | ***** | 4.41 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 3,368 | ***** | ***** | ***** | ***** | 8.15 | ***** | 1.53 | ***** | 1.25 ( 0.29, 5.37) | 0.764 |
| ARBs (183-day prior, 14-day gap) | 37,443 | ***** | ***** | ***** | ***** | 6.61 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,215 | ***** | ***** | ***** | ***** | 6.58 | ***** | 6.58 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 2,215 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 3,361 | ***** | ***** | ***** | ***** | 8.16 | ***** | 8.16 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 4,686 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,573 | ***** | ***** | ***** | ***** | 2.18 | ***** | -2.05 | ***** | 0.53 ( 0.07, 3.92) | 0.533 |
| ARBs (183-day prior, 14-day gap) | 32,130 | ***** | ***** | ***** | ***** | 4.23 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,452 | ***** | ***** | ***** | ***** | 0 | ***** | -5.49 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,452 | ***** | ***** | ***** | ***** | 5.49 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 2,568 | ***** | ***** | ***** | ***** | 2.18 | ***** | -2.3 | ***** | 0.49 ( 0.05, 4.74) | 0.54 |
| ARBs (183-day prior, 14-day gap) | 3,985 | ***** | ***** | ***** | ***** | 4.48 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,423 | ***** | ***** | ***** | ***** | 3.49 | ***** | -0.69 | ***** | 0.85 ( 0.11, 6.44) | 0.872 |
| ARBs (183-day prior, 14-day gap) | 17,230 | ***** | ***** | ***** | ***** | 4.18 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 415 | ***** | ***** | ***** | ***** | 0 | ***** | -14.54 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 415 | ***** | ***** | ***** | ***** | 14.54 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,420 | ***** | ***** | ***** | ***** | 3.49 | ***** | 1 | ***** | 1.42 ( 0.09, 22.73) | 0.804 |
| ARBs (183-day prior, 14-day gap) | 2,097 | ***** | ***** | ***** | ***** | 2.49 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 965 | ***** | ***** | ***** | ***** | 4.89 | ***** | 1.99 | ***** | 1.80 ( 0.22, 14.65) | 0.585 |
| ARBs (183-day prior, 14-day gap) | 11,238 | ***** | ***** | ***** | ***** | 2.9 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 194 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 194 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 966 | ***** | ***** | ***** | ***** | 4.89 | ***** | 1.24 | ***** | 1.32 ( 0.08, 21.03) | 0.846 |
| ARBs (183-day prior, 14-day gap) | 1,324 | ***** | ***** | ***** | ***** | 3.64 | ***** | | | | |
| **Race: Pacific Islander** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 61 | ***** | ***** | ***** | ***** | 0 | ***** | -8.97 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 478 | ***** | ***** | ***** | ***** | 8.97 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 50 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 50 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 50 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 50 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 61 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 478 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 50 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 50 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 50 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 50 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 52 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 447 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 41 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 41 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 45 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 46 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 34 | ***** | ***** | ***** | ***** | 0 | ***** | -34.82 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 362 | ***** | ***** | ***** | ***** | 34.82 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 21 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 21 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 29 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 39 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 22 | ***** | ***** | ***** | ***** | 0 | ***** | -17.55 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 337 | ***** | ***** | ***** | ***** | 17.55 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 12 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 12 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 19 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 35 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 13 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 192 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 11 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 21 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 138 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | ***** | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 15 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Race: White** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 32,805 | ***** | ***** | ***** | ***** | 2.48 | ***** | 0.07 | ***** | 0.97 ( 0.66, 1.42) | 0.858 |
| ARBs (183-day prior, 14-day gap) | 223,252 | ***** | ***** | ***** | ***** | 2.4 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 32,796 | ***** | ***** | ***** | ***** | 3.61 | ***** | 0 | ***** | 1.00 ( 0.58, 1.72) | 1 |
| ARBs (183-day prior, 14-day gap) | 32,796 | ***** | ***** | ***** | ***** | 3.61 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 32,796 | ***** | ***** | ***** | ***** | 2.48 | ***** | -0.16 | ***** | 0.89 ( 0.55, 1.44) | 0.647 |
| ARBs (183-day prior, 14-day gap) | 32,796 | ***** | ***** | ***** | ***** | 2.63 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 32,805 | ***** | ***** | ***** | ***** | 3.69 | ***** | -1.11 | ***** | 0.75 ( 0.38, 1.49) | 0.413 |
| ARBs (183-day prior, 14-day gap) | 223,252 | ***** | ***** | ***** | ***** | 4.81 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 32,796 | ***** | ***** | ***** | ***** | 3.37 | ***** | -2.11 | ***** | 0.62 ( 0.26, 1.48) | 0.28 |
| ARBs (183-day prior, 14-day gap) | 32,796 | ***** | ***** | ***** | ***** | 5.48 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 32,796 | ***** | ***** | ***** | ***** | 3.69 | ***** | -2.03 | ***** | 0.64 ( 0.28, 1.46) | 0.287 |
| ARBs (183-day prior, 14-day gap) | 32,796 | ***** | ***** | ***** | ***** | 5.73 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 26,529 | ***** | ***** | ***** | ***** | 3.29 | ***** | 0.49 | ***** | 1.16 ( 0.50, 2.74) | 0.727 |
| ARBs (183-day prior, 14-day gap) | 209,760 | ***** | ***** | ***** | ***** | 2.81 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 24,768 | ***** | ***** | ***** | ***** | 3.9 | ***** | 0 | ***** | 1.00 ( 0.32, 3.10) | 1 |
| ARBs (183-day prior, 14-day gap) | 24,768 | ***** | ***** | ***** | ***** | 3.9 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 26,520 | ***** | ***** | ***** | ***** | 3.3 | ***** | -1.17 | ***** | 0.74 ( 0.27, 2.04) | 0.564 |
| ARBs (183-day prior, 14-day gap) | 30,621 | ***** | ***** | ***** | ***** | 4.47 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 18,317 | ***** | ***** | ***** | ***** | 2.92 | ***** | 0.74 | ***** | 1.35 ( 0.47, 3.85) | 0.575 |
| ARBs (183-day prior, 14-day gap) | 165,181 | ***** | ***** | ***** | ***** | 2.18 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 13,479 | ***** | ***** | ***** | ***** | 3.15 | ***** | 3.15 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 13,479 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 18,311 | ***** | ***** | ***** | ***** | 2.92 | ***** | 2.92 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 24,143 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 14,962 | ***** | ***** | ***** | ***** | 2.48 | ***** | 0.79 | ***** | 1.47 ( 0.66, 3.25) | 0.346 |
| ARBs (183-day prior, 14-day gap) | 146,922 | ***** | ***** | ***** | ***** | 1.69 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 9,689 | ***** | ***** | ***** | ***** | 4.33 | ***** | 0.72 | ***** | 1.20 ( 0.37, 3.93) | 0.763 |
| ARBs (183-day prior, 14-day gap) | 9,689 | ***** | ***** | ***** | ***** | 3.61 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 14,956 | ***** | ***** | ***** | ***** | 2.48 | ***** | 0.42 | ***** | 1.20 ( 0.44, 3.31) | 0.724 |
| ARBs (183-day prior, 14-day gap) | 21,311 | ***** | ***** | ***** | ***** | 2.06 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 9,241 | ***** | ***** | ***** | ***** | 1.07 | ***** | -0.67 | ***** | 0.63 ( 0.15, 2.64) | 0.529 |
| ARBs (183-day prior, 14-day gap) | 92,122 | ***** | ***** | ***** | ***** | 1.74 | ***** | | | | |

**Table 23. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Race and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 3,652 | ***** | ***** | ***** | ***** | 3.25 | ***** | 0 | ***** | 1.00 ( 0.14, 7.10) | 1 |
| ARBs (183-day prior, 14-day gap) | 3,652 | ***** | ***** | ***** | ***** | 3.25 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 9,237 | ***** | ***** | ***** | ***** | 1.07 | ***** | -0.08 | ***** | 0.96 ( 0.16, 5.74) | 0.963 |
| ARBs (183-day prior, 14-day gap) | 12,898 | ***** | ***** | ***** | ***** | 1.15 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 6,366 | ***** | ***** | ***** | ***** | 0.72 | ***** | -0.75 | ***** | 0.49 ( 0.07, 3.65) | 0.487 |
| ARBs (183-day prior, 14-day gap) | 66,936 | ***** | ***** | ***** | ***** | 1.47 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 1,767 | ***** | ***** | ***** | ***** | 3.02 | ***** | 3.02 | ***** | - | - |
| ARBs (183-day prior, 14-day gap) | 1,767 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (183-day prior, 14-day gap) | 6,363 | ***** | ***** | ***** | ***** | 0.72 | ***** | -1.31 | ***** | 0.37 ( 0.04, 3.27) | 0.368 |
| ARBs (183-day prior, 14-day gap) | 8,999 | ***** | ***** | ***** | ***** | 2.03 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 24. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 49,629 | ***** | ***** | ***** | ***** | 2.43 | ***** | -4.3 | ***** | 0.34 ( 0.25, 0.47) | <0.001 |
| ACEI (14-day gap) | 695,068 | ***** | ***** | ***** | ***** | 6.74 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 49,628 | ***** | ***** | ***** | ***** | 2.52 | ***** | -6.73 | ***** | 0.27 ( 0.17, 0.43) | <0.001 |
| ACEI (14-day gap) | 49,628 | ***** | ***** | ***** | ***** | 9.26 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 49,628 | ***** | ***** | ***** | ***** | 2.43 | ***** | -3.65 | ***** | 0.37 ( 0.26, 0.53) | <0.001 |
| ACEI (14-day gap) | 49,628 | ***** | ***** | ***** | ***** | 6.08 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 25. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-Up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 49,629 | ***** | ***** | ***** | ***** | 2.43 | ***** | -4.3 | ***** | 0.34 ( 0.25, 0.47) | <0.001 |
| ACEI (14-day prior, 14-day gap) | 695,068 | ***** | ***** | ***** | ***** | 6.74 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 49,628 | ***** | ***** | ***** | ***** | 2.52 | ***** | -6.73 | ***** | 0.27 ( 0.17, 0.43) | <0.001 |
| ACEI (14-day prior, 14-day gap) | 49,628 | ***** | ***** | ***** | ***** | 9.26 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 49,628 | ***** | ***** | ***** | ***** | 2.43 | ***** | -3.65 | ***** | 0.37 ( 0.26, 0.53) | <0.001 |
| ACEI (14-day prior, 14-day gap) | 49,628 | ***** | ***** | ***** | ***** | 6.08 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 49,629 | ***** | ***** | ***** | ***** | 3.93 | ***** | -11.42 | ***** | 0.25 ( 0.15, 0.42) | <0.001 |
| ACEI (14-day prior, 14-day gap) | 695,068 | ***** | ***** | ***** | ***** | 15.35 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 49,628 | ***** | ***** | ***** | ***** | 3.77 | ***** | -13.06 | ***** | 0.22 ( 0.12, 0.41) | <0.001 |
| ACEI (14-day prior, 14-day gap) | 49,628 | ***** | ***** | ***** | ***** | 16.83 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 49,628 | ***** | ***** | ***** | ***** | 3.93 | ***** | -11.34 | ***** | 0.25 ( 0.14, 0.45) | <0.001 |
| ACEI (14-day prior, 14-day gap) | 49,628 | ***** | ***** | ***** | ***** | 15.26 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 37,404 | ***** | ***** | ***** | ***** | 3.94 | ***** | -2.1 | ***** | 0.65 ( 0.35, 1.23) | 0.188 |
| ACEI (14-day prior, 14-day gap) | 638,536 | ***** | ***** | ***** | ***** | 6.05 | ***** | | | | |

**Table 25. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-Up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 34,305 | ***** | ***** | ***** | ***** | 2.92 | ***** | -3.89 | ***** | 0.43 ( 0.16, 1.12) | 0.082 |
| ACEI (14-day prior, 14-day gap) | 34,305 | ***** | ***** | ***** | ***** | 6.8 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 37,403 | ***** | ***** | ***** | ***** | 3.94 | ***** | -1.3 | ***** | 0.74 ( 0.34, 1.63) | 0.46 |
| ACEI (14-day prior, 14-day gap) | 45,509 | ***** | ***** | ***** | ***** | 5.25 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 25,147 | ***** | ***** | ***** | ***** | 2.69 | ***** | -3.09 | ***** | 0.47 ( 0.19, 1.13) | 0.092 |
| ACEI (14-day prior, 14-day gap) | 463,084 | ***** | ***** | ***** | ***** | 5.78 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 17,306 | ***** | ***** | ***** | ***** | 1.67 | ***** | -5 | ***** | 0.25 ( 0.05, 1.18) | 0.08 |
| ACEI (14-day prior, 14-day gap) | 17,306 | ***** | ***** | ***** | ***** | 6.67 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 25,146 | ***** | ***** | ***** | ***** | 2.69 | ***** | -4.2 | ***** | 0.39 ( 0.14, 1.04) | 0.06 |
| ACEI (14-day prior, 14-day gap) | 34,002 | ***** | ***** | ***** | ***** | 6.89 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 19,929 | ***** | ***** | ***** | ***** | 0.78 | ***** | -3.61 | ***** | 0.18 ( 0.06, 0.55) | 0.003 |
| ACEI (14-day prior, 14-day gap) | 397,797 | ***** | ***** | ***** | ***** | 4.39 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 11,912 | ***** | ***** | ***** | ***** | 0.59 | ***** | -2.34 | ***** | 0.20 ( 0.02, 1.71) | 0.142 |
| ACEI (14-day prior, 14-day gap) | 11,912 | ***** | ***** | ***** | ***** | 2.93 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 19,928 | ***** | ***** | ***** | ***** | 0.78 | ***** | -1.11 | ***** | 0.40 ( 0.11, 1.45) | 0.162 |
| ACEI (14-day prior, 14-day gap) | 29,452 | ***** | ***** | ***** | ***** | 1.89 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 12,764 | ***** | ***** | ***** | ***** | 1.9 | ***** | -2.22 | ***** | 0.46 ( 0.19, 1.12) | 0.086 |
| ACEI (14-day prior, 14-day gap) | 235,571 | ***** | ***** | ***** | ***** | 4.12 | ***** | | | | |

**Table 25. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-Up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 4,378 | ***** | ***** | ***** | ***** | 2.77 | ***** | -1.39 | ***** | 0.67 ( 0.11, 3.99) | 0.657 |
| ACEI (14-day prior, 14-day gap) | 4,378 | ***** | ***** | ***** | ***** | 4.16 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 12,766 | ***** | ***** | ***** | ***** | 1.9 | ***** | -1.65 | ***** | 0.52 ( 0.18, 1.48) | 0.222 |
| ACEI (14-day prior, 14-day gap) | 17,106 | ***** | ***** | ***** | ***** | 3.55 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 9,031 | ***** | ***** | ***** | ***** | 1.5 | ***** | -2.05 | ***** | 0.42 ( 0.13, 1.31) | 0.133 |
| ACEI (14-day prior, 14-day gap) | 164,784 | ***** | ***** | ***** | ***** | 3.54 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 2,024 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day prior, 14-day gap) | 2,024 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 9,030 | ***** | ***** | ***** | ***** | 1.5 | ***** | -2.59 | ***** | 0.36 ( 0.10, 1.32) | 0.124 |
| ACEI (14-day prior, 14-day gap) | 11,426 | ***** | ***** | ***** | ***** | 4.09 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 26. Effect Estimates forNew Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (-183, -1)**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Angioedema (-183, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 49,583 | ***** | ***** | ***** | ***** | 2.37 | ***** | -4.1 | ***** | 0.35 ( 0.25, 0.48) | <0.001 |
| ACEI (14-day gap) | 694,204 | ***** | ***** | ***** | ***** | 6.48 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 49,582 | ***** | ***** | ***** | ***** | 2.42 | ***** | -6.42 | ***** | 0.27 ( 0.17, 0.43) | <0.001 |
| ACEI (14-day gap) | 49,582 | ***** | ***** | ***** | ***** | 8.84 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 49,582 | ***** | ***** | ***** | ***** | 2.37 | ***** | -3.47 | ***** | 0.38 ( 0.27, 0.55) | <0.001 |
| ACEI (14-day gap) | 49,582 | ***** | ***** | ***** | ***** | 5.85 | ***** | | | | |
| **Angioedema (-183, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 46 | ***** | ***** | ***** | ***** | 77.34 | ***** | -190.86 | ***** | 0.26 ( 0.04, 1.91) | 0.186 |
| ACEI (14-day gap) | 864 | ***** | ***** | ***** | ***** | 268.2 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 39 | ***** | ***** | ***** | ***** | 186.22 | ***** | -186.22 | ***** | 0.50 ( 0.05, 5.51) | 0.571 |
| ACEI (14-day gap) | 39 | ***** | ***** | ***** | ***** | 372.44 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 39 | ***** | ***** | ***** | ***** | 88.73 | ***** | -143.29 | ***** | 0.37 ( 0.04, 3.58) | 0.392 |
| ACEI (14-day gap) | 39 | ***** | ***** | ***** | ***** | 232.02 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 27: Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (ever, -1)**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Angioedema (ever, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 49,296 | ***** | ***** | ***** | ***** | 2.26 | ***** | -3.61 | ***** | 0.37 ( 0.26, 0.51) | <0.001 |
| ACEI (14-day gap) | 687,748 | ***** | ***** | ***** | ***** | 5.88 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 49,295 | ***** | ***** | ***** | ***** | 2.54 | ***** | -4.87 | ***** | 0.34 ( 0.22, 0.55) | <0.001 |
| ACEI (14-day gap) | 49,295 | ***** | ***** | ***** | ***** | 7.41 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 49,295 | ***** | ***** | ***** | ***** | 2.26 | ***** | -2.7 | ***** | 0.43 ( 0.29, 0.62) | <0.001 |
| ACEI (14-day gap) | 49,295 | ***** | ***** | ***** | ***** | 4.97 | ***** | | | | |
| **Angioedema (ever, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 333 | ***** | ***** | ***** | ***** | 31.78 | ***** | -65.3 | ***** | 0.30 ( 0.10, 0.93) | 0.037 |
| ACEI (14-day gap) | 7,320 | ***** | ***** | ***** | ***** | 97.08 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 327 | ***** | ***** | ***** | ***** | 35.77 | ***** | -107.3 | ***** | 0.25 ( 0.05, 1.18) | 0.08 |
| ACEI (14-day gap) | 327 | ***** | ***** | ***** | ***** | 143.06 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 327 | ***** | ***** | ***** | ***** | 32.31 | ***** | -88.41 | ***** | 0.23 ( 0.07, 0.80) | 0.021 |
| ACEI (14-day gap) | 327 | ***** | ***** | ***** | ***** | 120.71 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 28. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Serious Allergies**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Serious allergies** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 44,259 | ***** | ***** | ***** | ***** | 2.23 | ***** | -4.24 | ***** | 0.33 ( 0.23, 0.46) | <0.001 |
| ACEI (14-day gap) | 584,072 | ***** | ***** | ***** | ***** | 6.47 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 44,253 | ***** | ***** | ***** | ***** | 2.21 | ***** | -5.94 | ***** | 0.27 ( 0.16, 0.45) | <0.001 |
| ACEI (14-day gap) | 44,253 | ***** | ***** | ***** | ***** | 8.15 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 44,253 | ***** | ***** | ***** | ***** | 2.23 | ***** | -3 | ***** | 0.40 ( 0.27, 0.59) | <0.001 |
| ACEI (14-day gap) | 44,253 | ***** | ***** | ***** | ***** | 5.22 | ***** | | | | |
| **Serious allergies** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 5,370 | ***** | ***** | ***** | ***** | 4.27 | ***** | -4.05 | ***** | 0.49 ( 0.23, 1.04) | 0.063 |
| ACEI (14-day gap) | 110,996 | ***** | ***** | ***** | ***** | 8.31 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 5,365 | ***** | ***** | ***** | ***** | 4.36 | ***** | -8.72 | ***** | 0.33 ( 0.11, 1.03) | 0.057 |
| ACEI (14-day gap) | 5,365 | ***** | ***** | ***** | ***** | 13.09 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 5,365 | ***** | ***** | ***** | ***** | 4.27 | ***** | -4.11 | ***** | 0.47 ( 0.20, 1.14) | 0.094 |
| ACEI (14-day gap) | 5,365 | ***** | ***** | ***** | ***** | 8.38 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

Table 29. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin-Converting Enzyme Inhibitors (ACEI) 14-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, and Follow-up Time

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Sex: Male** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 34,743 | ***** | ***** | ***** | ***** | 2.57 | ***** | -3.41 | ***** | 0.41 ( 0.28, 0.58) | <0.001 |
| ACEI (14-day gap) | 353,146 | ***** | ***** | ***** | ***** | 5.98 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 34,715 | ***** | ***** | ***** | ***** | 2.82 | ***** | -4.46 | ***** | 0.39 ( 0.23, 0.66) | <0.001 |
| ACEI (14-day gap) | 34,715 | ***** | ***** | ***** | ***** | 7.28 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 34,715 | ***** | ***** | ***** | ***** | 2.57 | ***** | -1.87 | ***** | 0.54 ( 0.35, 0.84) | 0.006 |
| ACEI (14-day gap) | 34,715 | ***** | ***** | ***** | ***** | 4.44 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 34,743 | ***** | ***** | ***** | ***** | 3.19 | ***** | -11.41 | ***** | 0.21 ( 0.11, 0.43) | <0.001 |
| ACEI (14-day gap) | 353,146 | ***** | ***** | ***** | ***** | 14.6 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 34,715 | ***** | ***** | ***** | ***** | 3.31 | ***** | -9.92 | ***** | 0.25 ( 0.12, 0.54) | <0.001 |
| ACEI (14-day gap) | 34,715 | ***** | ***** | ***** | ***** | 13.23 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 34,715 | ***** | ***** | ***** | ***** | 3.19 | ***** | -8.46 | ***** | 0.27 ( 0.12, 0.58) | <0.001 |
| ACEI (14-day gap) | 34,715 | ***** | ***** | ***** | ***** | 11.65 | ***** | | | | |

**Table 29. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin-Converting Enzyme Inhibitors (ACEI) 14-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 26,387 | ***** | ***** | ***** | ***** | 4.46 | ***** | -1.13 | ***** | 0.79 ( 0.39, 1.62) | 0.52 |
| ACEI (14-day gap) | 325,667 | ***** | ***** | ***** | ***** | 5.59 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 24,158 | ***** | ***** | ***** | ***** | 3.44 | ***** | -0.69 | ***** | 0.83 ( 0.25, 2.73) | 0.763 |
| ACEI (14-day gap) | 24,158 | ***** | ***** | ***** | ***** | 4.13 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 26,368 | ***** | ***** | ***** | ***** | 4.46 | ***** | 0.49 | ***** | 1.09 ( 0.42, 2.83) | 0.857 |
| ACEI (14-day gap) | 31,762 | ***** | ***** | ***** | ***** | 3.97 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 17,862 | ***** | ***** | ***** | ***** | 3.79 | ***** | -0.95 | ***** | 0.80 ( 0.33, 1.98) | 0.636 |
| ACEI (14-day gap) | 236,803 | ***** | ***** | ***** | ***** | 4.74 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 12,310 | ***** | ***** | ***** | ***** | 2.34 | ***** | -3.52 | ***** | 0.40 ( 0.08, 2.06) | 0.273 |
| ACEI (14-day gap) | 12,310 | ***** | ***** | ***** | ***** | 5.86 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 17,847 | ***** | ***** | ***** | ***** | 3.79 | ***** | -0.58 | ***** | 0.87 ( 0.28, 2.66) | 0.806 |
| ACEI (14-day gap) | 23,871 | ***** | ***** | ***** | ***** | 4.37 | ***** | | | | |

**Table 29. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin-Converting Enzyme Inhibitors (ACEI) 14-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 14,181 | ***** | ***** | ***** | ***** | 0.36 | ***** | -3.14 | ***** | 0.10 ( 0.01, 0.74) | 0.024 |
| ACEI (14-day gap) | 203,937 | ***** | ***** | ***** | ***** | 3.5 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 8,440 | ***** | ***** | ***** | ***** | 0.82 | ***** | -1.64 | ***** | 0.33 ( 0.03, 3.20) | 0.341 |
| ACEI (14-day gap) | 8,440 | ***** | ***** | ***** | ***** | 2.47 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 14,171 | ***** | ***** | ***** | ***** | 0.36 | ***** | -1.26 | ***** | 0.22 ( 0.03, 1.79) | 0.155 |
| ACEI (14-day gap) | 20,616 | ***** | ***** | ***** | ***** | 1.62 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 9,105 | ***** | ***** | ***** | ***** | 2.67 | ***** | -0.74 | ***** | 0.78 ( 0.32, 1.92) | 0.587 |
| ACEI (14-day gap) | 120,273 | ***** | ***** | ***** | ***** | 3.41 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 3,136 | ***** | ***** | ***** | ***** | 5.81 | ***** | 1.94 | ***** | 1.50 ( 0.25, 8.98) | 0.657 |
| ACEI (14-day gap) | 3,136 | ***** | ***** | ***** | ***** | 3.87 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 9,101 | ***** | ***** | ***** | ***** | 2.67 | ***** | 0.56 | ***** | 1.23 ( 0.36, 4.25) | 0.744 |
| ACEI (14-day gap) | 12,007 | ***** | ***** | ***** | ***** | 2.11 | ***** | | | | |

Table 29. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin-Converting Enzyme Inhibitors (ACEI) 14-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, and Follow-up Time

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 6,443 | ***** | ***** | ***** | ***** | 2.1 | ***** | -0.81 | ***** | 0.70 ( 0.22, 2.25) | 0.553 |
| ACEI (14-day gap) | 84,138 | ***** | ***** | ***** | ***** | 2.91 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 1,481 | ***** | ***** | ***** | ***** | 0 | ***** | -3.62 | ***** | - | - |
| ACEI (14-day gap) | 1,481 | ***** | ***** | ***** | ***** | 3.62 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 6,440 | ***** | ***** | ***** | ***** | 2.1 | ***** | -0.82 | ***** | 0.69 ( 0.16, 2.88) | 0.608 |
| ACEI (14-day gap) | 8,010 | ***** | ***** | ***** | ***** | 2.92 | ***** | | | | |
| **Sex: Female** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 14,886 | ***** | ***** | ***** | ***** | 2.09 | ***** | -5.43 | ***** | 0.26 ( 0.14, 0.49) | <0.001 |
| ACEI (14-day gap) | 341,922 | ***** | ***** | ***** | ***** | 7.53 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 14,885 | ***** | ***** | ***** | ***** | 2.94 | ***** | -8.82 | ***** | 0.25 ( 0.12, 0.54) | <0.001 |
| ACEI (14-day gap) | 14,885 | ***** | ***** | ***** | ***** | 11.76 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 14,885 | ***** | ***** | ***** | ***** | 2.09 | ***** | -6.87 | ***** | 0.22 ( 0.11, 0.43) | <0.001 |
| ACEI (14-day gap) | 14,885 | ***** | ***** | ***** | ***** | 8.96 | ***** | | | | |

**Table 29. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin-Converting Enzyme Inhibitors (ACEI) 14-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 14,886 | ***** | ***** | ***** | ***** | 5.67 | ***** | -10.46 | ***** | 0.34 ( 0.15, 0.77) | 0.01 |
| ACEI (14-day gap) | 341,922 | ***** | ***** | ***** | ***** | 16.13 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 14,885 | ***** | ***** | ***** | ***** | 5.91 | ***** | -15.75 | ***** | 0.27 ( 0.11, 0.67) | 0.005 |
| ACEI (14-day gap) | 14,885 | ***** | ***** | ***** | ***** | 21.65 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 14,885 | ***** | ***** | ***** | ***** | 5.67 | ***** | -16.55 | ***** | 0.25 ( 0.10, 0.61) | 0.002 |
| ACEI (14-day gap) | 14,885 | ***** | ***** | ***** | ***** | 22.22 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 11,017 | ***** | ***** | ***** | ***** | 2.7 | ***** | -3.82 | ***** | 0.42 ( 0.10, 1.69) | 0.223 |
| ACEI (14-day gap) | 312,869 | ***** | ***** | ***** | ***** | 6.52 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 9,881 | ***** | ***** | ***** | ***** | 3.41 | ***** | -3.41 | ***** | 0.50 ( 0.09, 2.73) | 0.423 |
| ACEI (14-day gap) | 9,881 | ***** | ***** | ***** | ***** | 6.83 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 11,016 | ***** | ***** | ***** | ***** | 2.7 | ***** | -2.59 | ***** | 0.52 ( 0.10, 2.68) | 0.434 |
| ACEI (14-day gap) | 13,364 | ***** | ***** | ***** | ***** | 5.29 | ***** | | | | |

**Table 29. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin-Converting Enzyme Inhibitors (ACEI) 14-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 7,285 | ***** | ***** | ***** | ***** | 0 | ***** | -6.88 | ***** | - | - |
| ACEI (14-day gap) | 226,281 | ***** | ***** | ***** | ***** | 6.88 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 4,861 | ***** | ***** | ***** | ***** | 0 | ***** | -8.99 | ***** | - | - |
| ACEI (14-day gap) | 4,861 | ***** | ***** | ***** | ***** | 8.99 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 7,285 | ***** | ***** | ***** | ***** | 0 | ***** | -10.6 | ***** | - | - |
| ACEI (14-day gap) | 9,880 | ***** | ***** | ***** | ***** | 10.6 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 5,748 | ***** | ***** | ***** | ***** | 1.81 | ***** | -3.5 | ***** | 0.34 ( 0.08, 1.37) | 0.128 |
| ACEI (14-day gap) | 193,860 | ***** | ***** | ***** | ***** | 5.31 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 3,298 | ***** | ***** | ***** | ***** | 0 | ***** | -4.16 | ***** | - | - |
| ACEI (14-day gap) | 3,298 | ***** | ***** | ***** | ***** | 4.16 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 5,748 | ***** | ***** | ***** | ***** | 1.81 | ***** | -0.82 | ***** | 0.67 ( 0.12, 3.65) | 0.642 |
| ACEI (14-day gap) | 8,472 | ***** | ***** | ***** | ***** | 2.63 | ***** | | | | |

**Table 29. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin-Converting Enzyme Inhibitors (ACEI) 14-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 3,659 | ***** | ***** | ***** | ***** | 0 | ***** | -4.87 | ***** | - | - |
| ACEI (14-day gap) | 115,298 | ***** | ***** | ***** | ***** | 4.87 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 1,223 | ***** | ***** | ***** | ***** | 0 | ***** | -4.95 | ***** | - | - |
| ACEI (14-day gap) | 1,223 | ***** | ***** | ***** | ***** | 4.95 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 3,661 | ***** | ***** | ***** | ***** | 0 | ***** | -8.41 | ***** | - | - |
| ACEI (14-day gap) | 4,853 | ***** | ***** | ***** | ***** | 8.41 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 2,588 | ***** | ***** | ***** | ***** | 0 | ***** | -4.21 | ***** | - | - |
| ACEI (14-day gap) | 80,646 | ***** | ***** | ***** | ***** | 4.21 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 565 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 565 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 2,588 | ***** | ***** | ***** | ***** | 0 | ***** | -4.37 | ***** | - | - |
| ACEI (14-day gap) | 3,182 | ***** | ***** | ***** | ***** | 4.37 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 30. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 18-44 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 1,592 | ***** | ***** | ***** | ***** | 2.03 | ***** | -7.12 | ***** | 0.22 ( 0.03, 1.60) | 0.136 |
| ACEI (14-day gap) | 21,593 | ***** | ***** | ***** | ***** | 9.15 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 1,576 | ***** | ***** | ***** | ***** | 4.04 | ***** | -4.04 | ***** | 0.50 ( 0.05, 5.51) | 0.571 |
| ACEI (14-day gap) | 1,576 | ***** | ***** | ***** | ***** | 8.07 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 1,576 | ***** | ***** | ***** | ***** | 2.04 | ***** | -5.55 | ***** | 0.27 ( 0.03, 2.40) | 0.239 |
| ACEI (14-day gap) | 1,576 | ***** | ***** | ***** | ***** | 7.6 | ***** | | | | |
| **Age Group: 45-54 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 3,425 | ***** | ***** | ***** | ***** | 3.64 | ***** | -6.64 | ***** | 0.35 ( 0.13, 0.94) | 0.037 |
| ACEI (14-day gap) | 45,072 | ***** | ***** | ***** | ***** | 10.28 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 3,386 | ***** | ***** | ***** | ***** | 6.79 | ***** | -5.1 | ***** | 0.57 ( 0.17, 1.95) | 0.372 |
| ACEI (14-day gap) | 3,386 | ***** | ***** | ***** | ***** | 11.89 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 3,386 | ***** | ***** | ***** | ***** | 3.68 | ***** | -5.1 | ***** | 0.42 ( 0.13, 1.31) | 0.135 |
| ACEI (14-day gap) | 3,386 | ***** | ***** | ***** | ***** | 8.77 | ***** | | | | |

**Table 30. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 55-64 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 8,067 | ***** | ***** | ***** | ***** | 1.58 | ***** | -7.36 | ***** | 0.17 ( 0.06, 0.46) | <0.001 |
| ACEI (14-day gap) | 97,279 | ***** | ***** | ***** | ***** | 8.94 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 8,048 | ***** | ***** | ***** | ***** | 2.83 | ***** | -6.37 | ***** | 0.31 ( 0.10, 0.94) | 0.039 |
| ACEI (14-day gap) | 8,048 | ***** | ***** | ***** | ***** | 9.2 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 8,048 | ***** | ***** | ***** | ***** | 1.58 | ***** | -4.72 | ***** | 0.23 ( 0.08, 0.68) | 0.008 |
| ACEI (14-day gap) | 8,048 | ***** | ***** | ***** | ***** | 6.3 | ***** | | | | |
| **Age Group: 65+ Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 36,545 | ***** | ***** | ***** | ***** | 2.52 | ***** | -3.51 | ***** | 0.39 ( 0.28, 0.56) | <0.001 |
| ACEI (14-day gap) | 531,124 | ***** | ***** | ***** | ***** | 6.03 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 36,459 | ***** | ***** | ***** | ***** | 2.51 | ***** | -5.44 | ***** | 0.32 ( 0.19, 0.54) | <0.001 |
| ACEI (14-day gap) | 36,459 | ***** | ***** | ***** | ***** | 7.96 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 36,459 | ***** | ***** | ***** | ***** | 2.44 | ***** | -2.71 | ***** | 0.44 ( 0.29, 0.67) | <0.001 |
| ACEI (14-day gap) | 36,459 | ***** | ***** | ***** | ***** | 5.15 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 31. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Unknown** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 8,192 | ***** | ***** | ***** | ***** | 1.55 | ***** | -5.22 | ***** | 0.22 ( 0.08, 0.58) | 0.002 |
| ACEI (14-day gap) | 99,667 | ***** | ***** | ***** | ***** | 6.76 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 8,189 | ***** | ***** | ***** | ***** | 1.38 | ***** | -4.83 | ***** | 0.22 ( 0.05, 1.03) | 0.054 |
| ACEI (14-day gap) | 8,189 | ***** | ***** | ***** | ***** | 6.21 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 8,189 | ***** | ***** | ***** | ***** | 1.55 | ***** | -3.39 | ***** | 0.30 ( 0.10, 0.89) | 0.03 |
| ACEI (14-day gap) | 8,189 | ***** | ***** | ***** | ***** | 4.93 | ***** | | | | |
| **Race: American Indian** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 165 | ***** | ***** | ***** | ***** | 0 | ***** | -2.38 | ***** | - | - |
| ACEI (14-day gap) | 4,526 | ***** | ***** | ***** | ***** | 2.38 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 159 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 159 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 159 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 159 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 31. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Asian** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 526 | ***** | ***** | ***** | ***** | 0 | ***** | -2.63 | ***** | - | - |
| ACEI (14-day gap) | 7,873 | ***** | ***** | ***** | ***** | 2.63 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 520 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 520 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 520 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 520 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Race: Black** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 6,074 | ***** | ***** | ***** | ***** | 6.91 | ***** | -15.66 | ***** | 0.29 ( 0.16, 0.51) | <0.001 |
| ACEI (14-day gap) | 92,135 | ***** | ***** | ***** | ***** | 22.57 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 6,067 | ***** | ***** | ***** | ***** | 8.07 | ***** | -19.17 | ***** | 0.30 ( 0.13, 0.65) | 0.003 |
| ACEI (14-day gap) | 6,067 | ***** | ***** | ***** | ***** | 27.24 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 6,067 | ***** | ***** | ***** | ***** | 6.92 | ***** | -10.88 | ***** | 0.36 ( 0.19, 0.69) | 0.002 |
| ACEI (14-day gap) | 6,067 | ***** | ***** | ***** | ***** | 17.8 | ***** | | | | |

**Table 31. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Pacific Islander** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 46 | ***** | ***** | ***** | ***** | 0 | ***** | -14.36 | ***** | - | - |
| ACEI (14-day gap) | 741 | ***** | ***** | ***** | ***** | 14.36 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 41 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 41 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 41 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 41 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Race: White** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 34,626 | ***** | ***** | ***** | ***** | 2.02 | ***** | -2.33 | ***** | 0.44 ( 0.30, 0.67) | <0.001 |
| ACEI (14-day gap) | 490,126 | ***** | ***** | ***** | ***** | 4.35 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 34,613 | ***** | ***** | ***** | ***** | 1.58 | ***** | -4.18 | ***** | 0.28 ( 0.14, 0.54) | <0.001 |
| ACEI (14-day gap) | 34,613 | ***** | ***** | ***** | ***** | 5.76 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-14, -1)) | 34,613 | ***** | ***** | ***** | ***** | 2.02 | ***** | -1.91 | ***** | 0.49 ( 0.30, 0.78) | 0.003 |
| ACEI (14-day gap) | 34,613 | ***** | ***** | ***** | ***** | 3.93 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 32. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 35,703 | ***** | ***** | ***** | ***** | 3.18 | ***** | 0.16 | ***** | 0.99 ( 0.71, 1.38) | 0.937 |
| ARBs (14-day gap) | 337,204 | ***** | ***** | ***** | ***** | 3.01 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 35,702 | ***** | ***** | ***** | ***** | 3.78 | ***** | 1.12 | ***** | 1.42 ( 0.79, 2.56) | 0.241 |
| ARBs (14-day gap) | 35,702 | ***** | ***** | ***** | ***** | 2.66 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 35,702 | ***** | ***** | ***** | ***** | 3.18 | ***** | 0.51 | ***** | 1.14 ( 0.73, 1.77) | 0.556 |
| ARBs (14-day gap) | 35,702 | ***** | ***** | ***** | ***** | 2.67 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 33. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 35,703 | ***** | ***** | ***** | ***** | 3.18 | ***** | 0.16 | ***** | 0.99 ( 0.71, 1.38) | 0.937 |
| ARBs (14-day prior, 14-day gap) | 337,204 | ***** | ***** | ***** | ***** | 3.01 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 35,702 | ***** | ***** | ***** | ***** | 3.78 | ***** | 1.12 | ***** | 1.42 ( 0.79, 2.56) | 0.241 |
| ARBs (14-day prior, 14-day gap) | 35,702 | ***** | ***** | ***** | ***** | 2.66 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 35,702 | ***** | ***** | ***** | ***** | 3.18 | ***** | 0.51 | ***** | 1.14 ( 0.73, 1.77) | 0.556 |
| ARBs (14-day prior, 14-day gap) | 35,702 | ***** | ***** | ***** | ***** | 2.67 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 35,703 | ***** | ***** | ***** | ***** | 5.08 | ***** | -0.88 | ***** | 0.83 ( 0.47, 1.45) | 0.508 |
| ARBs (14-day prior, 14-day gap) | 337,204 | ***** | ***** | ***** | ***** | 5.96 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 35,702 | ***** | ***** | ***** | ***** | 5.22 | ***** | 2.01 | ***** | 1.62 ( 0.67, 3.92) | 0.28 |
| ARBs (14-day prior, 14-day gap) | 35,702 | ***** | ***** | ***** | ***** | 3.21 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 35,702 | ***** | ***** | ***** | ***** | 5.08 | ***** | 1.22 | ***** | 1.28 ( 0.58, 2.87) | 0.542 |
| ARBs (14-day prior, 14-day gap) | 35,702 | ***** | ***** | ***** | ***** | 3.86 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 26,796 | ***** | ***** | ***** | ***** | 3.85 | ***** | 0.44 | ***** | 1.13 ( 0.52, 2.45) | 0.757 |
| ARBs (14-day prior, 14-day gap) | 316,333 | ***** | ***** | ***** | ***** | 3.42 | ***** | | | | |

**Table 33. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 25,007 | ***** | ***** | ***** | ***** | 4.58 | ***** | 1.96 | ***** | 1.75 ( 0.51, 5.98) | 0.372 |
| ARBs (14-day prior, 14-day gap) | 25,007 | ***** | ***** | ***** | ***** | 2.62 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 26,796 | ***** | ***** | ***** | ***** | 3.85 | ***** | 1.37 | ***** | 1.53 ( 0.51, 4.54) | 0.447 |
| ARBs (14-day prior, 14-day gap) | 33,308 | ***** | ***** | ***** | ***** | 2.48 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 18,018 | ***** | ***** | ***** | ***** | 3.76 | ***** | 0.95 | ***** | 1.37 ( 0.55, 3.43) | 0.5 |
| ARBs (14-day prior, 14-day gap) | 243,524 | ***** | ***** | ***** | ***** | 2.81 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 13,146 | ***** | ***** | ***** | ***** | 2.18 | ***** | 1.09 | ***** | 2.00 ( 0.18, 22.06) | 0.571 |
| ARBs (14-day prior, 14-day gap) | 13,146 | ***** | ***** | ***** | ***** | 1.09 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 18,018 | ***** | ***** | ***** | ***** | 3.76 | ***** | 2.76 | ***** | 3.76 ( 0.73, 19.41) | 0.113 |
| ARBs (14-day prior, 14-day gap) | 25,950 | ***** | ***** | ***** | ***** | 1 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 14,327 | ***** | ***** | ***** | ***** | 2.56 | ***** | 0.31 | ***** | 1.13 ( 0.52, 2.45) | 0.752 |
| ARBs (14-day prior, 14-day gap) | 214,300 | ***** | ***** | ***** | ***** | 2.25 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 9,233 | ***** | ***** | ***** | ***** | 3.04 | ***** | -0.76 | ***** | 0.80 ( 0.21, 2.98) | 0.739 |
| ARBs (14-day prior, 14-day gap) | 9,233 | ***** | ***** | ***** | ***** | 3.8 | ***** | | | | |

**Table 33. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 14,327 | ***** | ***** | ***** | ***** | 2.56 | ***** | -1.58 | ***** | 0.62 ( 0.26, 1.49) | 0.284 |
| ARBs (14-day prior, 14-day gap) | 22,771 | ***** | ***** | ***** | ***** | 4.14 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 9,006 | ***** | ***** | ***** | ***** | 1.63 | ***** | -0.44 | ***** | 0.80 ( 0.25, 2.57) | 0.714 |
| ARBs (14-day prior, 14-day gap) | 130,102 | ***** | ***** | ***** | ***** | 2.07 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 3,388 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day prior, 14-day gap) | 3,388 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 9,006 | ***** | ***** | ***** | ***** | 1.63 | ***** | -0.21 | ***** | 0.87 ( 0.21, 3.66) | 0.854 |
| ARBs (14-day prior, 14-day gap) | 13,456 | ***** | ***** | ***** | ***** | 1.84 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 6,275 | ***** | ***** | ***** | ***** | 1.47 | ***** | -0.09 | ***** | 0.97 ( 0.23, 4.03) | 0.962 |
| ARBs (14-day prior, 14-day gap) | 92,658 | ***** | ***** | ***** | ***** | 1.56 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 1,660 | ***** | ***** | ***** | ***** | 3.26 | ***** | 0 | ***** | 1.00 ( 0.06, 15.99) | 1 |
| ARBs (14-day prior, 14-day gap) | 1,660 | ***** | ***** | ***** | ***** | 3.26 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day prior, 14-day gap) | 6,275 | ***** | ***** | ***** | ***** | 1.47 | ***** | 0.48 | ***** | 1.48 ( 0.21, 10.48) | 0.697 |
| ARBs (14-day prior, 14-day gap) | 9,317 | ***** | ***** | ***** | ***** | 0.99 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 34. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (-183, -1)**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Angioedema (-183, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 35,668 | ***** | ***** | ***** | ***** | 2.84 | ***** | 0.4 | ***** | 1.12 ( 0.78, 1.59) | 0.546 |
| ARBs (14-day gap) | 336,379 | ***** | ***** | ***** | ***** | 2.43 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 35,667 | ***** | ***** | ***** | ***** | 3.23 | ***** | 0.98 | ***** | 1.44 ( 0.76, 2.72) | 0.265 |
| ARBs (14-day gap) | 35,667 | ***** | ***** | ***** | ***** | 2.24 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 35,667 | ***** | ***** | ***** | ***** | 2.84 | ***** | 0.41 | ***** | 1.14 ( 0.71, 1.81) | 0.591 |
| ARBs (14-day gap) | 35,667 | ***** | ***** | ***** | ***** | 2.42 | ***** | | | | |
| **Angioedema (-183, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 35 | ***** | ***** | ***** | ***** | 390.63 | ***** | 118.99 | ***** | 1.30 ( 0.48, 3.57) | 0.605 |
| ARBs (14-day gap) | 825 | ***** | ***** | ***** | ***** | 271.63 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 33 | ***** | ***** | ***** | ***** | 776.7 | ***** | 776.7 | ***** | - | - |
| ARBs (14-day gap) | 33 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 33 | ***** | ***** | ***** | ***** | 439.08 | ***** | 330.56 | ***** | 2.84 ( 0.51, 15.71) | 0.233 |
| ARBs (14-day gap) | 33 | ***** | ***** | ***** | ***** | 108.52 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 35. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (ever, -1)**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Angioedema (ever, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 35,162 | ***** | ***** | ***** | ***** | 2.53 | ***** | 0.49 | ***** | 1.19 ( 0.81, 1.74) | 0.369 |
| ARBs (14-day gap) | 329,845 | ***** | ***** | ***** | ***** | 2.03 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 35,157 | ***** | ***** | ***** | ***** | 2.85 | ***** | 1.14 | ***** | 1.67 ( 0.81, 3.41) | 0.162 |
| ARBs (14-day gap) | 35,157 | ***** | ***** | ***** | ***** | 1.71 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 35,157 | ***** | ***** | ***** | ***** | 2.53 | ***** | 0.63 | ***** | 1.29 ( 0.77, 2.15) | 0.329 |
| ARBs (14-day gap) | 35,157 | ***** | ***** | ***** | ***** | 1.89 | ***** | | | | |
| **Angioedema (ever, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 541 | ***** | ***** | ***** | ***** | 49.9 | ***** | 1.96 | ***** | 0.87 ( 0.43, 1.78) | 0.705 |
| ARBs (14-day gap) | 7,359 | ***** | ***** | ***** | ***** | 47.94 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 535 | ***** | ***** | ***** | ***** | 81.05 | ***** | 30.39 | ***** | 1.60 ( 0.52, 4.89) | 0.41 |
| ARBs (14-day gap) | 535 | ***** | ***** | ***** | ***** | 50.65 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 535 | ***** | ***** | ***** | ***** | 50.8 | ***** | 13.01 | ***** | 1.20 ( 0.46, 3.14) | 0.706 |
| ARBs (14-day gap) | 535 | ***** | ***** | ***** | ***** | 37.79 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 36. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Serious Allergies**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Serious allergies** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 31,231 | ***** | ***** | ***** | ***** | 2.8 | ***** | 0.22 | ***** | 1.02 ( 0.70, 1.49) | 0.925 |
| ARBs (14-day gap) | 282,750 | ***** | ***** | ***** | ***** | 2.59 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 31,227 | ***** | ***** | ***** | ***** | 3.32 | ***** | 0.47 | ***** | 1.17 ( 0.62, 2.19) | 0.631 |
| ARBs (14-day gap) | 31,227 | ***** | ***** | ***** | ***** | 2.85 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 31,227 | ***** | ***** | ***** | ***** | 2.8 | ***** | 0.12 | ***** | 0.99 ( 0.61, 1.61) | 0.975 |
| ARBs (14-day gap) | 31,227 | ***** | ***** | ***** | ***** | 2.68 | ***** | | | | |
| **Serious allergies** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 4,472 | ***** | ***** | ***** | ***** | 6.14 | ***** | 0.65 | ***** | 1.03 ( 0.50, 2.11) | 0.931 |
| ARBs (14-day gap) | 54,454 | ***** | ***** | ***** | ***** | 5.5 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 4,459 | ***** | ***** | ***** | ***** | 6.37 | ***** | 5.09 | ***** | 5.00 ( 0.58, 42.80) | 0.142 |
| ARBs (14-day gap) | 4,459 | ***** | ***** | ***** | ***** | 1.27 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 4,459 | ***** | ***** | ***** | ***** | 6.16 | ***** | 2.81 | ***** | 1.80 ( 0.62, 5.21) | 0.278 |
| ARBs (14-day gap) | 4,459 | ***** | ***** | ***** | ***** | 3.36 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 37. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin II Receptor Blockers (ARB) 14-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Sex: Male** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 21,802 | ***** | ***** | ***** | ***** | 2.21 | ***** | -0.69 | ***** | 0.72 ( 0.43, 1.20) | 0.206 |
| ARBs (14-day gap) | 149,279 | ***** | ***** | ***** | ***** | 2.9 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 21,792 | ***** | ***** | ***** | ***** | 2.74 | ***** | 0.46 | ***** | 1.20 ( 0.52, 2.78) | 0.67 |
| ARBs (14-day gap) | 21,792 | ***** | ***** | ***** | ***** | 2.29 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 21,792 | ***** | ***** | ***** | ***** | 2.21 | ***** | -0.37 | ***** | 0.81 ( 0.43, 1.53) | 0.519 |
| ARBs (14-day gap) | 21,792 | ***** | ***** | ***** | ***** | 2.58 | ***** | | | | |
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 21,802 | ***** | ***** | ***** | ***** | 5.1 | ***** | 0.08 | ***** | 0.97 ( 0.46, 2.03) | 0.941 |
| ARBs (14-day gap) | 149,279 | ***** | ***** | ***** | ***** | 5.02 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 21,792 | ***** | ***** | ***** | ***** | 5.27 | ***** | 1.98 | ***** | 1.60 ( 0.52, 4.89) | 0.41 |
| ARBs (14-day gap) | 21,792 | ***** | ***** | ***** | ***** | 3.29 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 21,792 | ***** | ***** | ***** | ***** | 5.11 | ***** | 1.64 | ***** | 1.43 ( 0.50, 4.12) | 0.509 |
| ARBs (14-day gap) | 21,792 | ***** | ***** | ***** | ***** | 3.47 | ***** | | | | |

**Table 37. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin II Receptor Blockers (ARB) 14-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 16,532 | ***** | ***** | ***** | ***** | 1.78 | ***** | -1.1 | ***** | 0.61 ( 0.14, 2.54) | 0.493 |
| ARBs (14-day gap) | 139,809 | ***** | ***** | ***** | ***** | 2.88 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 15,257 | ***** | ***** | ***** | ***** | 2.13 | ***** | 1.07 | ***** | 2.00 ( 0.18, 22.06) | 0.571 |
| ARBs (14-day gap) | 15,257 | ***** | ***** | ***** | ***** | 1.07 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 16,525 | ***** | ***** | ***** | ***** | 1.78 | ***** | -0.96 | ***** | 0.65 ( 0.12, 3.54) | 0.616 |
| ARBs (14-day gap) | 20,080 | ***** | ***** | ***** | ***** | 2.74 | ***** | | | | |
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 11,206 | ***** | ***** | ***** | ***** | 2.42 | ***** | 0.01 | ***** | 1.03 ( 0.24, 4.41) | 0.968 |
| ARBs (14-day gap) | 107,362 | ***** | ***** | ***** | ***** | 2.41 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 8,113 | ***** | ***** | ***** | ***** | 1.77 | ***** | 1.77 | ***** | - | - |
| ARBs (14-day gap) | 8,113 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 11,204 | ***** | ***** | ***** | ***** | 2.42 | ***** | 2.42 | ***** | - | - |
| ARBs (14-day gap) | 15,670 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 37. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin II Receptor Blockers (ARB) 14-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 8,904 | ***** | ***** | ***** | ***** | 1.76 | ***** | -1 | ***** | 0.63 ( 0.19, 2.01) | 0.431 |
| ARBs (14-day gap) | 94,229 | ***** | ***** | ***** | ***** | 2.76 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 5,669 | ***** | ***** | ***** | ***** | 1.24 | ***** | -2.48 | ***** | 0.33 ( 0.03, 3.20) | 0.341 |
| ARBs (14-day gap) | 5,669 | ***** | ***** | ***** | ***** | 3.72 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 8,901 | ***** | ***** | ***** | ***** | 1.76 | ***** | -2.7 | ***** | 0.39 ( 0.11, 1.40) | 0.149 |
| ARBs (14-day gap) | 13,656 | ***** | ***** | ***** | ***** | 4.46 | ***** | | | | |
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 5,643 | ***** | ***** | ***** | ***** | 0.87 | ***** | -0.96 | ***** | 0.50 ( 0.07, 3.69) | 0.493 |
| ARBs (14-day gap) | 56,419 | ***** | ***** | ***** | ***** | 1.83 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 2,082 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 2,082 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 5,641 | ***** | ***** | ***** | ***** | 0.87 | ***** | -0.98 | ***** | 0.46 ( 0.05, 4.40) | 0.498 |
| ARBs (14-day gap) | 8,063 | ***** | ***** | ***** | ***** | 1.85 | ***** | | | | |

**Table 37. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin II Receptor Blockers (ARB) 14-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 3,939 | ***** | ***** | ***** | ***** | 0 | ***** | -2.15 | ***** | - | - |
| ARBs (14-day gap) | 39,965 | ***** | ***** | ***** | ***** | 2.15 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 1,043 | ***** | ***** | ***** | ***** | 0 | ***** | -5.18 | ***** | - | - |
| ARBs (14-day gap) | 1,043 | ***** | ***** | ***** | ***** | 5.18 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 3,939 | ***** | ***** | ***** | ***** | 0 | ***** | -0.84 | ***** | - | - |
| ARBs (14-day gap) | 5,566 | ***** | ***** | ***** | ***** | 0.84 | ***** | | | | |
| **Sex: Female** | | | | | | | | | | | |
| **Overall** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 13,901 | ***** | ***** | ***** | ***** | 4.77 | ***** | 1.66 | ***** | 1.42 ( 0.91, 2.21) | 0.125 |
| ARBs (14-day gap) | 187,925 | ***** | ***** | ***** | ***** | 3.1 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 13,901 | ***** | ***** | ***** | ***** | 5.57 | ***** | 2.6 | ***** | 1.87 ( 0.79, 4.42) | 0.151 |
| ARBs (14-day gap) | 13,901 | ***** | ***** | ***** | ***** | 2.97 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 13,901 | ***** | ***** | ***** | ***** | 4.77 | ***** | 1.86 | ***** | 1.59 ( 0.85, 3.00) | 0.148 |
| ARBs (14-day gap) | 13,901 | ***** | ***** | ***** | ***** | 2.9 | ***** | | | | |

**Table 37. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin II Receptor Blockers (ARB) 14-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **0 - 30 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 13,901 | ***** | ***** | ***** | ***** | 5.05 | ***** | -1.65 | ***** | 0.73 ( 0.30, 1.80) | 0.501 |
| ARBs (14-day gap) | 187,925 | ***** | ***** | ***** | ***** | 6.71 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 13,901 | ***** | ***** | ***** | ***** | 5.2 | ***** | 0 | ***** | 1.00 ( 0.29, 3.45) | 1 |
| ARBs (14-day gap) | 13,901 | ***** | ***** | ***** | ***** | 5.2 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 13,901 | ***** | ***** | ***** | ***** | 5.05 | ***** | -0.36 | ***** | 0.92 ( 0.28, 3.00) | 0.885 |
| ARBs (14-day gap) | 13,901 | ***** | ***** | ***** | ***** | 5.42 | ***** | | | | |
| **31 - 60 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 10,264 | ***** | ***** | ***** | ***** | 7.23 | ***** | 3.39 | ***** | 1.88 ( 0.75, 4.72) | 0.178 |
| ARBs (14-day gap) | 176,524 | ***** | ***** | ***** | ***** | 3.84 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 9,530 | ***** | ***** | ***** | ***** | 8.68 | ***** | 6.94 | ***** | 5.00 ( 0.58, 42.80) | 0.142 |
| ARBs (14-day gap) | 9,530 | ***** | ***** | ***** | ***** | 1.74 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 10,264 | ***** | ***** | ***** | ***** | 7.23 | ***** | 6.16 | ***** | 6.54 ( 0.76, 56.04) | 0.086 |
| ARBs (14-day gap) | 12,900 | ***** | ***** | ***** | ***** | 1.07 | ***** | | | | |

**Table 37. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin II Receptor Blockers (ARB) 14-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **61 - 90 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 6,812 | ***** | ***** | ***** | ***** | 5.97 | ***** | 2.84 | ***** | 1.95 ( 0.60, 6.35) | 0.269 |
| ARBs (14-day gap) | 136,162 | ***** | ***** | ***** | ***** | 3.13 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 4,891 | ***** | ***** | ***** | ***** | 2.92 | ***** | 0 | ***** | 1.00 ( 0.06, 15.99) | 1 |
| ARBs (14-day gap) | 4,891 | ***** | ***** | ***** | ***** | 2.92 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 6,812 | ***** | ***** | ***** | ***** | 5.97 | ***** | 3.37 | ***** | 2.30 ( 0.38, 13.78) | 0.361 |
| ARBs (14-day gap) | 9,983 | ***** | ***** | ***** | ***** | 2.59 | ***** | | | | |
| **91 - 180 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 5,423 | ***** | ***** | ***** | ***** | 3.88 | ***** | 2.02 | ***** | 2.13 ( 0.76, 5.96) | 0.148 |
| ARBs (14-day gap) | 120,071 | ***** | ***** | ***** | ***** | 1.86 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 3,431 | ***** | ***** | ***** | ***** | 6.16 | ***** | 4.11 | ***** | 3.00 ( 0.31, 28.84) | 0.341 |
| ARBs (14-day gap) | 3,431 | ***** | ***** | ***** | ***** | 2.05 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 5,423 | ***** | ***** | ***** | ***** | 3.88 | ***** | 0.07 | ***** | 1.03 ( 0.29, 3.64) | 0.969 |
| ARBs (14-day gap) | 8,740 | ***** | ***** | ***** | ***** | 3.81 | ***** | | | | |

**Table 37. Effect Estimates for Risk of Angioedema Sacubitril/Valsartan (SV) and Angiotensin II Receptor Blockers (ARB) 14-Day Inclusion 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type, Sex, Follow-up Time**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **181 - 270 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 3,363 | ***** | ***** | ***** | ***** | 2.92 | ***** | 0.67 | ***** | 1.31 ( 0.32, 5.47) | 0.708 |
| ARBs (14-day gap) | 73,683 | ***** | ***** | ***** | ***** | 2.25 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 1,256 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 1,256 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 3,363 | ***** | ***** | ***** | ***** | 2.92 | ***** | 1 | ***** | 1.54 ( 0.22, 10.93) | 0.666 |
| ARBs (14-day gap) | 5,149 | ***** | ***** | ***** | ***** | 1.92 | ***** | | | | |
| **271 - 365 Days** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 2,336 | ***** | ***** | ***** | ***** | 3.95 | ***** | 2.84 | ***** | 3.91 ( 0.88, 17.36) | 0.073 |
| ARBs (14-day gap) | 52,693 | ***** | ***** | ***** | ***** | 1.11 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 618 | ***** | ***** | ***** | ***** | 8.8 | ***** | 8.8 | ***** | - | - |
| ARBs (14-day gap) | 618 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 2,337 | ***** | ***** | ***** | ***** | 3.95 | ***** | 2.66 | ***** | 3.08 ( 0.28, 33.93) | 0.359 |
| ARBs (14-day gap) | 3,560 | ***** | ***** | ***** | ***** | 1.28 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 38. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 18-44 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 774 | ***** | ***** | ***** | ***** | 0 | ***** | -7.89 | ***** | - | - |
| ARBs (14-day gap) | 8,505 | ***** | ***** | ***** | ***** | 7.89 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 762 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 762 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 762 | ***** | ***** | ***** | ***** | 0 | ***** | -4.13 | ***** | - | - |
| ARBs (14-day gap) | 762 | ***** | ***** | ***** | ***** | 4.13 | ***** | | | | |
| **Age Group: 45-54 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 1,794 | ***** | ***** | ***** | ***** | 3.8 | ***** | -0.52 | ***** | 0.88 ( 0.21, 3.71) | 0.866 |
| ARBs (14-day gap) | 18,304 | ***** | ***** | ***** | ***** | 4.32 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 1,786 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 1,786 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 1,786 | ***** | ***** | ***** | ***** | 3.81 | ***** | 2.31 | ***** | 2.49 ( 0.23, 27.53) | 0.456 |
| ARBs (14-day gap) | 1,786 | ***** | ***** | ***** | ***** | 1.5 | ***** | | | | |

**Table 38. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 55-64 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 4,275 | ***** | ***** | ***** | ***** | 6.8 | ***** | 2.8 | ***** | 1.62 ( 0.81, 3.27) | 0.173 |
| ARBs (14-day gap) | 40,567 | ***** | ***** | ***** | ***** | 3.99 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 4,246 | ***** | ***** | ***** | ***** | 9.29 | ***** | 6.64 | ***** | 3.50 ( 0.73, 16.85) | 0.118 |
| ARBs (14-day gap) | 4,246 | ***** | ***** | ***** | ***** | 2.66 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 4,246 | ***** | ***** | ***** | ***** | 6.83 | ***** | 4.46 | ***** | 2.68 ( 0.83, 8.74) | 0.101 |
| ARBs (14-day gap) | 4,246 | ***** | ***** | ***** | ***** | 2.37 | ***** | | | | |
| **Age Group: 65+ Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 28,860 | ***** | ***** | ***** | ***** | 2.72 | ***** | 0.02 | ***** | 0.94 ( 0.63, 1.40) | 0.747 |
| ARBs (14-day gap) | 269,828 | ***** | ***** | ***** | ***** | 2.71 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 28,797 | ***** | ***** | ***** | ***** | 3.24 | ***** | 0.17 | ***** | 1.06 ( 0.55, 2.01) | 0.869 |
| ARBs (14-day gap) | 28,797 | ***** | ***** | ***** | ***** | 3.07 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 28,797 | ***** | ***** | ***** | ***** | 2.73 | ***** | -0.14 | ***** | 0.91 ( 0.55, 1.50) | 0.705 |
| ARBs (14-day gap) | 28,797 | ***** | ***** | ***** | ***** | 2.87 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 39. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Unknown** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 5,777 | ***** | ***** | ***** | ***** | 2.23 | ***** | -0.28 | ***** | 0.85 ( 0.31, 2.35) | 0.751 |
| ARBs (14-day gap) | 47,811 | ***** | ***** | ***** | ***** | 2.51 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 5,748 | ***** | ***** | ***** | ***** | 3.87 | ***** | 1.93 | ***** | 2.00 ( 0.37, 10.92) | 0.423 |
| ARBs (14-day gap) | 5,748 | ***** | ***** | ***** | ***** | 1.93 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 5,748 | ***** | ***** | ***** | ***** | 2.24 | ***** | -2.31 | ***** | 0.48 ( 0.15, 1.50) | 0.205 |
| ARBs (14-day gap) | 5,748 | ***** | ***** | ***** | ***** | 4.55 | ***** | | | | |
| **Race: American Indian** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 86 | ***** | ***** | ***** | ***** | 0 | ***** | -1.36 | ***** | - | - |
| ARBs (14-day gap) | 1,948 | ***** | ***** | ***** | ***** | 1.36 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 83 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 83 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 83 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 83 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 39. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Asian** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 863 | ***** | ***** | ***** | ***** | 0 | ***** | -0.81 | ***** | - | - |
| ARBs (14-day gap) | 7,814 | ***** | ***** | ***** | ***** | 0.81 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 834 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 834 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 834 | ***** | ***** | ***** | ***** | 0 | ***** | -2.55 | ***** | - | - |
| ARBs (14-day gap) | 834 | ***** | ***** | ***** | ***** | 2.55 | ***** | | | | |
| **Race: Black** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 4,832 | ***** | ***** | ***** | ***** | 4.4 | ***** | -2.4 | ***** | 0.60 ( 0.27, 1.36) | 0.222 |
| ARBs (14-day gap) | 55,825 | ***** | ***** | ***** | ***** | 6.8 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 4,829 | ***** | ***** | ***** | ***** | 4.93 | ***** | -3.7 | ***** | 0.57 ( 0.17, 1.95) | 0.372 |
| ARBs (14-day gap) | 4,829 | ***** | ***** | ***** | ***** | 8.62 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 4,829 | ***** | ***** | ***** | ***** | 4.4 | ***** | -0.4 | ***** | 0.82 ( 0.29, 2.31) | 0.704 |
| ARBs (14-day gap) | 4,829 | ***** | ***** | ***** | ***** | 4.8 | ***** | | | | |

**Table 39. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Pacific Islander** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 46 | ***** | ***** | ***** | ***** | 0 | ***** | -8.97 | ***** | - | - |
| ARBs (14-day gap) | 478 | ***** | ***** | ***** | ***** | 8.97 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 40 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 40 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 40 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 40 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Race: White** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 24,099 | ***** | ***** | ***** | ***** | 3.29 | ***** | 0.89 | ***** | 1.28 ( 0.86, 1.90) | 0.229 |
| ARBs (14-day gap) | 223,328 | ***** | ***** | ***** | ***** | 2.4 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 24,091 | ***** | ***** | ***** | ***** | 3.56 | ***** | 0.99 | ***** | 1.38 ( 0.68, 2.83) | 0.371 |
| ARBs (14-day gap) | 24,091 | ***** | ***** | ***** | ***** | 2.57 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-14, -1)) | 24,091 | ***** | ***** | ***** | ***** | 3.3 | ***** | 1.24 | ***** | 1.55 ( 0.89, 2.70) | 0.124 |
| ARBs (14-day gap) | 24,091 | ***** | ***** | ***** | ***** | 2.06 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 40. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (7-day gap, history of ACEI (-183, -1)) | 69,639 | ***** | ***** | ***** | ***** | 2.14 | ***** | -4.77 | ***** | 0.29 ( 0.21, 0.39) | <0.001 |
| ACEI (7-day gap) | 694,882 | ***** | ***** | ***** | ***** | 6.91 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (7-day gap, history of ACEI (-183, -1)) | 69,639 | ***** | ***** | ***** | ***** | 2.84 | ***** | -8.42 | ***** | 0.25 ( 0.17, 0.37) | <0.001 |
| ACEI (7-day gap) | 69,639 | ***** | ***** | ***** | ***** | 11.26 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (7-day gap, history of ACEI (-183, -1)) | 69,639 | ***** | ***** | ***** | ***** | 2.14 | ***** | -4.48 | ***** | 0.30 ( 0.21, 0.41) | <0.001 |
| ACEI (7-day gap) | 69,639 | ***** | ***** | ***** | ***** | 6.62 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 41. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (7-day gap, history of ARBs (-183, -1)) | 49,140 | ***** | ***** | ***** | ***** | 2.85 | ***** | -0.19 | ***** | 0.87 ( 0.63, 1.20) | 0.388 |
| ARBs (7-day gap) | 337,083 | ***** | ***** | ***** | ***** | 3.04 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (7-day gap, history of ARBs (-183, -1)) | 49,137 | ***** | ***** | ***** | ***** | 3.48 | ***** | 0 | ***** | 1.00 ( 0.60, 1.66) | 1 |
| ARBs (7-day gap) | 49,137 | ***** | ***** | ***** | ***** | 3.48 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (7-day gap, history of ARBs (-183, -1)) | 49,137 | ***** | ***** | ***** | ***** | 2.85 | ***** | -0.1 | ***** | 0.91 ( 0.61, 1.35) | 0.626 |
| ARBs (7-day gap) | 49,137 | ***** | ***** | ***** | ***** | 2.95 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 42. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,639 | ***** | ***** | ***** | ***** | 0.86 | ***** | -1.14 | ***** | 0.42 ( 0.27, 0.64) | <0.001 |
| ACEI (14-day gap) | 694,882 | ***** | ***** | ***** | ***** | 2 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,639 | ***** | ***** | ***** | ***** | 1.07 | ***** | -1.93 | ***** | 0.36 ( 0.20, 0.64) | <0.001 |
| ACEI (14-day gap) | 69,639 | ***** | ***** | ***** | ***** | 3 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,639 | ***** | ***** | ***** | ***** | 0.86 | ***** | -0.99 | ***** | 0.44 ( 0.27, 0.73) | 0.001 |
| ACEI (14-day gap) | 69,639 | ***** | ***** | ***** | ***** | 1.86 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 43. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (-183, -1)**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Angioedema (-183, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,556 | ***** | ***** | ***** | ***** | 0.82 | ***** | -1.1 | ***** | 0.41 ( 0.26, 0.65) | <0.001 |
| ACEI (14-day gap) | 694,018 | ***** | ***** | ***** | ***** | 1.93 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,556 | ***** | ***** | ***** | ***** | 1 | ***** | -1.86 | ***** | 0.35 ( 0.19, 0.64) | <0.001 |
| ACEI (14-day gap) | 69,556 | ***** | ***** | ***** | ***** | 2.86 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,556 | ***** | ***** | ***** | ***** | 0.82 | ***** | -0.97 | ***** | 0.44 ( 0.26, 0.73) | 0.002 |
| ACEI (14-day gap) | 69,556 | ***** | ***** | ***** | ***** | 1.79 | ***** | | | | |
| **Angioedema (-183, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 83 | ***** | ***** | ***** | ***** | 34.92 | ***** | -40.45 | ***** | 0.54 ( 0.07, 4.00) | 0.547 |
| ACEI (14-day gap) | 864 | ***** | ***** | ***** | ***** | 75.37 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 68 | ***** | ***** | ***** | ***** | 80.52 | ***** | 0 | ***** | 1.00 ( 0.06, 15.99) | 1 |
| ACEI (14-day gap) | 68 | ***** | ***** | ***** | ***** | 80.52 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 68 | ***** | ***** | ***** | ***** | 43.22 | ***** | -4.54 | ***** | 1.06 ( 0.07, 16.94) | 0.967 |
| ACEI (14-day gap) | 68 | ***** | ***** | ***** | ***** | 47.76 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 44. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (ever, -1)**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Angioedema (ever, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,145 | ***** | ***** | ***** | ***** | 0.83 | ***** | -0.92 | ***** | 0.46 ( 0.29, 0.72) | <0.001 |
| ACEI (14-day gap) | 687,565 | ***** | ***** | ***** | ***** | 1.75 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,144 | ***** | ***** | ***** | ***** | 1.01 | ***** | -1.58 | ***** | 0.39 ( 0.21, 0.72) | 0.003 |
| ACEI (14-day gap) | 69,144 | ***** | ***** | ***** | ***** | 2.59 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 69,144 | ***** | ***** | ***** | ***** | 0.83 | ***** | -0.77 | ***** | 0.49 ( 0.29, 0.84) | 0.009 |
| ACEI (14-day gap) | 69,144 | ***** | ***** | ***** | ***** | 1.59 | ***** | | | | |
| **Angioedema (ever, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 494 | ***** | ***** | ***** | ***** | 6.3 | ***** | -22.43 | ***** | 0.22 ( 0.03, 1.56) | 0.128 |
| ACEI (14-day gap) | 7,317 | ***** | ***** | ***** | ***** | 28.73 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 487 | ***** | ***** | ***** | ***** | 11.83 | ***** | -23.66 | ***** | 0.33 ( 0.03, 3.20) | 0.341 |
| ACEI (14-day gap) | 487 | ***** | ***** | ***** | ***** | 35.49 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 487 | ***** | ***** | ***** | ***** | 6.38 | ***** | -16.84 | ***** | 0.28 ( 0.03, 2.48) | 0.251 |
| ACEI (14-day gap) | 487 | ***** | ***** | ***** | ***** | 23.22 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 45. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Serious Allergies**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Serious allergies** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 61,592 | ***** | ***** | ***** | ***** | 0.83 | ***** | -1.02 | ***** | 0.43 ( 0.27, 0.69) | <0.001 |
| ACEI (14-day gap) | 583,922 | ***** | ***** | ***** | ***** | 1.85 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 61,582 | ***** | ***** | ***** | ***** | 0.96 | ***** | -1.52 | ***** | 0.39 ( 0.20, 0.75) | 0.005 |
| ACEI (14-day gap) | 61,582 | ***** | ***** | ***** | ***** | 2.48 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 61,582 | ***** | ***** | ***** | ***** | 0.83 | ***** | -0.8 | ***** | 0.48 ( 0.28, 0.84) | 0.01 |
| ACEI (14-day gap) | 61,582 | ***** | ***** | ***** | ***** | 1.63 | ***** | | | | |
| **Serious allergies** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 8,047 | ***** | ***** | ***** | ***** | 1.15 | ***** | -1.77 | ***** | 0.39 ( 0.12, 1.22) | 0.105 |
| ACEI (14-day gap) | 110,960 | ***** | ***** | ***** | ***** | 2.92 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 8,038 | ***** | ***** | ***** | ***** | 1.38 | ***** | -3.45 | ***** | 0.29 ( 0.06, 1.38) | 0.118 |
| ACEI (14-day gap) | 8,038 | ***** | ***** | ***** | ***** | 4.84 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 8,038 | ***** | ***** | ***** | ***** | 1.15 | ***** | -1.88 | ***** | 0.37 ( 0.10, 1.36) | 0.135 |
| ACEI (14-day gap) | 8,038 | ***** | ***** | ***** | ***** | 3.03 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 46. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Sex**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Sex: Male** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 48,440 | ***** | ***** | ***** | ***** | 1 | ***** | -0.58 | ***** | 0.60 ( 0.37, 0.99) | 0.044 |
| ACEI (14-day gap) | 353,015 | ***** | ***** | ***** | ***** | 1.57 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 48,398 | ***** | ***** | ***** | ***** | 1.02 | ***** | -1.13 | ***** | 0.48 ( 0.22, 1.01) | 0.053 |
| ACEI (14-day gap) | 48,398 | ***** | ***** | ***** | ***** | 2.15 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 48,398 | ***** | ***** | ***** | ***** | 1 | ***** | -0.44 | ***** | 0.66 ( 0.36, 1.19) | 0.166 |
| ACEI (14-day gap) | 48,398 | ***** | ***** | ***** | ***** | 1.43 | ***** | | | | |
| **Sex: Female** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 21,199 | ***** | ***** | ***** | ***** | 0.55 | ***** | -1.9 | ***** | 0.22 ( 0.08, 0.59) | 0.002 |
| ACEI (14-day gap) | 341,867 | ***** | ***** | ***** | ***** | 2.45 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 21,198 | ***** | ***** | ***** | ***** | 0.74 | ***** | -2.22 | ***** | 0.25 ( 0.07, 0.89) | 0.032 |
| ACEI (14-day gap) | 21,198 | ***** | ***** | ***** | ***** | 2.96 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 21,198 | ***** | ***** | ***** | ***** | 0.55 | ***** | -1.32 | ***** | 0.28 ( 0.09, 0.85) | 0.024 |
| ACEI (14-day gap) | 21,198 | ***** | ***** | ***** | ***** | 1.87 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 47. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 18-44 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 2,412 | ***** | ***** | ***** | ***** | 0 | ***** | -3.36 | ***** | - | - |
| ACEI (14-day gap) | 21,587 | ***** | ***** | ***** | ***** | 3.36 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 2,385 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 2,385 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 2,385 | ***** | ***** | ***** | ***** | 0 | ***** | -1.24 | ***** | - | - |
| ACEI (14-day gap) | 2,385 | ***** | ***** | ***** | ***** | 1.24 | ***** | | | | |
| **Age Group: 45-54 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 5,115 | ***** | ***** | ***** | ***** | 1.17 | ***** | -1.62 | ***** | 0.45 ( 0.11, 1.84) | 0.264 |
| ACEI (14-day gap) | 45,057 | ***** | ***** | ***** | ***** | 2.79 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 5,075 | ***** | ***** | ***** | ***** | 1.09 | ***** | -1.09 | ***** | 0.50 ( 0.05, 5.51) | 0.571 |
| ACEI (14-day gap) | 5,075 | ***** | ***** | ***** | ***** | 2.17 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 5,075 | ***** | ***** | ***** | ***** | 1.18 | ***** | -0.43 | ***** | 0.68 ( 0.11, 4.05) | 0.669 |
| ACEI (14-day gap) | 5,075 | ***** | ***** | ***** | ***** | 1.61 | ***** | | | | |

**Table 47. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 55-64 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 11,494 | ***** | ***** | ***** | ***** | 1.83 | ***** | -1.41 | ***** | 0.57 ( 0.27, 1.22) | 0.148 |
| ACEI (14-day gap) | 97,244 | ***** | ***** | ***** | ***** | 3.25 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 11,435 | ***** | ***** | ***** | ***** | 1.88 | ***** | -4.22 | ***** | 0.31 ( 0.10, 0.94) | 0.039 |
| ACEI (14-day gap) | 11,435 | ***** | ***** | ***** | ***** | 6.1 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 11,435 | ***** | ***** | ***** | ***** | 1.84 | ***** | -2.15 | ***** | 0.45 ( 0.19, 1.07) | 0.071 |
| ACEI (14-day gap) | 11,435 | ***** | ***** | ***** | ***** | 4 | ***** | | | | |
| **Age Group: 65+ Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 50,618 | ***** | ***** | ***** | ***** | 0.67 | ***** | -1.03 | ***** | 0.38 ( 0.21, 0.67) | <0.001 |
| ACEI (14-day gap) | 530,994 | ***** | ***** | ***** | ***** | 1.69 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 50,470 | ***** | ***** | ***** | ***** | 0.77 | ***** | -1.53 | ***** | 0.33 ( 0.15, 0.74) | 0.007 |
| ACEI (14-day gap) | 50,470 | ***** | ***** | ***** | ***** | 2.3 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 50,470 | ***** | ***** | ***** | ***** | 0.67 | ***** | -0.63 | ***** | 0.48 ( 0.24, 0.94) | 0.034 |
| ACEI (14-day gap) | 50,470 | ***** | ***** | ***** | ***** | 1.3 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 48. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Unknown** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 11,656 | ***** | ***** | ***** | ***** | 0.25 | ***** | -1.68 | ***** | 0.13 ( 0.02, 0.92) | 0.041 |
| ACEI (14-day gap) | 99,645 | ***** | ***** | ***** | ***** | 1.93 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 11,647 | ***** | ***** | ***** | ***** | 0.45 | ***** | -0.45 | ***** | 0.50 ( 0.05, 5.51) | 0.571 |
| ACEI (14-day gap) | 11,647 | ***** | ***** | ***** | ***** | 0.91 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 11,647 | ***** | ***** | ***** | ***** | 0.25 | ***** | -1.06 | ***** | 0.20 ( 0.02, 1.63) | 0.132 |
| ACEI (14-day gap) | 11,647 | ***** | ***** | ***** | ***** | 1.31 | ***** | | | | |
| **Race: American Indian** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 242 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 4,525 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 234 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 48. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Asian** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 666 | ***** | ***** | ***** | ***** | 0 | ***** | -0.99 | ***** | - | - |
| ACEI (14-day gap) | 7,871 | ***** | ***** | ***** | ***** | 0.99 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 656 | ***** | ***** | ***** | ***** | 0 | ***** | -8.2 | ***** | - | - |
| ACEI (14-day gap) | 656 | ***** | ***** | ***** | ***** | 8.2 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 656 | ***** | ***** | ***** | ***** | 0 | ***** | -3.98 | ***** | - | - |
| ACEI (14-day gap) | 656 | ***** | ***** | ***** | ***** | 3.98 | ***** | | | | |
| **Race: Black** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 9,015 | ***** | ***** | ***** | ***** | 2.61 | ***** | -4.74 | ***** | 0.34 ( 0.16, 0.73) | 0.005 |
| ACEI (14-day gap) | 92,098 | ***** | ***** | ***** | ***** | 7.35 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 8,997 | ***** | ***** | ***** | ***** | 3.33 | ***** | -3.33 | ***** | 0.50 ( 0.17, 1.46) | 0.206 |
| ACEI (14-day gap) | 8,997 | ***** | ***** | ***** | ***** | 6.67 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 8,997 | ***** | ***** | ***** | ***** | 2.62 | ***** | -2.4 | ***** | 0.50 ( 0.20, 1.21) | 0.125 |
| ACEI (14-day gap) | 8,997 | ***** | ***** | ***** | ***** | 5.02 | ***** | | | | |

**Table 48. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Pacific Islander** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 66 | ***** | ***** | ***** | ***** | 0 | ***** | -3.59 | ***** | - | - |
| ACEI (14-day gap) | 741 | ***** | ***** | ***** | ***** | 3.59 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ACEI (14-day gap) | 59 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Race: White** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 47,994 | ***** | ***** | ***** | ***** | 0.75 | ***** | -0.46 | ***** | 0.60 ( 0.34, 1.04) | 0.069 |
| ACEI (14-day gap) | 490,002 | ***** | ***** | ***** | ***** | 1.21 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 47,950 | ***** | ***** | ***** | ***** | 0.79 | ***** | -1.19 | ***** | 0.40 ( 0.18, 0.91) | 0.028 |
| ACEI (14-day gap) | 47,950 | ***** | ***** | ***** | ***** | 1.99 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ACEI (-183, -1)) | 47,950 | ***** | ***** | ***** | ***** | 0.75 | ***** | -0.51 | ***** | 0.56 ( 0.29, 1.10) | 0.091 |
| ACEI (14-day gap) | 47,950 | ***** | ***** | ***** | ***** | 1.26 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 49. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 49,140 | ***** | ***** | ***** | ***** | 0.53 | ***** | -0.36 | ***** | 0.57 ( 0.29, 1.12) | 0.101 |
| ARBs (14-day gap) | 337,083 | ***** | ***** | ***** | ***** | 0.9 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 49,137 | ***** | ***** | ***** | ***** | 0.78 | ***** | -0.19 | ***** | 0.80 ( 0.32, 2.03) | 0.638 |
| ARBs (14-day gap) | 49,137 | ***** | ***** | ***** | ***** | 0.97 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 49,137 | ***** | ***** | ***** | ***** | 0.53 | ***** | -0.33 | ***** | 0.59 ( 0.27, 1.31) | 0.193 |
| ARBs (14-day gap) | 49,137 | ***** | ***** | ***** | ***** | 0.86 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 50. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (-183, -1)**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Angioedema (-183, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 49,082 | ***** | ***** | ***** | ***** | 0.53 | ***** | -0.24 | ***** | 0.66 ( 0.34, 1.31) | 0.234 |
| ARBs (14-day gap) | 336,258 | ***** | ***** | ***** | ***** | 0.78 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 49,079 | ***** | ***** | ***** | ***** | 0.78 | ***** | 0 | ***** | 1.00 ( 0.38, 2.66) | 1 |
| ARBs (14-day gap) | 49,079 | ***** | ***** | ***** | ***** | 0.78 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 49,079 | ***** | ***** | ***** | ***** | 0.53 | ***** | -0.24 | ***** | 0.67 ( 0.30, 1.50) | 0.329 |
| ARBs (14-day gap) | 49,079 | ***** | ***** | ***** | ***** | 0.77 | ***** | | | | |
| **Angioedema (-183, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 58 | ***** | ***** | ***** | ***** | 0 | ***** | -52.37 | ***** | - | - |
| ARBs (14-day gap) | 825 | ***** | ***** | ***** | ***** | 52.37 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 55 | ***** | ***** | ***** | ***** | 0 | ***** | -186.22 | ***** | - | - |
| ARBs (14-day gap) | 55 | ***** | ***** | ***** | ***** | 186.22 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 55 | ***** | ***** | ***** | ***** | 0 | ***** | -74.99 | ***** | - | - |
| ARBs (14-day gap) | 55 | ***** | ***** | ***** | ***** | 74.99 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 51. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Prior Angioedema (ever, -1)**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Angioedema (ever, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 48,390 | ***** | ***** | ***** | ***** | 0.54 | ***** | -0.14 | ***** | 0.77 ( 0.39, 1.53) | 0.459 |
| ARBs (14-day gap) | 329,726 | ***** | ***** | ***** | ***** | 0.68 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 48,383 | ***** | ***** | ***** | ***** | 0.79 | ***** | 0.2 | ***** | 1.33 ( 0.46, 3.84) | 0.594 |
| ARBs (14-day gap) | 48,383 | ***** | ***** | ***** | ***** | 0.59 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 48,383 | ***** | ***** | ***** | ***** | 0.54 | ***** | -0.15 | ***** | 0.76 ( 0.33, 1.74) | 0.515 |
| ARBs (14-day gap) | 48,383 | ***** | ***** | ***** | ***** | 0.69 | ***** | | | | |
| **Angioedema (ever, -1)** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 750 | ***** | ***** | ***** | ***** | 0 | ***** | -10.71 | ***** | - | - |
| ARBs (14-day gap) | 7,357 | ***** | ***** | ***** | ***** | 10.71 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 744 | ***** | ***** | ***** | ***** | 0 | ***** | -19.05 | ***** | - | - |
| ARBs (14-day gap) | 744 | ***** | ***** | ***** | ***** | 19.05 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 744 | ***** | ***** | ***** | ***** | 0 | ***** | -8.72 | ***** | - | - |
| ARBs (14-day gap) | 744 | ***** | ***** | ***** | ***** | 8.72 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 52. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Serious Allergies**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No Serious allergies** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 42,674 | ***** | ***** | ***** | ***** | 0.54 | ***** | -0.15 | ***** | 0.74 ( 0.36, 1.53) | 0.418 |
| ARBs (14-day gap) | 282,648 | ***** | ***** | ***** | ***** | 0.69 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 42,666 | ***** | ***** | ***** | ***** | 0.77 | ***** | 0.11 | ***** | 1.17 ( 0.39, 3.47) | 0.782 |
| ARBs (14-day gap) | 42,666 | ***** | ***** | ***** | ***** | 0.66 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 42,666 | ***** | ***** | ***** | ***** | 0.54 | ***** | -0.09 | ***** | 0.84 ( 0.34, 2.05) | 0.7 |
| ARBs (14-day gap) | 42,666 | ***** | ***** | ***** | ***** | 0.62 | ***** | | | | |
| **Serious allergies** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 6,466 | ***** | ***** | ***** | ***** | 0.5 | ***** | -1.61 | ***** | 0.23 ( 0.03, 1.68) | 0.147 |
| ARBs (14-day gap) | 54,435 | ***** | ***** | ***** | ***** | 2.11 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 6,436 | ***** | ***** | ***** | ***** | 0.84 | ***** | -1.69 | ***** | 0.33 ( 0.03, 3.20) | 0.341 |
| ARBs (14-day gap) | 6,436 | ***** | ***** | ***** | ***** | 2.53 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 6,436 | ***** | ***** | ***** | ***** | 0.5 | ***** | -1.42 | ***** | 0.25 ( 0.03, 2.11) | 0.201 |
| ARBs (14-day gap) | 6,436 | ***** | ***** | ***** | ***** | 1.92 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 53. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Sex**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval) | Wald P-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Sex: Male** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 29,914 | ***** | ***** | ***** | ***** | 0.29 | ***** | -0.61 | ***** | 0.31 ( 0.10, 0.98) | 0.045 |
| ARBs (14-day gap) | 149,212 | ***** | ***** | ***** | ***** | 0.9 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 29,883 | ***** | ***** | ***** | ***** | 0.48 | ***** | -0.32 | ***** | 0.60 ( 0.14, 2.51) | 0.484 |
| ARBs (14-day gap) | 29,883 | ***** | ***** | ***** | ***** | 0.8 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 29,883 | ***** | ***** | ***** | ***** | 0.29 | ***** | -0.55 | ***** | 0.33 ( 0.09, 1.20) | 0.092 |
| ARBs (14-day gap) | 29,883 | ***** | ***** | ***** | ***** | 0.83 | ***** | | | | |
| **Sex: Female** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 19,226 | ***** | ***** | ***** | ***** | 0.93 | ***** | 0.03 | ***** | 0.98 ( 0.43, 2.26) | 0.971 |
| ARBs (14-day gap) | 187,871 | ***** | ***** | ***** | ***** | 0.89 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 19,218 | ***** | ***** | ***** | ***** | 1.51 | ***** | 0.5 | ***** | 1.50 ( 0.42, 5.32) | 0.53 |
| ARBs (14-day gap) | 19,218 | ***** | ***** | ***** | ***** | 1 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 19,218 | ***** | ***** | ***** | ***** | 0.93 | ***** | 0.35 | ***** | 1.53 ( 0.47, 5.03) | 0.482 |
| ARBs (14-day gap) | 19,218 | ***** | ***** | ***** | ***** | 0.58 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 54. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 18-44 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 1,164 | ***** | ***** | ***** | ***** | 0 | ***** | -2.74 | ***** | - | - |
| ARBs (14-day gap) | 8,502 | ***** | ***** | ***** | ***** | 2.74 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 1,154 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 1,154 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 1,154 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 1,154 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Age Group: 45-54 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 2,653 | ***** | ***** | ***** | ***** | 0 | ***** | -2.01 | ***** | - | - |
| ARBs (14-day gap) | 18,293 | ***** | ***** | ***** | ***** | 2.01 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 2,641 | ***** | ***** | ***** | ***** | 0 | ***** | -4.24 | ***** | - | - |
| ARBs (14-day gap) | 2,641 | ***** | ***** | ***** | ***** | 4.24 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 2,641 | ***** | ***** | ***** | ***** | 0 | ***** | -2.03 | ***** | - | - |
| ARBs (14-day gap) | 2,641 | ***** | ***** | ***** | ***** | 2.03 | ***** | | | | |

**Table 54. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Age Group**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Group: 55-64 Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 5,990 | ***** | ***** | ***** | ***** | 1.03 | ***** | -0.88 | ***** | 0.58 ( 0.14, 2.44) | 0.461 |
| ARBs (14-day gap) | 40,547 | ***** | ***** | ***** | ***** | 1.91 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 5,945 | ***** | ***** | ***** | ***** | 1.79 | ***** | 0 | ***** | 1.00 ( 0.14, 7.10) | 1 |
| ARBs (14-day gap) | 5,945 | ***** | ***** | ***** | ***** | 1.79 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 5,945 | ***** | ***** | ***** | ***** | 1.03 | ***** | 0.19 | ***** | 1.17 ( 0.16, 8.33) | 0.876 |
| ARBs (14-day gap) | 5,945 | ***** | ***** | ***** | ***** | 0.85 | ***** | | | | |
| **Age Group: 65+ Years** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 39,333 | ***** | ***** | ***** | ***** | 0.51 | ***** | -0.15 | ***** | 0.72 ( 0.33, 1.55) | 0.399 |
| ARBs (14-day gap) | 269,741 | ***** | ***** | ***** | ***** | 0.66 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 39,269 | ***** | ***** | ***** | ***** | 0.7 | ***** | -0.23 | ***** | 0.75 ( 0.26, 2.16) | 0.594 |
| ARBs (14-day gap) | 39,269 | ***** | ***** | ***** | ***** | 0.94 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 39,269 | ***** | ***** | ***** | ***** | 0.51 | ***** | -0.26 | ***** | 0.63 ( 0.25, 1.55) | 0.311 |
| ARBs (14-day gap) | 39,269 | ***** | ***** | ***** | ***** | 0.77 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Table 55. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Unknown** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 8,082 | ***** | ***** | ***** | ***** | 0 | ***** | -0.63 | ***** | - | - |
| ARBs (14-day gap) | 47,793 | ***** | ***** | ***** | ***** | 0.63 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 8,026 | ***** | ***** | ***** | ***** | 0 | ***** | -1.28 | ***** | - | - |
| ARBs (14-day gap) | 8,026 | ***** | ***** | ***** | ***** | 1.28 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 8,026 | ***** | ***** | ***** | ***** | 0 | ***** | -0.59 | ***** | - | - |
| ARBs (14-day gap) | 8,026 | ***** | ***** | ***** | ***** | 0.59 | ***** | | | | |
| **Race: American Indian** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 133 | ***** | ***** | ***** | ***** | 0 | ***** | -1.36 | ***** | - | - |
| ARBs (14-day gap) | 1,948 | ***** | ***** | ***** | ***** | 1.36 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 131 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 131 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 131 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 131 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |

**Table 55. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Asian** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 1,070 | ***** | ***** | ***** | ***** | 0 | ***** | -0.54 | ***** | - | - |
| ARBs (14-day gap) | 7,811 | ***** | ***** | ***** | ***** | 0.54 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 1,026 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 1,026 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 1,026 | ***** | ***** | ***** | ***** | 0 | ***** | -2.15 | ***** | - | - |
| ARBs (14-day gap) | 1,026 | ***** | ***** | ***** | ***** | 2.15 | ***** | | | | |
| **Race: Black** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 6,989 | ***** | ***** | ***** | ***** | 0.97 | ***** | -1.82 | ***** | 0.33 ( 0.08, 1.35) | 0.122 |
| ARBs (14-day gap) | 55,801 | ***** | ***** | ***** | ***** | 2.79 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 6,967 | ***** | ***** | ***** | ***** | 0.82 | ***** | -2.46 | ***** | 0.25 ( 0.03, 2.24) | 0.215 |
| ARBs (14-day gap) | 6,967 | ***** | ***** | ***** | ***** | 3.28 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 6,967 | ***** | ***** | ***** | ***** | 0.97 | ***** | -1.24 | ***** | 0.39 ( 0.08, 1.95) | 0.253 |
| ARBs (14-day gap) | 6,967 | ***** | ***** | ***** | ***** | 2.21 | ***** | | | | |

**Table 55. Effect Estimates for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020 by Analysis Type and Race**

| Medical Product | Number of New Users | Person Years at Risk | Average Person Days at Risk | Average Person Years at Risk | Number of Events | Incidence Rate per 1,000 Person Years | Risk per 1,000 New Users | Incidence Rate Difference per 1,000 Person Years | Difference in Risk per 1,000 New Users | Hazard Ratio (95% Confidence Interval)[2] | Wald P-Value[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Race: Pacific Islander** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 61 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 478 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 50 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 50 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 50 | ***** | ***** | ***** | ***** | 0 | ***** | 0 | ***** | - | - |
| ARBs (14-day gap) | 50 | ***** | ***** | ***** | ***** | 0 | ***** | | | | |
| **Race: White** | | | | | | | | | | | |
| **Site-Adjusted Analysis** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 32,805 | ***** | ***** | ***** | ***** | 0.6 | ***** | 0.03 | ***** | 1.00 ( 0.46, 2.19) | 0.996 |
| ARBs (14-day gap) | 223,252 | ***** | ***** | ***** | ***** | 0.57 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Conditional Analysis; Caliper= 0.05[1]** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 32,796 | ***** | ***** | ***** | ***** | 0.83 | ***** | -0.14 | ***** | 0.86 ( 0.29, 2.55) | 0.782 |
| ARBs (14-day gap) | 32,796 | ***** | ***** | ***** | ***** | 0.97 | ***** | | | | |
| **Fixed Ratio 1:1 Propensity Score Matched Unconditional Analysis; Caliper= 0.05** | | | | | | | | | | | |
| SV (14-day gap, history of ARBs (-183, -1)) | 32,796 | ***** | ***** | ***** | ***** | 0.6 | ***** | 0.07 | ***** | 1.10 ( 0.40, 3.04) | 0.854 |
| ARBs (14-day gap) | 32,796 | ***** | ***** | ***** | ***** | 0.53 | ***** | | | | |

[1]Conditional analysis accounts for informative events and person-time.

[2]Data presented by a dash are unable to be calculated. This table may not use all data representations.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

**Figure 1a. Histograms of Propensity Score Distribution Aggregated, Before Adjustment, Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

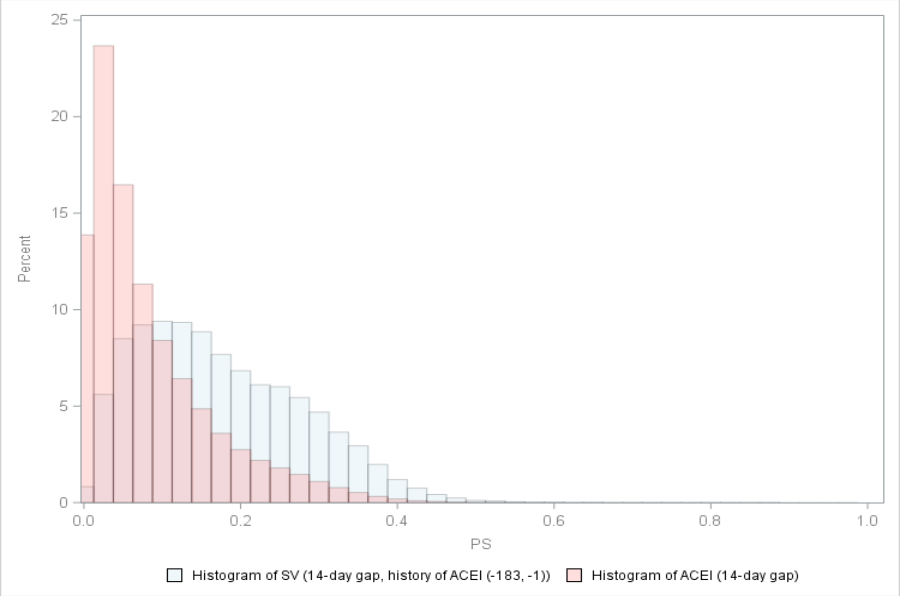


**Figure 1b. Histogram of Propensity Score Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

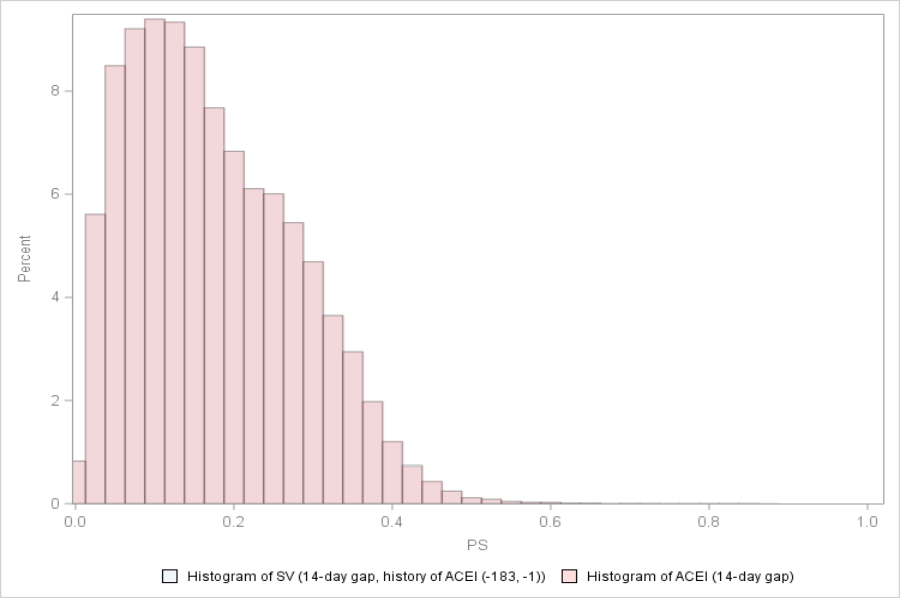


**Figure 2a. Histograms of Propensity Score Distribution Aggregated, Before Adjustment, Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

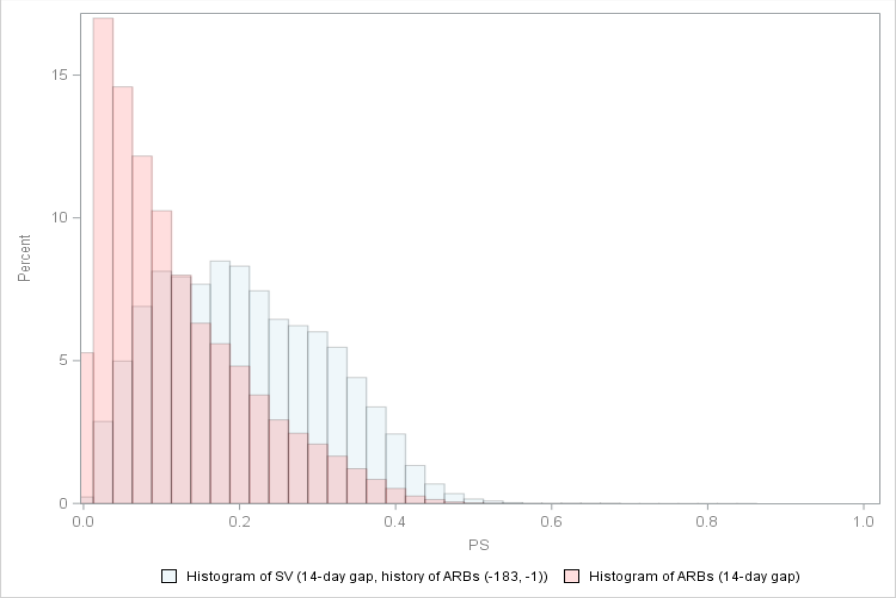


**Figure 2b. Histograms of Propensity Score Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

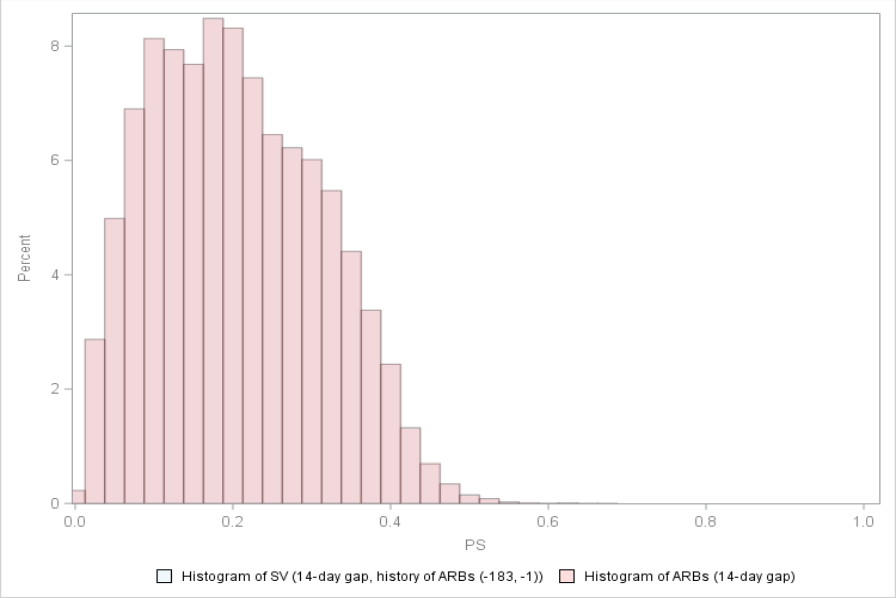


**Figure 3a. Histograms of Propensity Score Distribution Aggregated, Before Adjustment, Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

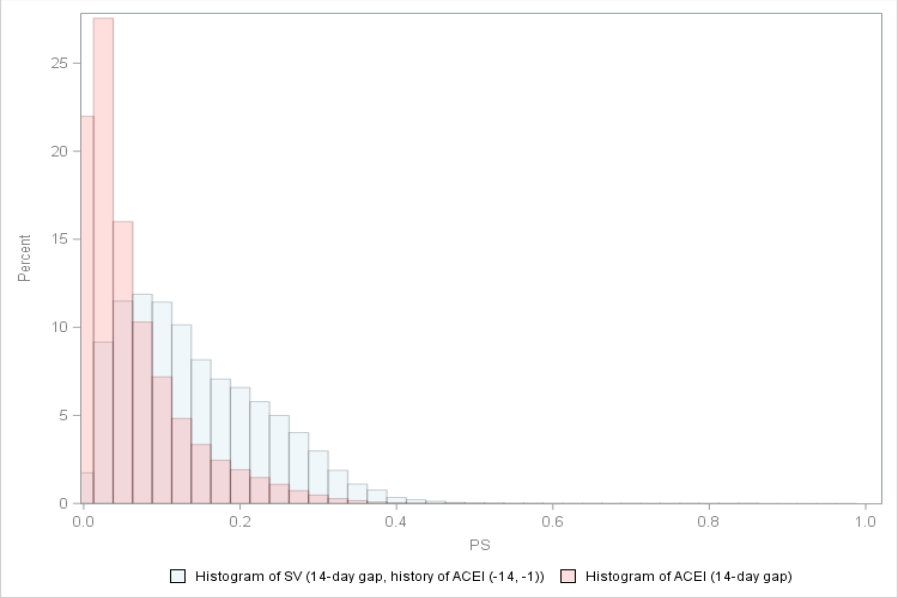


**Figure 3b. Histograms of Propensity Score Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

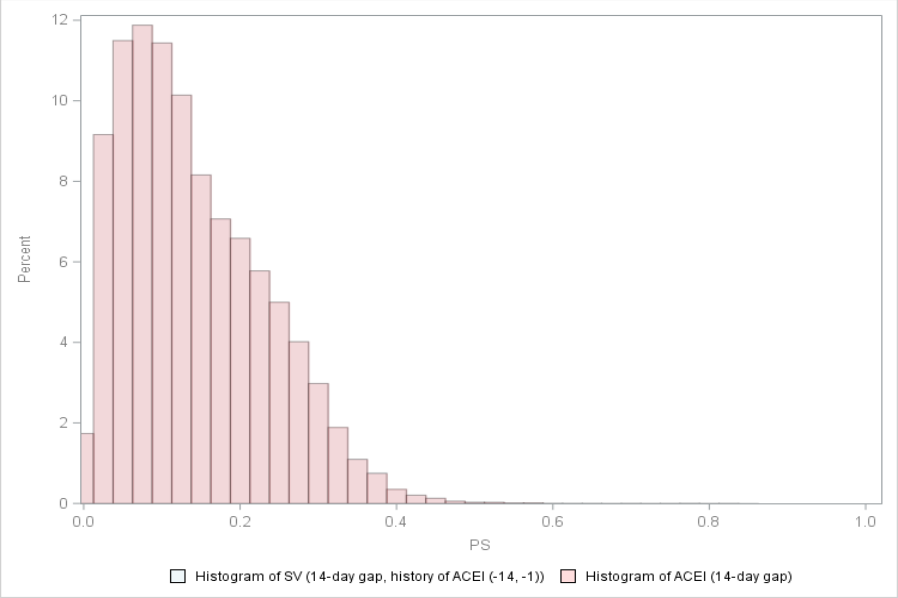


**Figure 4a. Histograms of Propensity Score Distribution Aggregated, Before Adjustment, Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

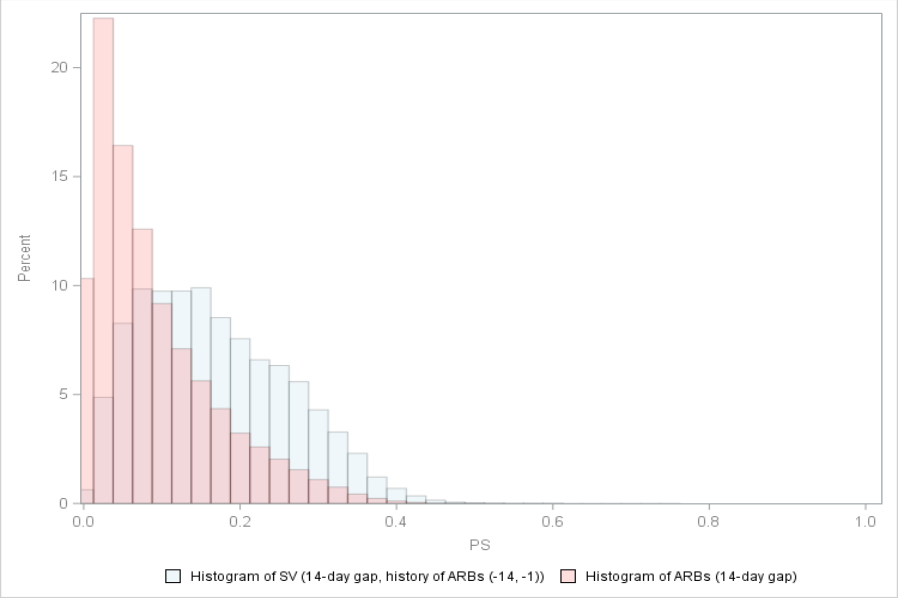


**Figure 4b. Histograms of Propensity Score Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

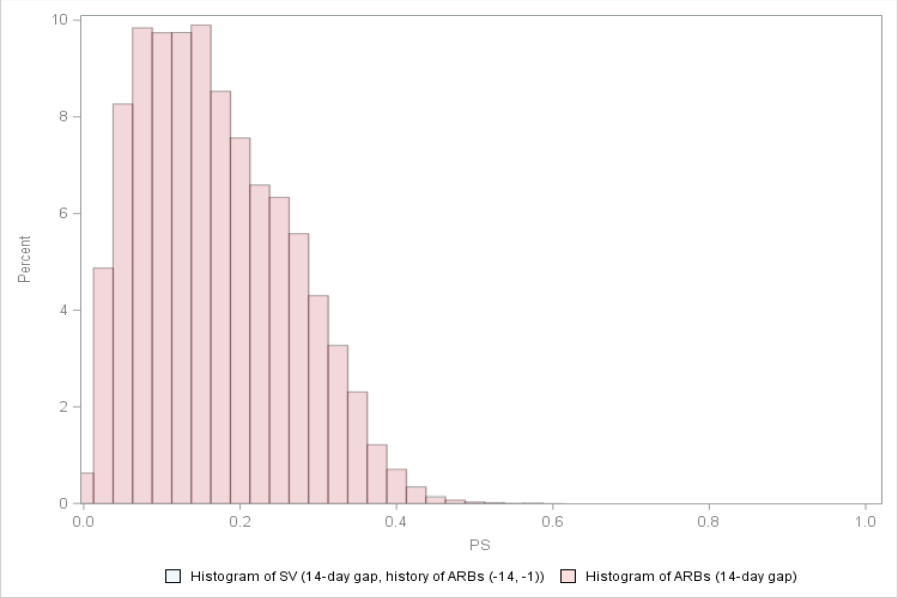


**Figure 5a. Histograms of Propensity Score Distribution Aggregated, Before Adjustment, Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 7-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

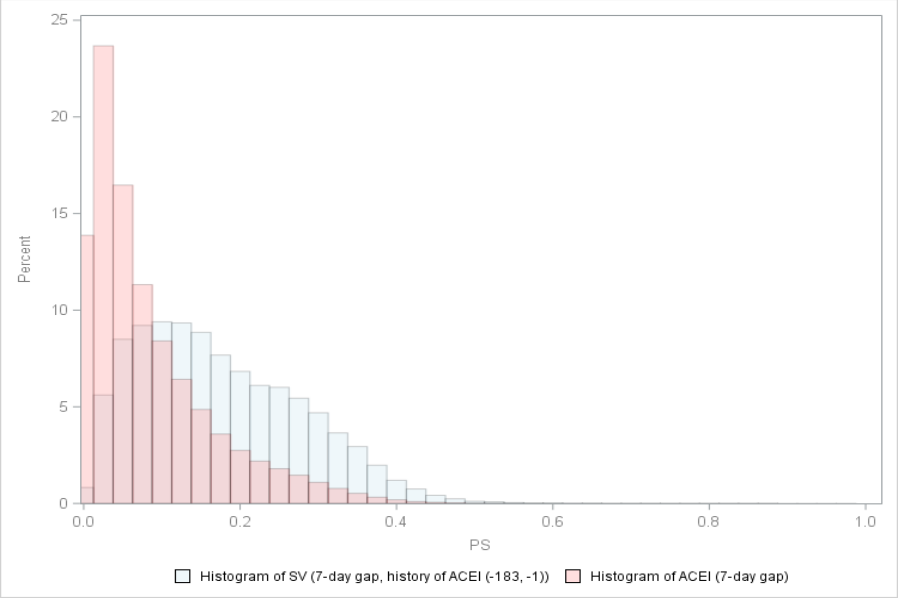


**Figure 5b. Histograms of Propensity Score Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 7-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

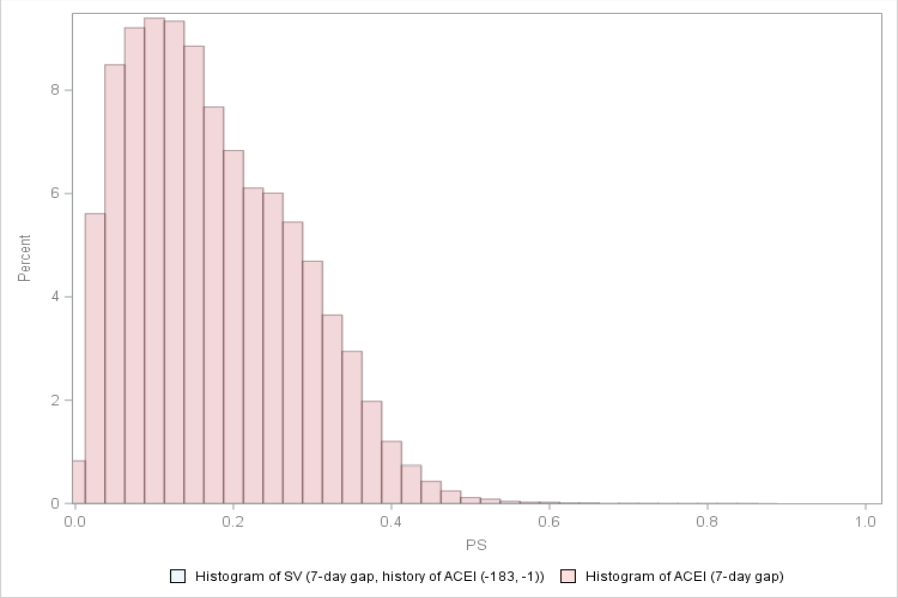


**Figure 6a. Histograms of Propensity Score Distribution Aggregated, Before Adjustment, Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

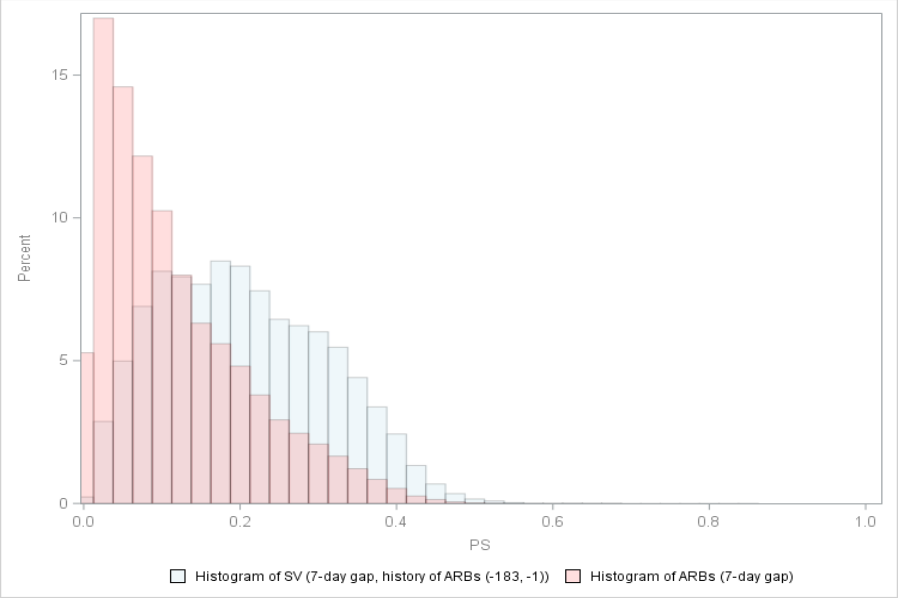


**Figure 6b. Histograms of Propensity Score Fixed Ratio 1:1 Aggregated Adjusted Cohort, Matched Caliper = 0.05, Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

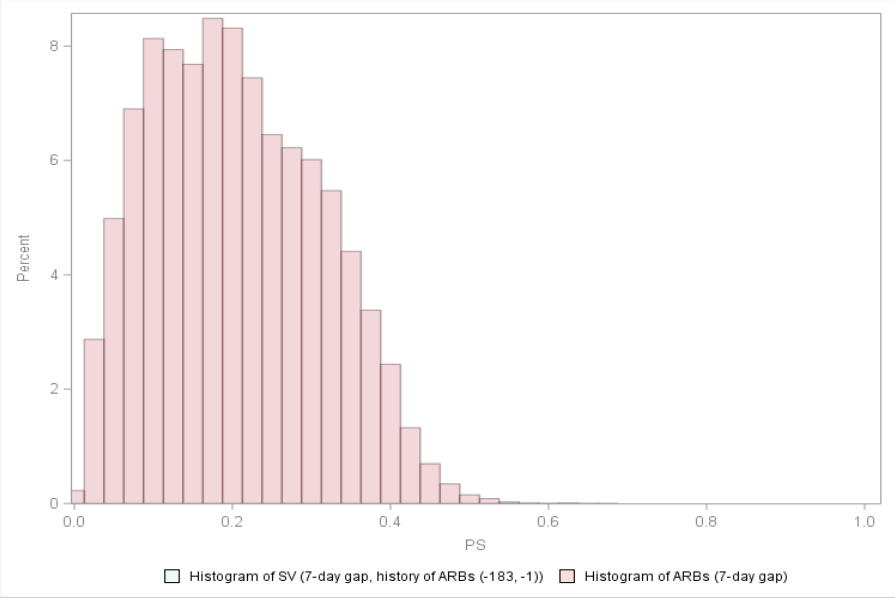


**Figure 7. Kaplan Meier Survival Curves for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

**Kaplan Meier Survival Curves of Events and Followup Time for Risk of Angioedema, Unconditional Propensity Score Adjusted Matched Cohort.**

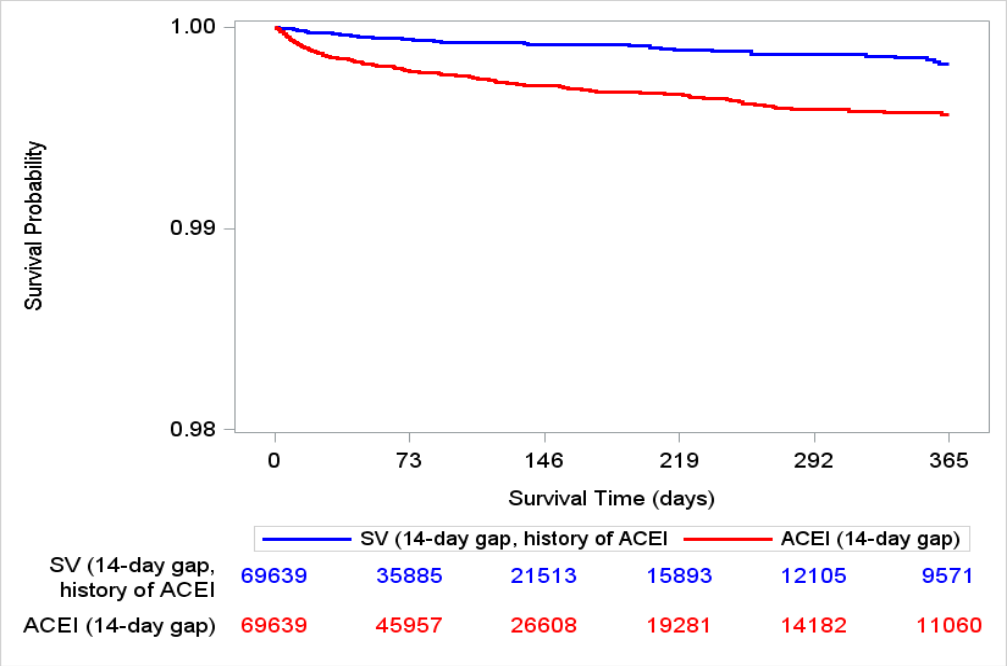


**Figure 8. Kaplan Meier Survival Curves for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

**Kaplan Meier Survival Curves of Events and Followup Time for Risk of Angioedema, Unconditional Propensity Score Adjusted Matched Cohort.**

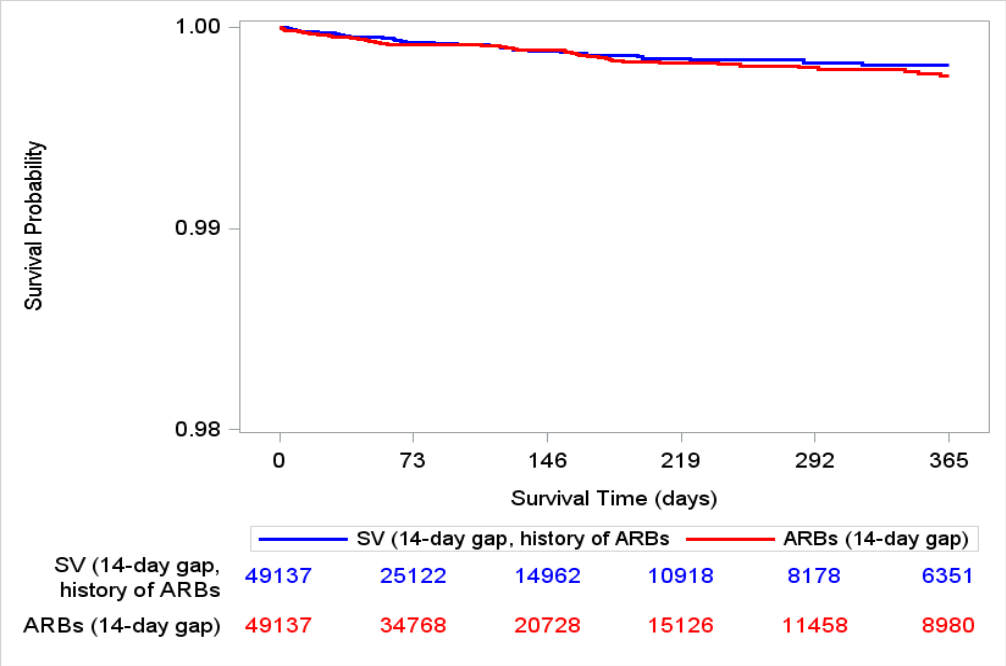


**Figure 9. Kaplan Meier Survival Curves for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 14 Days Prior, and ACEI, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

**Kaplan Meier Survival Curves of Events and Followup Time for Risk of Angioedema, Unconditional Propensity Score Adjusted Matched Cohort.**

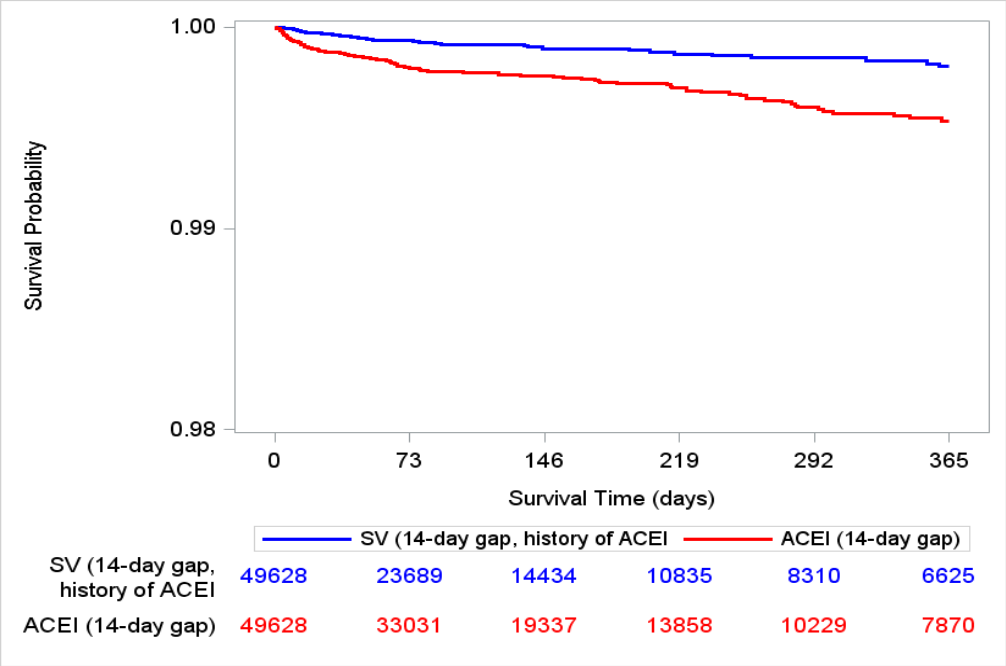


**Figure 10. Kaplan Meier Survival Curves for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 14 Days Prior, and ARBs, 14-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

**Kaplan Meier Survival Curves of Events and Followup Time for Risk of Angioedema, Unconditional Propensity Score Adjusted Matched Cohort.**

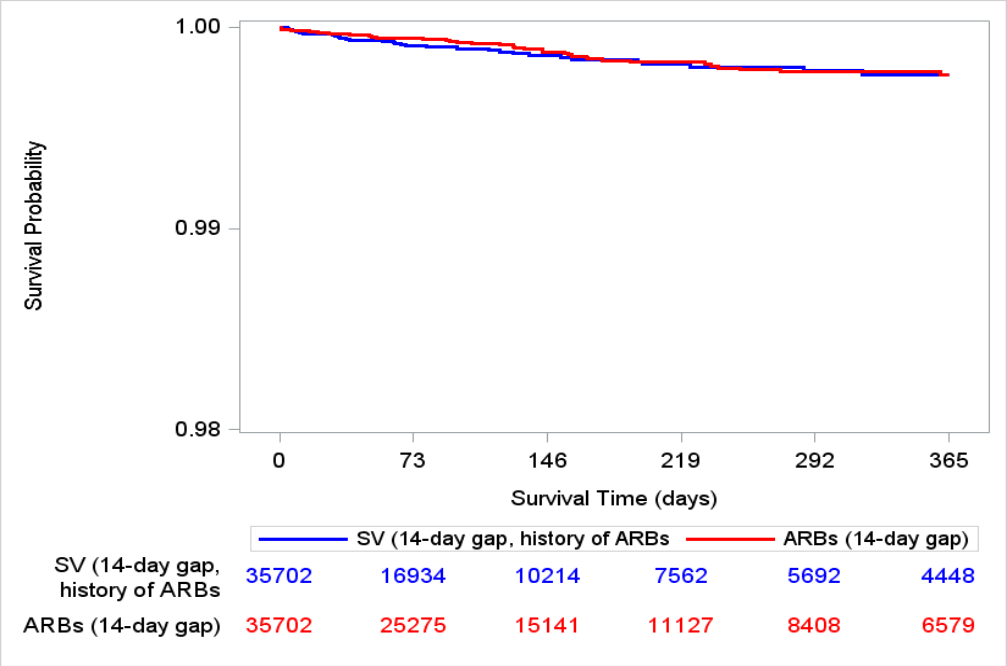


**Figure 11. Kaplan Meier Survival Curves for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

**Kaplan Meier Survival Curves of Events and Followup Time for Risk of Angioedema, Unconditional Propensity Score Adjusted Matched Cohort.**

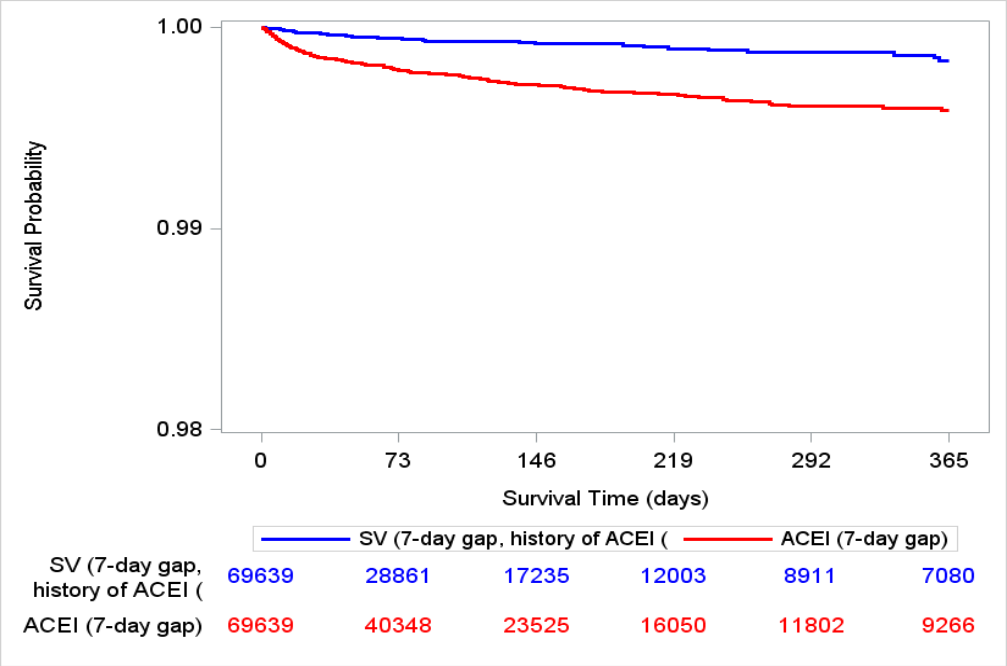


**Figure 12. Kaplan Meier Survival Curves for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 7-Day Gap, and Risk of Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

**Kaplan Meier Survival Curves of Events and Followup Time for Risk of Angioedema, Unconditional Propensity Score Adjusted Matched Cohort.**

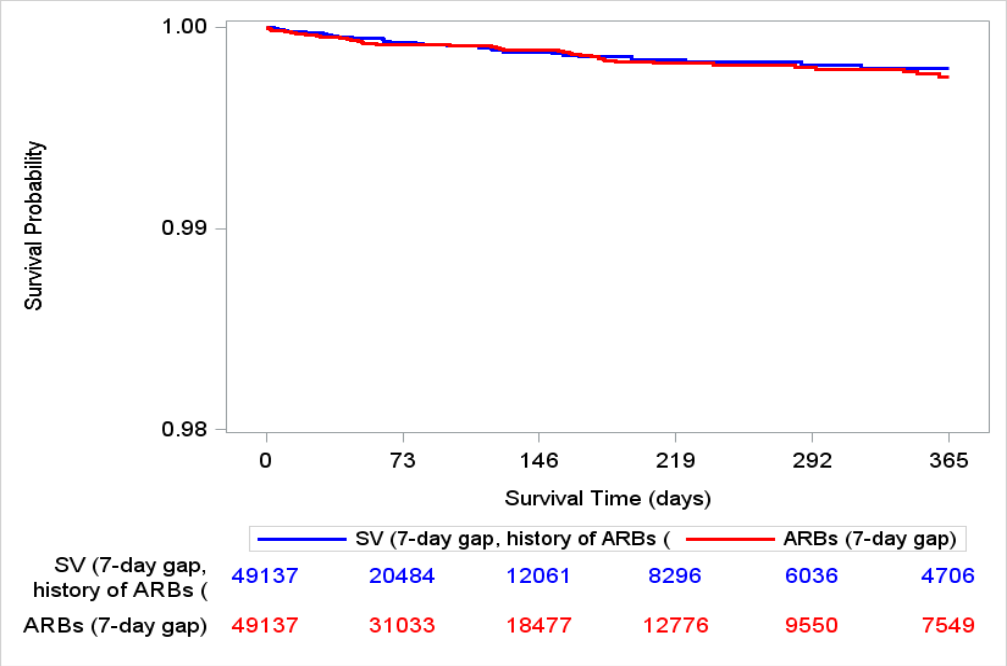


**Figure 13. Kaplan Meier Survival Curves for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin-Converting Enzyme Inhibitors (ACEI) in the 183 Days Prior, and ACEI, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

**Kaplan Meier Survival Curves of Events and Followup Time for Risk of Serious Angioedema, Unconditional Propensity Score Adjusted Matched Cohort.**

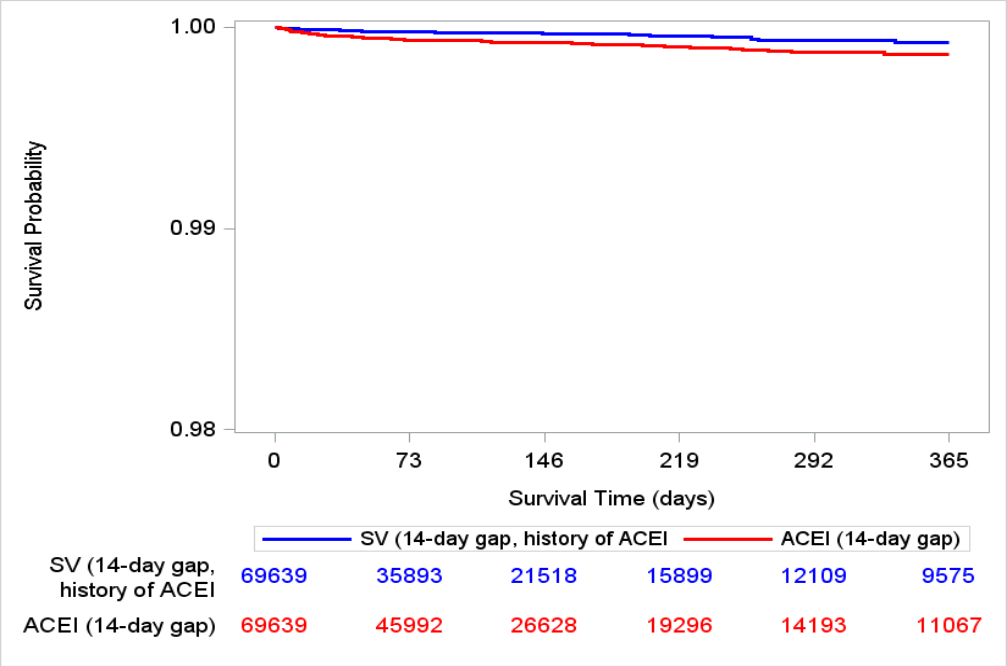


**Figure 14. Kaplan Meier Survival Curves for New Initiators of Sacubitril/Valsartan (SV) with use of Angiotensin II Receptor Blockers (ARBs) in the 183 Days Prior, and ARBs, 14-Day Gap, and Risk of Serious Angioedema in the Sentinel Distributed Database (SDD) between July 7, 2015 and February 29, 2020**

**Kaplan Meier Survival Curves of Events and Followup Time for Risk of Serious Angioedema, Unconditional Propensity Score Adjusted Matched Cohort.**

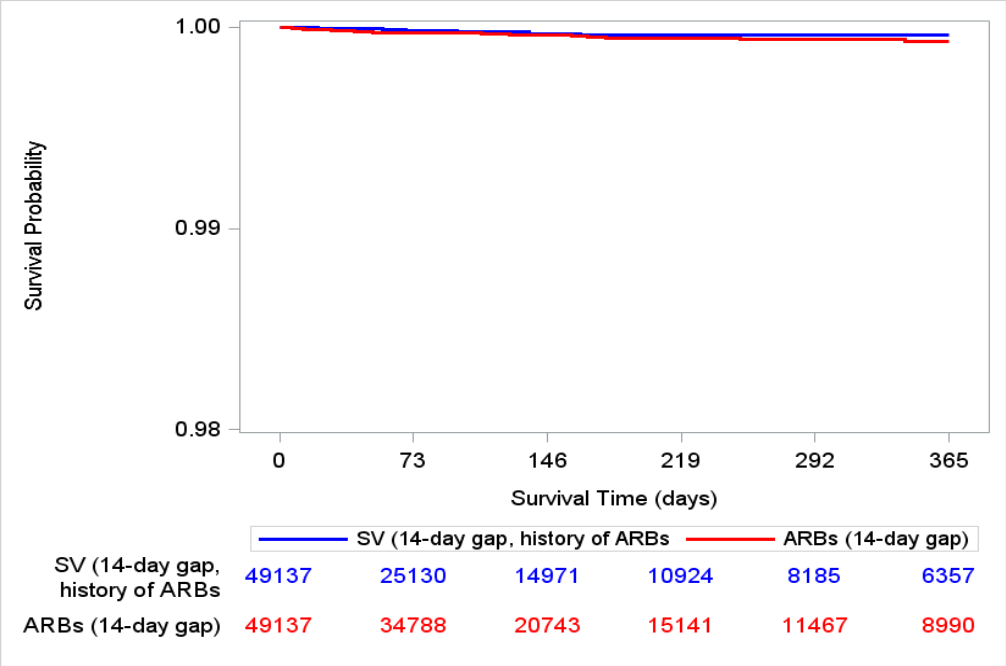


**Figure 15. Kaplan Meier Survival Curves for Risk of Angioedema, SV (183 days prior, 14-day gap) and ARBs (183 days prior, 14-day gap)**

**Kaplan Meier Survival Curves of Events and Followup Time for Risk of Angioedema, Unconditional Propensity Score Adjusted Matched Cohort, No Baseline Angioedema (-183, -1)**

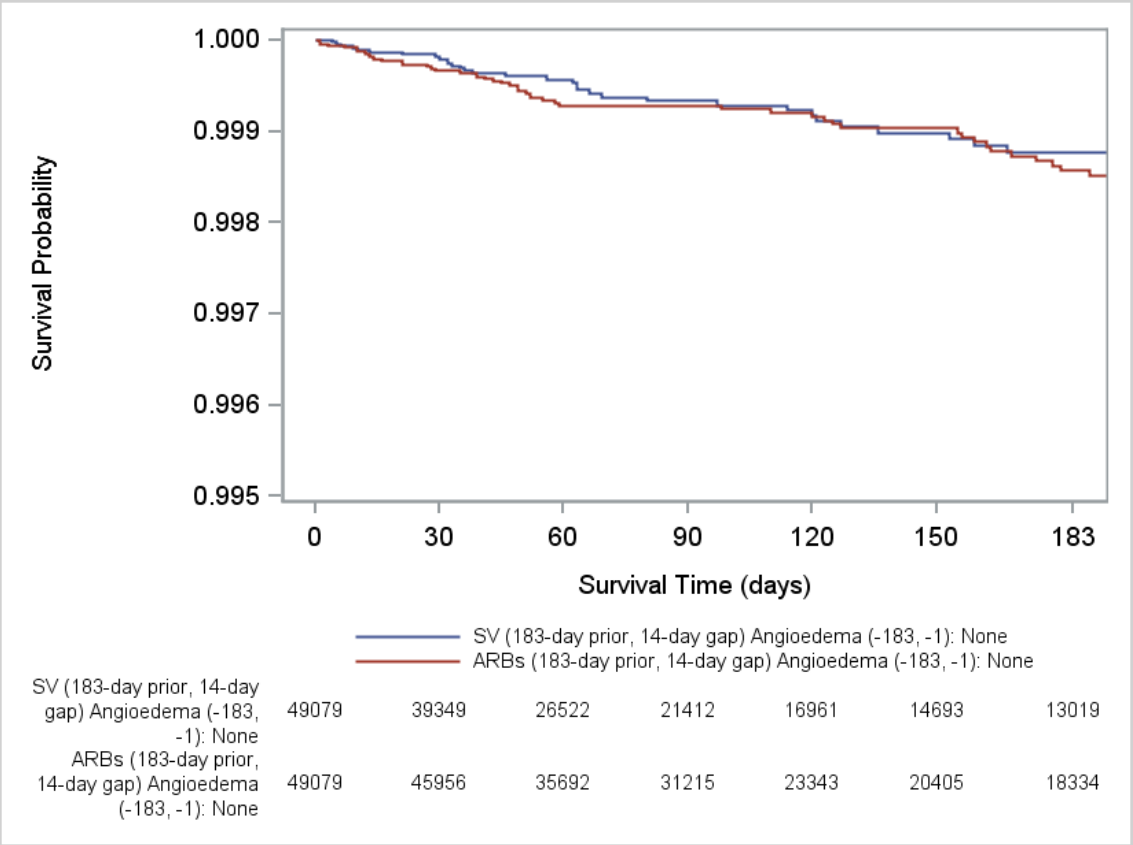
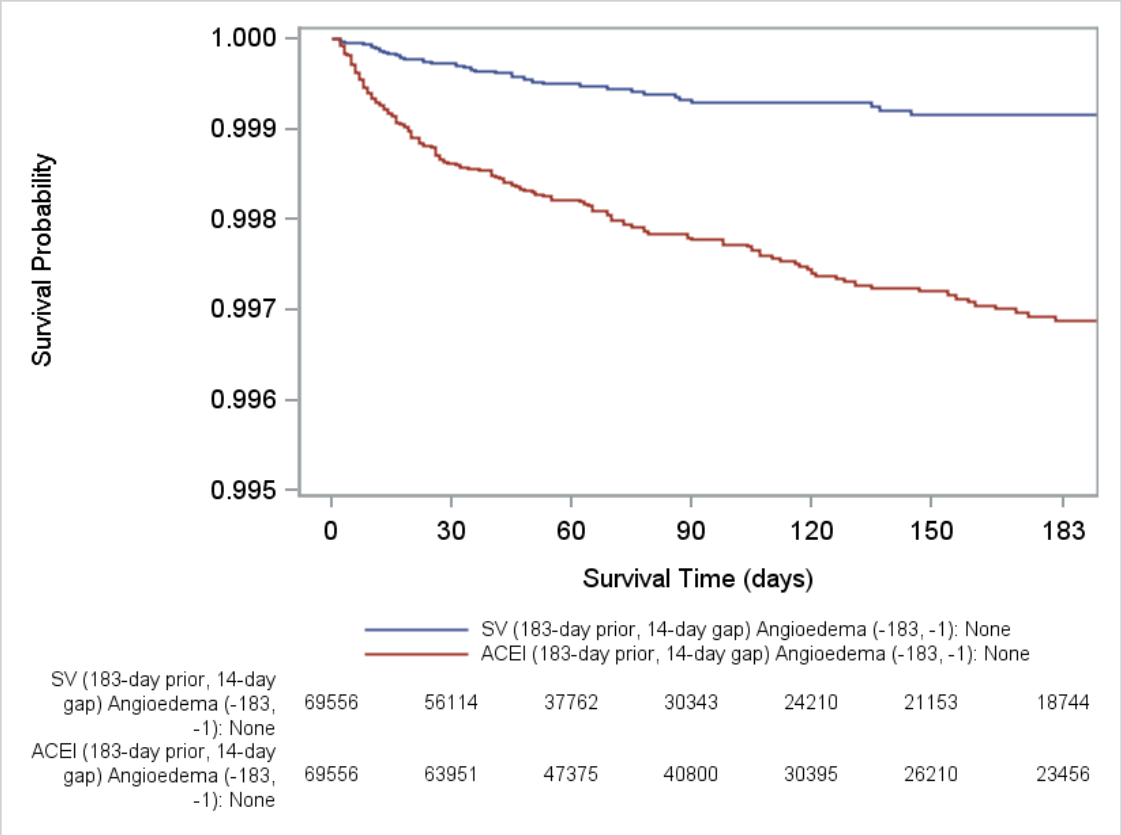


**Figure 16. Kaplan Meier Survival Curves for Risk of Angioedema, SV (183 days prior, 14-day gap) and ACEI (183 days prior, 14-day gap)**

**Kaplan Meier Survival Curves of Events and Followup Time for Risk of Angioedema, Unconditional Propensity Score Adjusted Matched Cohort, Angioedema, No Baseline Angioedema (-183, -1)**



## Appendix A. Dates of Available Data for Each Data Partner (DP) as of Request Distribution Date (January 13, 2021)

| DP ID | Start Date[1] | End Date[1] |
|---|---|---|
| DP01 | 1/1/2010 | 12/31/2019 |
| DP02 | 1/1/2008 | 12/31/2019 |
| DP03 | 1/1/2008 | 2/29/2020 |
| DP04 | 6/1/2007 | 10/31/2019 |
| DP05 | 1/1/2006 | 1/31/2020 |

[1]The start and end dates are based on the minimum and maximum dates within each DP. The month with the maximum date must have at least 80% of the number of records in the previous month.

**Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request**

| Generic Name | Brand Name |
|---|---|
| **Angiotensin-Converting Enzyme Inhibitors (ACEI)** | |
| AMLODIPINE BESYLATE/BENAZEPRIL HCL | Lotrel |
| AMLODIPINE BESYLATE/BENAZEPRIL HCL | amlodipine-benazepril |
| BENAZEPRIL HCL | Lotensin |
| BENAZEPRIL HCL | benazepril |
| BENAZEPRIL HCL/HYDROCHLOROTHIAZIDE | Lotensin HCT |
| BENAZEPRIL HCL/HYDROCHLOROTHIAZIDE | benazepril-hydrochlorothiazide |
| CAPTOPRIL | captopril |
| CAPTOPRIL/HYDROCHLOROTHIAZIDE | captopril-hydrochlorothiazide |
| ENALAPRIL MALEATE | Epaned |
| ENALAPRIL MALEATE | Vasotec |
| ENALAPRIL MALEATE | enalapril maleate |
| ENALAPRIL MALEATE/HYDROCHLOROTHIAZIDE | Vaseretic |
| ENALAPRIL MALEATE/HYDROCHLOROTHIAZIDE | enalapril-hydrochlorothiazide |
| FOSINOPRIL SODIUM | fosinopril |
| FOSINOPRIL SODIUM/HYDROCHLOROTHIAZIDE | fosinopril-hydrochlorothiazide |
| LISINOPRIL | Prinivil |
| LISINOPRIL | Qbrelis |
| LISINOPRIL | Zestril |
| LISINOPRIL | lisinopril |
| LISINOPRIL/HYDROCHLOROTHIAZIDE | Zestoretic |
| LISINOPRIL/HYDROCHLOROTHIAZIDE | lisinopril-hydrochlorothiazide |
| MOEXIPRIL HCL | Univasc |
| MOEXIPRIL HCL | moexipril |
| MOEXIPRIL HCL/HYDROCHLOROTHIAZIDE | Uniretic |
| MOEXIPRIL HCL/HYDROCHLOROTHIAZIDE | moexipril-hydrochlorothiazide |
| PERINDOPRIL ARGININE/AMLODIPINE BESYLATE | Prestalia |
| PERINDOPRIL ERBUMINE | Aceon |
| PERINDOPRIL ERBUMINE | perindopril erbumine |
| QUINAPRIL HCL | Accupril |
| QUINAPRIL HCL | quinapril |
| QUINAPRIL HCL/HYDROCHLOROTHIAZIDE | Accuretic |
| QUINAPRIL HCL/HYDROCHLOROTHIAZIDE | quinapril-hydrochlorothiazide |
| RAMIPRIL | Altace |
| RAMIPRIL | ramipril |
| TRANDOLAPRIL | Mavik |
| TRANDOLAPRIL | trandolapril |
| TRANDOLAPRIL/VERAPAMIL HCL | Tarka |
| TRANDOLAPRIL/VERAPAMIL HCL | trandolapril-verapamil |
| amlodipine besylate/benazepril HCl | amlodipine-benazepril |
| benazepril HCl | Lotensin |
| benazepril HCl | benazepril |
| captopril | captopril |
| enalapril maleate | enalapril maleate |
| lisinopril | lisinopril |
| lisinopril/hydrochlorothiazide | lisinopril-hydrochlorothiazide |
| quinapril HCl | quinapril |
| ramipril | ramipril |
| trandolapril | trandolapril |
| **Angiotensin II Receptor Blockers (ARB)** | |

**Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request**

| Generic Name | Brand Name |
|---|---|
| AMLODIPINE BESYLATE/OLMESARTAN MEDOXOMIL | Azor |
| AMLODIPINE BESYLATE/OLMESARTAN MEDOXOMIL | amlodipine-olmesartan |
| AMLODIPINE BESYLATE/VALSARTAN | Exforge |
| AMLODIPINE BESYLATE/VALSARTAN | amlodipine-valsartan |
| AMLODIPINE BESYLATE/VALSARTAN /HYDROCHLOROTHIAZIDE | Exforge HCT |
| AMLODIPINE BESYLATE/VALSARTAN /HYDROCHLOROTHIAZIDE | amlodipine-valsartan-hcthiazid |
| AZILSARTAN MEDOXOMIL | Edarbi |
| AZILSARTAN MEDOXOMIL/CHLORTHALIDONE | Edarbyclor |
| CANDESARTAN CILEXETIL | Atacand |
| CANDESARTAN CILEXETIL | candesartan |
| CANDESARTAN CILEXETIL/HYDROCHLOROTHIAZIDE | Atacand HCT |
| CANDESARTAN CILEXETIL/HYDROCHLOROTHIAZIDE | candesartan-hydrochlorothiazid |
| EPROSARTAN MESYLATE | Teveten |
| EPROSARTAN MESYLATE | eprosartan |
| EPROSARTAN MESYLATE/HYDROCHLOROTHIAZIDE | Teveten HCT |
| IRBESARTAN | Avapro |
| IRBESARTAN | irbesartan |
| IRBESARTAN/HYDROCHLOROTHIAZIDE | Avalide |
| IRBESARTAN/HYDROCHLOROTHIAZIDE | irbesartan-hydrochlorothiazide |
| LOSARTAN POTASSIUM | Cozaar |
| LOSARTAN POTASSIUM | losartan |
| LOSARTAN POTASSIUM/HYDROCHLOROTHIAZIDE | Hyzaar |
| LOSARTAN POTASSIUM/HYDROCHLOROTHIAZIDE | losartan-hydrochlorothiazide |
| NEBIVOLOL HCL/VALSARTAN | Byvalson |
| OLMESARTAN MEDOXOMIL | Benicar |
| OLMESARTAN MEDOXOMIL | olmesartan |
| OLMESARTAN MEDOXOMIL/AMLODIPINE BESYLATE/HYDROCHLOROTHIAZIDE | Tribenzor |
| OLMESARTAN MEDOXOMIL/AMLODIPINE BESYLATE/HYDROCHLOROTHIAZIDE | olmesartan-amlodipin-hcthiazid |
| OLMESARTAN MEDOXOMIL/HYDROCHLOROTHIAZIDE | Benicar HCT |
| OLMESARTAN MEDOXOMIL/HYDROCHLOROTHIAZIDE | olmesartan-hydrochlorothiazide |
| TELMISARTAN | Micardis |
| TELMISARTAN | telmisartan |
| TELMISARTAN/AMLODIPINE BESYLATE | Twynsta |
| TELMISARTAN/AMLODIPINE BESYLATE | telmisartan-amlodipine |
| TELMISARTAN/HYDROCHLOROTHIAZIDE | Micardis HCT |
| TELMISARTAN/HYDROCHLOROTHIAZIDE | telmisartan-hydrochlorothiazid |
| VALSARTAN | Diovan |
| VALSARTAN | valsartan |
| VALSARTAN/HYDROCHLOROTHIAZIDE | Diovan HCT |
| VALSARTAN/HYDROCHLOROTHIAZIDE | valsartan-hydrochlorothiazide |
| amlodipine besylate/olmesartan medoxomil | amlodipine-olmesartan |
| amlodipine besylate/valsartan | amlodipine-valsartan |
| amlodipine besylate/valsartan/hydrochlorothiazide | amlodipine-valsartan-hcthiazid |
| candesartan cilexetil | Atacand |
| candesartan cilexetil | candesartan |
| candesartan cilexetil/hydrochlorothiazide | Atacand HCT |
| candesartan cilexetil/hydrochlorothiazide | candesartan-hydrochlorothiazid |
| irbesartan | irbesartan |
| irbesartan/hydrochlorothiazide | irbesartan-hydrochlorothiazide |

**Appendix B. Generic and Brand Names of Medical Products Used to Define Exposures in this Request**

| Generic Name | Brand Name |
|---|---|
| losartan potassium | losartan |
| losartan potassium/hydrochlorothiazide | losartan-hydrochlorothiazide |
| olmesartan medoxomil | Benicar |
| olmesartan medoxomil | olmesartan |
| olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide | olmesartan-amlodipin-hcthiazid |
| olmesartan medoxomil/hydrochlorothiazide | Benicar HCT |
| telmisartan | telmisartan |
| telmisartan/hydrochlorothiazide | telmisartan-hydrochlorothiazid |
| valsartan | valsartan |
| valsartan/hydrochlorothiazide | valsartan-hydrochlorothiazide |
| **Sacubitril/Valsartan** | |
| SACUBITRIL/VALSARTAN | Entresto |

**Appendix C. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS), Current Procedural Terminology, Fourth Edition (CPT-4), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Outcome in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| | **Intensive Care Unit Admission, Intubation, Tracheostomy, or Laryngoscopy** | | |
| 09HN7BZ | Insertion of Airway into Nasopharynx, Via Natural or Artificial Opening | Procedure | ICD-10-PCS |
| 9HN8BZ | Insertion of Airway into Nasopharynx, Via Natural or Artificial Opening Endoscopic | Procedure | ICD-10-PCS |
| B110F4 | Bypass Trachea to Cutaneous with Tracheostomy Device, Open Approach | Procedure | ICD-10-PCS |
| 0B110Z4 | Bypass Trachea to Cutaneous, Open Approach | Procedure | ICD-10-PCS |
| 0B113F4 | Bypass Trachea to Cutaneous with Tracheostomy Device, Percutaneous Approach | Procedure | ICD-10-PCS |
| 0B113Z4 | Bypass Trachea to Cutaneous, Percutaneous Approach | Procedure | ICD-10-PCS |
| | Bypass Trachea to Cutaneous with Tracheostomy Device, Percutaneous Endoscopic Approach | Procedure | ICD-10-PCS |
| 0B114F4 | | | |
| 0B114Z4 | Bypass Trachea to Cutaneous, Percutaneous Endoscopic Approach | Procedure | ICD-10-PCS |
| 0B710DZ | Dilation of Trachea with Intraluminal Device, Open Approach | Procedure | ICD-10-PCS |
| 0B710ZZ | Dilation of Trachea, Open Approach | Procedure | ICD-10-PCS |
| 0B713DZ | Dilation of Trachea with Intraluminal Device, Percutaneous Approach | Procedure | ICD-10-PCS |
| 0B713ZZ | Dilation of Trachea, Percutaneous Approach | Procedure | ICD-10-PCS |
| 0B714DZ | Dilation of Trachea with Intraluminal Device, Percutaneous Endoscopic Approach | Procedure | ICD-10-PCS |
| 0B714ZZ | Dilation of Trachea, Percutaneous Endoscopic Approach | Procedure | ICD-10-PCS |
| 0B717DZ | Dilation of Trachea with Intraluminal Device, Via Natural or Artificial Opening | Procedure | ICD-10-PCS |
| 0B717ZZ | Dilation of Trachea, Via Natural or Artificial Opening | Procedure | ICD-10-PCS |
| | Dilation of Trachea with Intraluminal Device, Via Natural or Artificial Opening Endoscopic | Procedure | ICD-10-PCS |
| 0B718DZ | | | |
| 0B718ZZ | Dilation of Trachea, Via Natural or Artificial Opening Endoscopic | Procedure | ICD-10-PCS |
| 0B720DZ | Dilation of Carina with Intraluminal Device, Open Approach | Procedure | ICD-10-PCS |
| 0B720ZZ | Dilation of Carina, Open Approach | Procedure | ICD-10-PCS |
| 0B723DZ | Dilation of Carina with Intraluminal Device, Percutaneous Approach | Procedure | ICD-10-PCS |
| 0B723ZZ | Dilation of Carina, Percutaneous Approach | Procedure | ICD-10-PCS |
| 0B724DZ | Dilation of Carina with Intraluminal Device, Percutaneous Endoscopic Approach | Procedure | ICD-10-PCS |
| 0B724ZZ | Dilation of Carina, Percutaneous Endoscopic Approach | Procedure | ICD-10-PCS |
| 0B727DZ | Dilation of Carina with Intraluminal Device, Via Natural or Artificial Opening | Procedure | ICD-10-PCS |
| 0B727ZZ | Dilation of Carina, Via Natural or Artificial Opening | Procedure | ICD-10-PCS |
| | Dilation of Carina with Intraluminal Device, Via Natural or Artificial Opening Endoscopic | Procedure | ICD-10-PCS |
| 0B728DZ | | | |
| 0B728ZZ | Dilation of Carina, Via Natural or Artificial Opening Endoscopic | Procedure | ICD-10-PCS |
| | Insertion of Intraluminal Device into Tracheobronchial Tree, Via Natural or Artificial Opening | Procedure | ICD-10-PCS |
| 0BH07DZ | | | |
| 0BH17EZ | Insertion of Endotracheal Airway into Trachea, Via Natural or Artificial Opening | Procedure | ICD-10-PCS |
| | Insertion of Endotracheal Airway into Trachea, Via Natural or Artificial Opening Endoscopic | Procedure | ICD-10-PCS |
| 0BH18EZ | | | |
| 0BJ14ZZ | Inspection of Trachea, Percutaneous Endoscopic Approach | Procedure | ICD-10-PCS |
| 0BJ18ZZ | Inspection of Trachea, Via Natural or Artificial Opening Endoscopic | Procedure | ICD-10-PCS |
| 0BQ10ZZ | Repair Trachea, Open Approach | Procedure | ICD-10-PCS |
| 0BQ13ZZ | Repair Trachea, Percutaneous Approach | Procedure | ICD-10-PCS |
| 0BQ14ZZ | Repair Trachea, Percutaneous Endoscopic Approach | Procedure | ICD-10-PCS |
| 0BQ17ZZ | Repair Trachea, Via Natural or Artificial Opening | Procedure | ICD-10-PCS |
| 0BQ18ZZ | Repair Trachea, Via Natural or Artificial Opening Endoscopic | Procedure | ICD-10-PCS |
| 0BQ20ZZ | Repair Carina, Open Approach | Procedure | ICD-10-PCS |
| 0BQ23ZZ | Repair Carina, Percutaneous Approach | Procedure | ICD-10-PCS |
| 0BQ24ZZ | Repair Carina, Percutaneous Endoscopic Approach | Procedure | ICD-10-PCS |

**Appendix C. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS), Current Procedural Terminology, Fourth Edition (CPT-4), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Outcome in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| 0BQ27ZZ | Repair Carina, Via Natural or Artificial Opening | Procedure | ICD-10-PCS |
| 0BQ28ZZ | Repair Carina, Via Natural or Artificial Opening Endoscopic | Procedure | ICD-10-PCS |
| 0CHY7BZ | Insertion of Airway into Mouth and Throat, Via Natural or Artificial Opening | Procedure | ICD-10-PCS |
| 0CHY8BZ | Insertion of Airway into Mouth and Throat, Via Natural or Artificial Opening Endoscopic | Procedure | ICD-10-PCS |
| 0CJS4ZZ | Inspection of Larynx, Percutaneous Endoscopic Approach | Procedure | ICD-10-PCS |
| 0CJS8ZZ | Inspection of Larynx, Via Natural or Artificial Opening Endoscopic | Procedure | ICD-10-PCS |
| 0DH57BZ | Insertion of Airway into Esophagus, Via Natural or Artificial Opening | Procedure | ICD-10-PCS |
| 0DH58BZ | Insertion of Airway into Esophagus, Via Natural or Artificial Opening Endoscopic | Procedure | ICD-10-PCS |
| 0DL57DZ | Occlusion of Esophagus with Intraluminal Device, Via Natural or Artificial Opening | Procedure | ICD-10-PCS |
| 0DL58DZ | Occlusion of Esophagus with Intraluminal Device, Via Natural or Artificial Opening Endoscopic | Procedure | ICD-10-PCS |
| 0WHQ7YZ | Insertion of Other Device into Respiratory Tract, Via Natural or Artificial Opening | Procedure | ICD-10-PCS |
| 31.1 | Tracheostomy | Procedure | ICD-9-CM |
| 31.2 | Tracheostomy | Procedure | ICD-9-CM |
| 31.21 | Tracheostomy | Procedure | ICD-9-CM |
| 31.29 | Tracheostomy | Procedure | ICD-9-CM |
| 31.42 | Laryngoscopy | Procedure | ICD-9-CM |
| 31.99 | Intubation | Procedure | ICD-9-CM |
| 31231 | Laryngoscopy | Procedure | CPT-4 |
| 31502 | Intubation | Procedure | CPT-4 |
| 31505 | Laryngoscopy | Procedure | CPT-4 |
| 31525 | Laryngoscopy | Procedure | CPT-4 |
| 31526 | Laryngoscopy | Procedure | CPT-4 |
| 31527 | Laryngoscopy | Procedure | CPT-4 |
| 31528 | Laryngoscopy | Procedure | CPT-4 |
| 31529 | Laryngoscopy | Procedure | CPT-4 |
| 31560 | Laryngoscopy | Procedure | CPT-4 |
| 31561 | Laryngoscopy | Procedure | CPT-4 |
| 31603 | Tracheostomy | Procedure | CPT-4 |
| 31605 | Tracheostomy | Procedure | CPT-4 |
| 31610 | Tracheostomy | Procedure | CPT-4 |
| 31612 | Tracheostomy | Procedure | CPT-4 |
| 31615 | Tracheostomy | Procedure | CPT-4 |
| 3E1F78Z | Irrigation of Respiratory Tract using Irrigating Substance, Via Natural or Artificial Opening | Procedure | ICD-10-PCS |
| 3E1F88Z | Irrigation of Respiratory Tract using Irrigating Substance, Via Natural or Artificial Opening Endoscopic | Procedure | ICD-10-PCS |
| 5A1935Z | Respiratory Ventilation, Less than 24 Consecutive Hours | Procedure | ICD-10-PCS |
| 5A1945Z | Respiratory Ventilation, 24-96 Consecutive Hours | Procedure | ICD-10-PCS |
| 5A1955Z | Respiratory Ventilation, Greater than 96 Consecutive Hours | Procedure | ICD-10-PCS |
| 91000 | Intubation | Procedure | CPT-4 |
| 96 | Intubation | Procedure | ICD-9-CM |
| 96.0 | Intubation | Procedure | ICD-9-CM |
| 96.01 | Intubation | Procedure | ICD-9-CM |
| 96.02 | Intubation | Procedure | ICD-9-CM |
| 96.03 | Intubation | Procedure | ICD-9-CM |

**Appendix C. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS), Current Procedural Terminology, Fourth Edition (CPT-4), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Outcome in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| 96.04 | Intubation | Procedure | ICD-9-CM |
| 96.05 | Intubation | Procedure | ICD-9-CM |
| 96.06 | Intubation | Procedure | ICD-9-CM |
| 96.56 | Intubation | Procedure | ICD-9-CM |
| 96.7 | Intubation | Procedure | ICD-9-CM |
| 96.70 | Intubation | Procedure | ICD-9-CM |
| 96.71 | Intubation | Procedure | ICD-9-CM |
| 96.72 | Intubation | Procedure | ICD-9-CM |
| 99220 | ICU Admission | Procedure | CPT-4 |
| 99221 | ICU Admission | Procedure | CPT-4 |
| 99222 | ICU Admission | Procedure | CPT-4 |
| 99223 | ICU Admission | Procedure | CPT-4 |
| 99224 | ICU Admission | Procedure | CPT-4 |
| 99225 | ICU Admission | Procedure | CPT-4 |
| 99226 | ICU Admission | Procedure | CPT-4 |
| 99291 | ICU Admission | Procedure | CPT-4 |
| 99292 | ICU Admission | Procedure | CPT-4 |
| A0396 | Intubation | Procedure | HCPCS |
| V44.0 | Tracheostomy | Diagnosis | ICD-9-CM |
| V55.0 | Tracheostomy | Diagnosis | ICD-9-CM |
| Z43.0 | Encounter for Attention to Tracheostomy | Diagnosis | ICD-10-CM |
| Z93.0 | Tracheostomy Status | Diagnosis | ICD-10-CM |
| | **Angioedema** | | |
| 995.1 | Angioedema | Diagnosis | ICD-9-CM |
| T783XXA | Angioedema | Diagnosis | ICD-10-CM |

**Appendix D. Generic and Brand Names of Medical Products Used to Define Exposure Incidence and Exclusion Criteria in this Request**

| Generic Name | Brand Name |
|---|---|
| **Angiotensin-Converting Enzyme Inhibitors (ACEI)** | |
| AMLODIPINE BESYLATE/BENAZEPRIL HCL | Lotrel |
| AMLODIPINE BESYLATE/BENAZEPRIL HCL | amlodipine-benazepril |
| BENAZEPRIL HCL | Lotensin |
| BENAZEPRIL HCL | benazepril |
| BENAZEPRIL HCL/HYDROCHLOROTHIAZIDE | Lotensin HCT |
| BENAZEPRIL HCL/HYDROCHLOROTHIAZIDE | benazepril-hydrochlorothiazide |
| CAPTOPRIL | captopril |
| CAPTOPRIL/HYDROCHLOROTHIAZIDE | captopril-hydrochlorothiazide |
| ENALAPRIL MALEATE | Epaned |
| ENALAPRIL MALEATE | Vasotec |
| ENALAPRIL MALEATE | enalapril maleate |
| ENALAPRIL MALEATE/HYDROCHLOROTHIAZIDE | Vaseretic |
| ENALAPRIL MALEATE/HYDROCHLOROTHIAZIDE | enalapril-hydrochlorothiazide |
| FOSINOPRIL SODIUM | fosinopril |
| FOSINOPRIL SODIUM/HYDROCHLOROTHIAZIDE | fosinopril-hydrochlorothiazide |
| LISINOPRIL | Prinivil |
| LISINOPRIL | Qbrelis |
| LISINOPRIL | Zestril |
| LISINOPRIL | lisinopril |
| LISINOPRIL/HYDROCHLOROTHIAZIDE | Zestoretic |
| LISINOPRIL/HYDROCHLOROTHIAZIDE | lisinopril-hydrochlorothiazide |
| MOEXIPRIL HCL | Univasc |
| MOEXIPRIL HCL | moexipril |
| MOEXIPRIL HCL/HYDROCHLOROTHIAZIDE | Uniretic |
| MOEXIPRIL HCL/HYDROCHLOROTHIAZIDE | moexipril-hydrochlorothiazide |
| PERINDOPRIL ARGININE/AMLODIPINE BESYLATE | Prestalia |
| PERINDOPRIL ERBUMINE | Aceon |
| PERINDOPRIL ERBUMINE | perindopril erbumine |
| QUINAPRIL HCL | Accupril |
| QUINAPRIL HCL | quinapril |
| QUINAPRIL HCL/HYDROCHLOROTHIAZIDE | Accuretic |
| QUINAPRIL HCL/HYDROCHLOROTHIAZIDE | quinapril-hydrochlorothiazide |
| RAMIPRIL | Altace |
| RAMIPRIL | ramipril |
| TRANDOLAPRIL | Mavik |
| TRANDOLAPRIL | trandolapril |
| TRANDOLAPRIL/VERAPAMIL HCL | Tarka |
| TRANDOLAPRIL/VERAPAMIL HCL | trandolapril-verapamil |
| amlodipine besylate/benazepril HCl | amlodipine-benazepril |
| benazepril HCl | Lotensin |
| benazepril HCl | benazepril |
| captopril | captopril |
| enalapril maleate | enalapril maleate |
| lisinopril | lisinopril |
| lisinopril/hydrochlorothiazide | lisinopril-hydrochlorothiazide |
| quinapril HCl | quinapril |
| ramipril | ramipril |
| trandolapril | trandolapril |

**Appendix D. Generic and Brand Names of Medical Products Used to Define Exposure Incidence and Exclusion Criteria in this Request**

| Generic Name | Brand Name |
|---|---|
| **Angiotensin II Receptor Blockers (ARB)** | |
| AMLODIPINE BESYLATE/OLMESARTAN MEDOXOMIL | Azor |
| AMLODIPINE BESYLATE/OLMESARTAN MEDOXOMIL | amlodipine-olmesartan |
| AMLODIPINE BESYLATE/VALSARTAN | Exforge |
| AMLODIPINE BESYLATE/VALSARTAN | amlodipine-valsartan |
| AMLODIPINE BESYLATE/VALSARTAN/HYDROCHLOROTHIAZIDE | Exforge HCT |
| AMLODIPINE BESYLATE/VALSARTAN/HYDROCHLOROTHIAZIDE | amlodipine-valsartan-hcthiazid |
| AZILSARTAN MEDOXOMIL | Edarbi |
| AZILSARTAN MEDOXOMIL/CHLORTHALIDONE | Edarbyclor |
| CANDESARTAN CILEXETIL | Atacand |
| CANDESARTAN CILEXETIL | candesartan |
| CANDESARTAN CILEXETIL/HYDROCHLOROTHIAZIDE | Atacand HCT |
| CANDESARTAN CILEXETIL/HYDROCHLOROTHIAZIDE | candesartan-hydrochlorothiazid |
| EPROSARTAN MESYLATE | Teveten |
| EPROSARTAN MESYLATE | eprosartan |
| EPROSARTAN MESYLATE/HYDROCHLOROTHIAZIDE | Teveten HCT |
| IRBESARTAN | Avapro |
| IRBESARTAN | irbesartan |
| IRBESARTAN/HYDROCHLOROTHIAZIDE | Avalide |
| IRBESARTAN/HYDROCHLOROTHIAZIDE | irbesartan-hydrochlorothiazide |
| LOSARTAN POTASSIUM | Cozaar |
| LOSARTAN POTASSIUM | losartan |
| LOSARTAN POTASSIUM/HYDROCHLOROTHIAZIDE | Hyzaar |
| LOSARTAN POTASSIUM/HYDROCHLOROTHIAZIDE | losartan-hydrochlorothiazide |
| NEBIVOLOL HCL/VALSARTAN | Byvalson |
| OLMESARTAN MEDOXOMIL | Benicar |
| OLMESARTAN MEDOXOMIL | olmesartan |
| OLMESARTAN MEDOXOMIL/AMLODIPINE BESYLATE/HYDROCHLOROTHIAZIDE | Tribenzor |
| OLMESARTAN MEDOXOMIL/AMLODIPINE BESYLATE/HYDROCHLOROTHIAZIDE | olmesartan-amlodipin-hcthiazid |
| OLMESARTAN MEDOXOMIL/HYDROCHLOROTHIAZIDE | Benicar HCT |
| OLMESARTAN MEDOXOMIL/HYDROCHLOROTHIAZIDE | olmesartan-hydrochlorothiazide |
| TELMISARTAN | Micardis |
| TELMISARTAN | telmisartan |
| TELMISARTAN/AMLODIPINE BESYLATE | Twynsta |
| TELMISARTAN/AMLODIPINE BESYLATE | telmisartan-amlodipine |
| TELMISARTAN/HYDROCHLOROTHIAZIDE | Micardis HCT |
| TELMISARTAN/HYDROCHLOROTHIAZIDE | telmisartan-hydrochlorothiazid |
| VALSARTAN | Diovan |
| VALSARTAN | valsartan |
| VALSARTAN/HYDROCHLOROTHIAZIDE | Diovan HCT |
| VALSARTAN/HYDROCHLOROTHIAZIDE | valsartan-hydrochlorothiazide |
| amlodipine besylate/olmesartan medoxomil | amlodipine-olmesartan |
| amlodipine besylate/valsartan | amlodipine-valsartan |
| amlodipine besylate/valsartan/hydrochlorothiazide | amlodipine-valsartan-hcthiazid |
| candesartan cilexetil | Atacand |
| candesartan cilexetil | candesartan |
| candesartan cilexetil/hydrochlorothiazide | Atacand HCT |

**Appendix D. Generic and Brand Names of Medical Products Used to Define Exposure Incidence and Exclusion Criteria in this Request**

| Generic Name | Brand Name |
|---|---|
| candesartan cilexetil/hydrochlorothiazide | candesartan-hydrochlorothiazid |
| irbesartan | irbesartan |
| irbesartan/hydrochlorothiazide | irbesartan-hydrochlorothiazide |
| losartan potassium | losartan |
| losartan potassium/hydrochlorothiazide | losartan-hydrochlorothiazide |
| olmesartan medoxomil | Benicar |
| olmesartan medoxomil | olmesartan |
| olmesartan medoxomil/amlodipine besylate/hydrochlorothiazide | olmesartan-amlodipin-hcthiazid |
| olmesartan medoxomil/hydrochlorothiazide | Benicar HCT |
| telmisartan | telmisartan |
| telmisartan/hydrochlorothiazide | telmisartan-hydrochlorothiazid |
| valsartan | valsartan |
| valsartan/hydrochlorothiazide | valsartan-hydrochlorothiazide |

**Appendix E. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Codes Used to Define Inclusion Criteria in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| | **Heart Failure** | | |
| 402.01 | Malignant hypertensive heart disease with heart failure | Diagnosis | ICD-9-CM |
| 402.11 | Benign hypertensive heart disease with heart failure | Diagnosis | ICD-9-CM |
| 402.91 | Hypertensive heart disease, unspecified, with heart failure | Diagnosis | ICD-9-CM |
| 404.01 | Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified | Diagnosis | ICD-9-CM |
| 404.03 | Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage V or end stage renal disease | Diagnosis | ICD-9-CM |
| 404.11 | Hypertensive heart and chronic kidney disease, benign, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified | Diagnosis | ICD-9-CM |
| 404.13 | Hypertensive heart and chronic kidney disease, benign, with heart failure and chronic kidney disease stage V or end stage renal disease | Diagnosis | ICD-9-CM |
| 404.91 | Hypertensive heart and chronic kidney disease, unspecified, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified | Diagnosis | ICD-9-CM |
| 404.93 | Hypertensive heart and chronic kidney disease, unspecified, with heart failure and chronic kidney disease stage V or end stage renal disease | Diagnosis | ICD-9-CM |
| 428 | Heart failure | Diagnosis | ICD-9-CM |
| 428.0 | Congestive heart failure, unspecified | Diagnosis | ICD-9-CM |
| 428.1 | Left heart failure | Diagnosis | ICD-9-CM |
| 428.2 | Systolic heart failure | Diagnosis | ICD-9-CM |
| 428.20 | Unspecified systolic heart failure | Diagnosis | ICD-9-CM |
| 428.21 | Acute systolic heart failure | Diagnosis | ICD-9-CM |
| 428.22 | Chronic systolic heart failure | Diagnosis | ICD-9-CM |
| 428.23 | Acute on chronic systolic heart failure | Diagnosis | ICD-9-CM |
| 428.3 | Diastolic heart failure | Diagnosis | ICD-9-CM |
| 428.30 | Unspecified diastolic heart failure | Diagnosis | ICD-9-CM |
| 428.31 | Acute diastolic heart failure | Diagnosis | ICD-9-CM |
| 428.32 | Chronic diastolic heart failure | Diagnosis | ICD-9-CM |
| 428.33 | Acute on chronic diastolic heart failure | Diagnosis | ICD-9-CM |
| 428.4 | Combined systolic and diastolic heart failure | Diagnosis | ICD-9-CM |
| 428.40 | Unspecified combined systolic and diastolic heart failure | Diagnosis | ICD-9-CM |
| 428.41 | Acute combined systolic and diastolic heart failure | Diagnosis | ICD-9-CM |
| 428.42 | Chronic combined systolic and diastolic heart failure | Diagnosis | ICD-9-CM |
| 428.43 | Acute on chronic combined systolic and diastolic heart failure | Diagnosis | ICD-9-CM |
| 428.9 | Unspecified heart failure | Diagnosis | ICD-9-CM |
| I11.0 | Hypertensive heart disease with heart failure | Diagnosis | ICD-10-CM |
| I13.0 | Hypertensive heart and chronic kidney disease with heart failure and stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease | Diagnosis | ICD-10-CM |
| I13.2 | Hypertensive heart and chronic kidney disease with heart failure and with stage 5 chronic kidney disease, or end stage renal disease | Diagnosis | ICD-10-CM |
| I50 | Heart failure | Diagnosis | ICD-10-CM |
| I50.1 | Left ventricular failure, unspecified | Diagnosis | ICD-10-CM |
| I50.2 | Systolic (congestive) heart failure | Diagnosis | ICD-10-CM |
| I50.20 | Unspecified systolic (congestive) heart failure | Diagnosis | ICD-10-CM |
| I50.21 | Acute systolic (congestive) heart failure | Diagnosis | ICD-10-CM |
| I50.22 | Chronic systolic (congestive) heart failure | Diagnosis | ICD-10-CM |
| I50.23 | Acute on chronic systolic (congestive) heart failure | Diagnosis | ICD-10-CM |
| I50.3 | Diastolic (congestive) heart failure | Diagnosis | ICD-10-CM |

**Appendix E. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Codes Used to Define Inclusion Criteria in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| I50.30 | Unspecified diastolic (congestive) heart failure | Diagnosis | ICD-10-CM |
| I50.31 | Acute diastolic (congestive) heart failure | Diagnosis | ICD-10-CM |
| I50.32 | Chronic diastolic (congestive) heart failure | Diagnosis | ICD-10-CM |
| I50.33 | Acute on chronic diastolic (congestive) heart failure | Diagnosis | ICD-10-CM |
| I50.4 | Combined systolic (congestive) and diastolic (congestive) heart failure | Diagnosis | ICD-10-CM |
| I50.40 | Unspecified combined systolic (congestive) and diastolic (congestive) heart failure | Diagnosis | ICD-10-CM |
| I50.41 | Acute combined systolic (congestive) and diastolic (congestive) heart failure | Diagnosis | ICD-10-CM |
| I50.42 | Chronic combined systolic (congestive) and diastolic (congestive) heart failure | Diagnosis | ICD-10-CM |
| I50.43 | Acute on chronic combined systolic (congestive) and diastolic (congestive) heart failure | Diagnosis | ICD-10-CM |
| I50.810 | Right heart failure, unspecified | Diagnosis | ICD-10-CM |
| I50.811 | Acute right heart failure | Diagnosis | ICD-10-CM |
| I50.812 | Chronic right heart failure | Diagnosis | ICD-10-CM |
| I50.813 | Acute on chronic right heart failure | Diagnosis | ICD-10-CM |
| I50.814 | Right heart failure due to left heart failure | Diagnosis | ICD-10-CM |
| I50.82 | Biventricular heart failure | Diagnosis | ICD-10-CM |
| I50.83 | High output heart failure | Diagnosis | ICD-10-CM |
| I50.84 | End stage heart failure | Diagnosis | ICD-10-CM |
| I50.89 | Other heart failure | Diagnosis | ICD-10-CM |
| I50.9 | Heart failure, unspecified | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| | **Allergies** | | |
| 472.0 | Chronic rhinitis | Diagnosis | ICD-9-CM |
| 477.0 | Allergic rhinitis due to pollen | Diagnosis | ICD-9-CM |
| 477.1 | Allergic rhinitis, due to food | Diagnosis | ICD-9-CM |
| 477.2 | Allergic rhinitis due to animal (cat) (dog) hair and dander | Diagnosis | ICD-9-CM |
| 477.8 | Allergic rhinitis due to other allergen | Diagnosis | ICD-9-CM |
| 477.9 | Allergic rhinitis, cause unspecified | Diagnosis | ICD-9-CM |
| 478.8 | Upper respiratory tract hypersensitivity reaction, site unspecified | Diagnosis | ICD-9-CM |
| 558.3 | Gastroenteritis and colitis, allergic | Diagnosis | ICD-9-CM |
| 691.0 | Diaper or napkin rash | Diagnosis | ICD-9-CM |
| 691.8 | Other atopic dermatitis and related conditions | Diagnosis | ICD-9-CM |
| 692.0 | Contact dermatitis and other eczema due to detergents | Diagnosis | ICD-9-CM |
| 692.1 | Contact dermatitis and other eczema due to oils and greases | Diagnosis | ICD-9-CM |
| 692.2 | Contact dermatitis and other eczema due to solvents | Diagnosis | ICD-9-CM |
| 692.3 | Contact dermatitis and other eczema due to drugs and medicines in contact with skin | Diagnosis | ICD-9-CM |
| 692.4 | Contact dermatitis and other eczema due to other chemical products | Diagnosis | ICD-9-CM |
| 692.5 | Contact dermatitis and other eczema due to food in contact with skin | Diagnosis | ICD-9-CM |
| 692.6 | Contact dermatitis and other eczema due to plants (except food) | Diagnosis | ICD-9-CM |
| 692.70 | Unspecified dermatitis due to sun | Diagnosis | ICD-9-CM |
| 692.71 | Contact dermatitis and other eczema due to sunburn | Diagnosis | ICD-9-CM |
| 692.72 | Acute dermatitis due to solar radiation | Diagnosis | ICD-9-CM |
| 692.73 | Actinic reticuloid and actinic granuloma | Diagnosis | ICD-9-CM |
| 692.74 | Other chronic dermatitis due to solar radiation | Diagnosis | ICD-9-CM |
| 692.75 | Disseminated superficial actinic porokeratosis (DSAP) | Diagnosis | ICD-9-CM |
| 692.76 | Sunburn of second degree | Diagnosis | ICD-9-CM |
| 692.77 | Sunburn of third degree | Diagnosis | ICD-9-CM |
| 692.79 | Other dermatitis due to solar radiation | Diagnosis | ICD-9-CM |
| 692.81 | Dermatitis due to cosmetics | Diagnosis | ICD-9-CM |
| 692.82 | Dermatitis due to other radiation | Diagnosis | ICD-9-CM |
| 692.83 | Dermatitis due to metals | Diagnosis | ICD-9-CM |
| 692.84 | Contact dermatitis and other eczema due to animal (cat) (dog) dander | Diagnosis | ICD-9-CM |
| 692.89 | Contact dermatitis and other eczema due to other specified agent | Diagnosis | ICD-9-CM |
| 692.9 | Contact dermatitis and other eczema, due to unspecified cause | Diagnosis | ICD-9-CM |
| 693.0 | Dermatitis due to drugs and medicines taken internally | Diagnosis | ICD-9-CM |
| 693.1 | Dermatitis due to food taken internally | Diagnosis | ICD-9-CM |
| 693.8 | Dermatitis due to other specified substances taken internally | Diagnosis | ICD-9-CM |
| 693.9 | Dermatitis due to unspecified substance taken internally | Diagnosis | ICD-9-CM |
| 708.0 | Allergic urticaria | Diagnosis | ICD-9-CM |
| 708.1 | Idiopathic urticaria | Diagnosis | ICD-9-CM |
| 708.2 | Urticaria due to cold and heat | Diagnosis | ICD-9-CM |
| 708.3 | Dermatographic urticaria | Diagnosis | ICD-9-CM |
| 708.4 | Vibratory urticaria | Diagnosis | ICD-9-CM |
| 708.5 | Cholinergic urticaria | Diagnosis | ICD-9-CM |
| 708.8 | Other specified urticaria | Diagnosis | ICD-9-CM |
| 708.9 | Unspecified urticaria | Diagnosis | ICD-9-CM |
| 995.0 | Other anaphylactic reaction | Diagnosis | ICD-9-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| 995.27 | Other drug allergy | Diagnosis | ICD-9-CM |
| 995.3 | Allergy, unspecified not elsewhere classified | Diagnosis | ICD-9-CM |
| 995.7 | Other adverse food reactions, not elsewhere classified | Diagnosis | ICD-9-CM |
| J30.0 | Vasomotor rhinitis | Diagnosis | ICD-10-CM |
| J30.1 | Allergic rhinitis due to pollen | Diagnosis | ICD-10-CM |
| J30.2 | Other seasonal allergic rhinitis | Diagnosis | ICD-10-CM |
| J30.5 | Allergic rhinitis due to food | Diagnosis | ICD-10-CM |
| J30.81 | Allergic rhinitis due to animal (cat) (dog) hair and dander | Diagnosis | ICD-10-CM |
| J30.89 | Other allergic rhinitis | Diagnosis | ICD-10-CM |
| J30.9 | Allergic rhinitis, unspecified | Diagnosis | ICD-10-CM |
| J31.0 | Chronic rhinitis | Diagnosis | ICD-10-CM |
| J39.3 | Upper respiratory tract hypersensitivity reaction, site unspecified | Diagnosis | ICD-10-CM |
| K52.21 | Food protein-induced enterocolitis syndrome | Diagnosis | ICD-10-CM |
| K52.22 | Food protein-induced enteropathy | Diagnosis | ICD-10-CM |
| K52.29 | Other allergic and dietetic gastroenteritis and colitis | Diagnosis | ICD-10-CM |
| L20.0 | Besnier's prurigo | Diagnosis | ICD-10-CM |
| L20.81 | Atopic neurodermatitis | Diagnosis | ICD-10-CM |
| L20.82 | Flexural eczema | Diagnosis | ICD-10-CM |
| L20.84 | Intrinsic (allergic) eczema | Diagnosis | ICD-10-CM |
| L20.89 | Other atopic dermatitis | Diagnosis | ICD-10-CM |
| L20.9 | Atopic dermatitis, unspecified | Diagnosis | ICD-10-CM |
| L22 | Diaper dermatitis | Diagnosis | ICD-10-CM |
| L23.0 | Allergic contact dermatitis due to metals | Diagnosis | ICD-10-CM |
| L23.1 | Allergic contact dermatitis due to adhesives | Diagnosis | ICD-10-CM |
| L23.2 | Allergic contact dermatitis due to cosmetics | Diagnosis | ICD-10-CM |
| L23.3 | Allergic contact dermatitis due to drugs in contact with skin | Diagnosis | ICD-10-CM |
| L23.4 | Allergic contact dermatitis due to dyes | Diagnosis | ICD-10-CM |
| L23.5 | Allergic contact dermatitis due to other chemical products | Diagnosis | ICD-10-CM |
| L23.6 | Allergic contact dermatitis due to food in contact with the skin | Diagnosis | ICD-10-CM |
| L23.7 | Allergic contact dermatitis due to plants, except food | Diagnosis | ICD-10-CM |
| L23.81 | Allergic contact dermatitis due to animal (cat) (dog) dander | Diagnosis | ICD-10-CM |
| L23.89 | Allergic contact dermatitis due to other agents | Diagnosis | ICD-10-CM |
| L23.9 | Allergic contact dermatitis, unspecified cause | Diagnosis | ICD-10-CM |
| L24.0 | Irritant contact dermatitis due to detergents | Diagnosis | ICD-10-CM |
| L24.1 | Irritant contact dermatitis due to oils and greases | Diagnosis | ICD-10-CM |
| L24.2 | Irritant contact dermatitis due to solvents | Diagnosis | ICD-10-CM |
| L24.3 | Irritant contact dermatitis due to cosmetics | Diagnosis | ICD-10-CM |
| L24.4 | Irritant contact dermatitis due to drugs in contact with skin | Diagnosis | ICD-10-CM |
| L24.5 | Irritant contact dermatitis due to other chemical products | Diagnosis | ICD-10-CM |
| L24.6 | Irritant contact dermatitis due to food in contact with skin | Diagnosis | ICD-10-CM |
| L24.7 | Irritant contact dermatitis due to plants, except food | Diagnosis | ICD-10-CM |
| L24.81 | Irritant contact dermatitis due to metals | Diagnosis | ICD-10-CM |
| L24.89 | Irritant contact dermatitis due to other agents | Diagnosis | ICD-10-CM |
| L24.9 | Irritant contact dermatitis, unspecified cause | Diagnosis | ICD-10-CM |
| L25.0 | Unspecified contact dermatitis due to cosmetics | Diagnosis | ICD-10-CM |
| L25.1 | Unspecified contact dermatitis due to drugs in contact with skin | Diagnosis | ICD-10-CM |
| L25.2 | Unspecified contact dermatitis due to dyes | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| L25.3 | Unspecified contact dermatitis due to other chemical products | Diagnosis | ICD-10-CM |
| L25.4 | Unspecified contact dermatitis due to food in contact with skin | Diagnosis | ICD-10-CM |
| L25.5 | Unspecified contact dermatitis due to plants, except food | Diagnosis | ICD-10-CM |
| L25.8 | Unspecified contact dermatitis due to other agents | Diagnosis | ICD-10-CM |
| L25.9 | Unspecified contact dermatitis, unspecified cause | Diagnosis | ICD-10-CM |
| L27.0 | Generalized skin eruption due to drugs and medicaments taken internally | Diagnosis | ICD-10-CM |
| L27.1 | Localized skin eruption due to drugs and medicaments taken internally | Diagnosis | ICD-10-CM |
| L27.2 | Dermatitis due to ingested food | Diagnosis | ICD-10-CM |
| L27.8 | Dermatitis due to other substances taken internally | Diagnosis | ICD-10-CM |
| L27.9 | Dermatitis due to unspecified substance taken internally | Diagnosis | ICD-10-CM |
| L50.0 | Allergic urticaria | Diagnosis | ICD-10-CM |
| L50.1 | Idiopathic urticaria | Diagnosis | ICD-10-CM |
| L50.2 | Urticaria due to cold and heat | Diagnosis | ICD-10-CM |
| L50.3 | Dermatographic urticaria | Diagnosis | ICD-10-CM |
| L50.4 | Vibratory urticaria | Diagnosis | ICD-10-CM |
| L50.5 | Cholinergic urticaria | Diagnosis | ICD-10-CM |
| L50.6 | Contact urticaria | Diagnosis | ICD-10-CM |
| L50.8 | Other urticaria | Diagnosis | ICD-10-CM |
| L50.9 | Urticaria, unspecified | Diagnosis | ICD-10-CM |
| L55.0 | Sunburn of first degree | Diagnosis | ICD-10-CM |
| L55.1 | Sunburn of second degree | Diagnosis | ICD-10-CM |
| L55.2 | Sunburn of third degree | Diagnosis | ICD-10-CM |
| L55.9 | Sunburn, unspecified | Diagnosis | ICD-10-CM |
| L56.0 | Drug phototoxic response | Diagnosis | ICD-10-CM |
| L56.1 | Drug photoallergic response | Diagnosis | ICD-10-CM |
| L56.2 | Photocontact dermatitis [berloque dermatitis] | Diagnosis | ICD-10-CM |
| L56.3 | Solar urticaria | Diagnosis | ICD-10-CM |
| L56.4 | Polymorphous light eruption | Diagnosis | ICD-10-CM |
| L56.5 | Disseminated superficial actinic porokeratosis (DSAP) | Diagnosis | ICD-10-CM |
| L56.8 | Other specified acute skin changes due to ultraviolet radiation | Diagnosis | ICD-10-CM |
| L56.9 | Acute skin change due to ultraviolet radiation, unspecified | Diagnosis | ICD-10-CM |
| L57.1 | Actinic reticuloid | Diagnosis | ICD-10-CM |
| L57.5 | Actinic granuloma | Diagnosis | ICD-10-CM |
| L57.8 | Other skin changes due to chronic exposure to nonionizing radiation | Diagnosis | ICD-10-CM |
| L57.9 | Skin changes due to chronic exposure to nonionizing radiation, unspecified | Diagnosis | ICD-10-CM |
| L58.0 | Acute radiodermatitis | Diagnosis | ICD-10-CM |
| L58.1 | Chronic radiodermatitis | Diagnosis | ICD-10-CM |
| L58.9 | Radiodermatitis, unspecified | Diagnosis | ICD-10-CM |
| T50.995A | Adverse effect of other drugs, medicaments and biological substances, initial encounter | Diagnosis | ICD-10-CM |
| | | | |
| T78.0 | Anaphylactic reaction due to food | Diagnosis | ICD-10-CM |
| T78.00 | Anaphylactic reaction due to unspecified food | Diagnosis | ICD-10-CM |
| T78.00XA | Anaphylactic reaction due to unspecified food, initial encounter | Diagnosis | ICD-10-CM |
| T78.00XD | Anaphylactic reaction due to unspecified food, subsequent encounter | Diagnosis | ICD-10-CM |
| T78.00XS | Anaphylactic reaction due to unspecified food, sequela | Diagnosis | ICD-10-CM |
| T78.01 | Anaphylactic reaction due to peanuts | Diagnosis | ICD-10-CM |
| T78.01XA | Anaphylactic reaction due to peanuts, initial encounter | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| T78.01XD | Anaphylactic reaction due to peanuts, subsequent encounter | Diagnosis | ICD-10-CM |
| T78.01XS | Anaphylactic reaction due to peanuts, sequela | Diagnosis | ICD-10-CM |
| T78.02 | Anaphylactic reaction due to shellfish (crustaceans) | Diagnosis | ICD-10-CM |
| T78.02XA | Anaphylactic reaction due to shellfish (crustaceans), initial encounter | Diagnosis | ICD-10-CM |
| T78.02XD | Anaphylactic reaction due to shellfish (crustaceans), subsequent encounter | Diagnosis | ICD-10-CM |
| T78.02XS | Anaphylactic reaction due to shellfish (crustaceans), sequela | Diagnosis | ICD-10-CM |
| T78.03 | Anaphylactic reaction due to other fish | Diagnosis | ICD-10-CM |
| T78.03XA | Anaphylactic reaction due to other fish, initial encounter | Diagnosis | ICD-10-CM |
| T78.03XD | Anaphylactic reaction due to other fish, subsequent encounter | Diagnosis | ICD-10-CM |
| T78.03XS | Anaphylactic reaction due to other fish, sequela | Diagnosis | ICD-10-CM |
| T78.04 | Anaphylactic reaction due to fruits and vegetables | Diagnosis | ICD-10-CM |
| T78.04XA | Anaphylactic reaction due to fruits and vegetables, initial encounter | Diagnosis | ICD-10-CM |
| T78.04XD | Anaphylactic reaction due to fruits and vegetables, subsequent encounter | Diagnosis | ICD-10-CM |
| T78.04XS | Anaphylactic reaction due to fruits and vegetables, sequela | Diagnosis | ICD-10-CM |
| T78.05 | Anaphylactic reaction due to tree nuts and seeds | Diagnosis | ICD-10-CM |
| T78.05XA | Anaphylactic reaction due to tree nuts and seeds, initial encounter | Diagnosis | ICD-10-CM |
| T78.05XD | Anaphylactic reaction due to tree nuts and seeds, subsequent encounter | Diagnosis | ICD-10-CM |
| T78.05XS | Anaphylactic reaction due to tree nuts and seeds, sequela | Diagnosis | ICD-10-CM |
| T78.06 | Anaphylactic reaction due to food additives | Diagnosis | ICD-10-CM |
| T78.06XA | Anaphylactic reaction due to food additives, initial encounter | Diagnosis | ICD-10-CM |
| T78.06XD | Anaphylactic reaction due to food additives, subsequent encounter | Diagnosis | ICD-10-CM |
| T78.06XS | Anaphylactic reaction due to food additives, sequela | Diagnosis | ICD-10-CM |
| T78.07 | Anaphylactic reaction due to milk and dairy products | Diagnosis | ICD-10-CM |
| T78.07XA | Anaphylactic reaction due to milk and dairy products, initial encounter | Diagnosis | ICD-10-CM |
| T78.07XD | Anaphylactic reaction due to milk and dairy products, subsequent encounter | Diagnosis | ICD-10-CM |
| T78.07XS | Anaphylactic reaction due to milk and dairy products, sequela | Diagnosis | ICD-10-CM |
| T78.08 | Anaphylactic reaction due to eggs | Diagnosis | ICD-10-CM |
| T78.08XA | Anaphylactic reaction due to eggs, initial encounter | Diagnosis | ICD-10-CM |
| T78.08XD | Anaphylactic reaction due to eggs, subsequent encounter | Diagnosis | ICD-10-CM |
| T78.08XS | Anaphylactic reaction due to eggs, sequela | Diagnosis | ICD-10-CM |
| T78.09 | Anaphylactic reaction due to other food products | Diagnosis | ICD-10-CM |
| T78.09XA | Anaphylactic reaction due to other food products, initial encounter | Diagnosis | ICD-10-CM |
| T78.09XD | Anaphylactic reaction due to other food products, subsequent encounter | Diagnosis | ICD-10-CM |
| T78.09XS | Anaphylactic reaction due to other food products, sequela | Diagnosis | ICD-10-CM |
| T78.1XXA | Other adverse food reactions, not elsewhere classified, initial encounter | Diagnosis | ICD-10-CM |
| T78.2 | Anaphylactic shock, unspecified | Diagnosis | ICD-10-CM |
| T78.2XXA | Anaphylactic shock, unspecified, initial encounter | Diagnosis | ICD-10-CM |
| T78.2XXD | Anaphylactic shock, unspecified, subsequent encounter | Diagnosis | ICD-10-CM |
| T78.2XXS | Anaphylactic shock, unspecified, sequela | Diagnosis | ICD-10-CM |
| T78.40 | Allergy, unspecified | Diagnosis | ICD-10-CM |
| T78.40XA | Allergy, unspecified, initial encounter | Diagnosis | ICD-10-CM |
| T78.40XD | Allergy, unspecified, subsequent encounter | Diagnosis | ICD-10-CM |
| T78.40XS | Allergy, unspecified, sequela | Diagnosis | ICD-10-CM |
| T78.49XA | Other allergy, initial encounter | Diagnosis | ICD-10-CM |
| T80.5 | Anaphylactic reaction due to serum | Diagnosis | ICD-10-CM |
| T80.51 | Anaphylactic reaction due to administration of blood and blood products | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| T80.51XA | Anaphylactic reaction due to administration of blood and blood products, initial encounter | Diagnosis | ICD-10-CM |
| T80.51XD | Anaphylactic reaction due to administration of blood and blood products, subsequent encounter | Diagnosis | ICD-10-CM |
| T80.51XS | Anaphylactic reaction due to administration of blood and blood products, sequela | Diagnosis | ICD-10-CM |
| T80.52 | Anaphylactic reaction due to vaccination | Diagnosis | ICD-10-CM |
| T80.52XA | Anaphylactic reaction due to vaccination, initial encounter | Diagnosis | ICD-10-CM |
| T80.52XD | Anaphylactic reaction due to vaccination, subsequent encounter | Diagnosis | ICD-10-CM |
| T80.52XS | Anaphylactic reaction due to vaccination, sequela | Diagnosis | ICD-10-CM |
| T80.59 | Anaphylactic reaction due to other serum | Diagnosis | ICD-10-CM |
| T80.59XA | Anaphylactic reaction due to other serum, initial encounter | Diagnosis | ICD-10-CM |
| T80.59XD | Anaphylactic reaction due to other serum, subsequent encounter | Diagnosis | ICD-10-CM |
| T80.59XS | Anaphylactic reaction due to other serum, sequela | Diagnosis | ICD-10-CM |
| T88.6 | Anaphylactic reaction due to adverse effect of correct drug or medicament properly administered | Diagnosis | ICD-10-CM |
| T88.6XXA | Anaphylactic reaction due to adverse effect of correct drug or medicament properly administered, initial encounter | Diagnosis | ICD-10-CM |
| T88.6XXD | Anaphylactic reaction due to adverse effect of correct drug or medicament properly administered, subsequent encounter | Diagnosis | ICD-10-CM |
| T88.6XXS | Anaphylactic reaction due to adverse effect of correct drug or medicament properly administered, sequela | Diagnosis | ICD-10-CM |
| V07.1 | Need for desensitization to allergens | Diagnosis | ICD-9-CM |
| V13.81 | Personal history of anaphylaxis | Diagnosis | ICD-9-CM |
| V14.0 | Personal history of allergy to penicillin | Diagnosis | ICD-9-CM |
| V14.1 | Personal history of allergy to other antibiotic agent | Diagnosis | ICD-9-CM |
| V14.2 | Personal history of allergy to sulfonamides | Diagnosis | ICD-9-CM |
| V14.3 | Personal history of allergy to other anti-infective agent | Diagnosis | ICD-9-CM |
| V14.4 | Personal history of allergy to anesthetic agent | Diagnosis | ICD-9-CM |
| V14.5 | Personal history of allergy to narcotic agent | Diagnosis | ICD-9-CM |
| V14.6 | Personal history of allergy to analgesic agent | Diagnosis | ICD-9-CM |
| V14.7 | Personal history of allergy to serum or vaccine | Diagnosis | ICD-9-CM |
| V14.8 | Personal history of allergy to other specified medicinal agents | Diagnosis | ICD-9-CM |
| V14.9 | Personal history of allergy to unspecified medicinal agent | Diagnosis | ICD-9-CM |
| V15.09 | Personal history of other allergy, other than to medicinal agents | Diagnosis | ICD-9-CM |
| V72.7 | Diagnostic skin and sensitization tests | Diagnosis | ICD-9-CM |
| Z01.82 | Encounter for allergy testing | Diagnosis | ICD-10-CM |
| Z01.89 | Encounter for other specified special examinations | Diagnosis | ICD-10-CM |
| Z51.6 | Encounter for desensitization to allergens | Diagnosis | ICD-10-CM |
| Z87.892 | Personal history of anaphylaxis | Diagnosis | ICD-10-CM |
| Z88.0 | Allergy status to penicillin | Diagnosis | ICD-10-CM |
| Z88.1 | Allergy status to other antibiotic agents status | Diagnosis | ICD-10-CM |
| Z88.2 | Allergy status to sulfonamides status | Diagnosis | ICD-10-CM |
| Z88.3 | Allergy status to other anti-infective agents status | Diagnosis | ICD-10-CM |
| Z88.4 | Allergy status to anesthetic agent status | Diagnosis | ICD-10-CM |
| Z88.5 | Allergy status to narcotic agent status | Diagnosis | ICD-10-CM |
| Z88.6 | Allergy status to analgesic agent status | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| Z88.7 | Allergy status to serum and vaccine status | Diagnosis | ICD-10-CM |
| Z88.8 | Allergy status to other drugs, medicaments and biological substances status | Diagnosis | ICD-10-CM |
| Z88.9 | Allergy status to unspecified drugs, medicaments and biological substances status | Diagnosis | ICD-10-CM |
| Z91.0 | Allergy status, other than to drugs and biological substances | Diagnosis | ICD-10-CM |
| Z91.01 | Food allergy status | Diagnosis | ICD-10-CM |
| Z91.010 | Allergy to peanuts | Diagnosis | ICD-10-CM |
| Z91.011 | Allergy to milk products | Diagnosis | ICD-10-CM |
| Z91.012 | Allergy to eggs | Diagnosis | ICD-10-CM |
| Z91.013 | Allergy to seafood | Diagnosis | ICD-10-CM |
| Z91.018 | Allergy to other foods | Diagnosis | ICD-10-CM |
| Z91.02 | Food additives allergy status | Diagnosis | ICD-10-CM |
| Z91.03 | Insect allergy status | Diagnosis | ICD-10-CM |
| Z91.030 | Bee allergy status | Diagnosis | ICD-10-CM |
| Z91.038 | Other insect allergy status | Diagnosis | ICD-10-CM |
| Z91.04 | Nonmedicinal substance allergy status | Diagnosis | ICD-10-CM |
| Z91.040 | Latex allergy status | Diagnosis | ICD-10-CM |
| Z91.041 | Radiographic dye allergy status | Diagnosis | ICD-10-CM |
| Z91.048 | Other nonmedicinal substance allergy status | Diagnosis | ICD-10-CM |
| Z91.09 | Other allergy status, other than to drugs and biological substances | Diagnosis | ICD-10-CM |
| | **Angioedema** | | |
| 995.1 | Angioedema | Diagnosis | ICD-9-CM |
| T783XXA | Angioedema | Diagnosis | ICD-10-CM |
| T783XXD | Angioneurotic edema, sequela | Diagnosis | ICD-10-CM |
| T783XXS | Angioneurotic edema, subsequent encounter | Diagnosis | ICD-10-CM |
| | **Diabetes** | | |
| 250 | Diabetes mellitus | Diagnosis | ICD-9-CM |
| 250.0 | Diabetes mellitus without mention of complication | Diagnosis | ICD-9-CM |
| 250.00 | Diabetes mellitus without mention of complication, type II or unspecified type, not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.01 | Diabetes mellitus without mention of complication, type I [juvenile type], not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.02 | Diabetes mellitus without mention of complication, type II or unspecified type, uncontrolled | Diagnosis | ICD-9-CM |
| 250.03 | Diabetes mellitus without mention of complication, type I [juvenile type], uncontrolled | Diagnosis | ICD-9-CM |
| 250.1 | Diabetes with ketoacidosis | Diagnosis | ICD-9-CM |
| 250.10 | Diabetes with ketoacidosis, type II or unspecified type, not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.11 | Diabetes with ketoacidosis, type I [juvenile type], not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.12 | Diabetes with ketoacidosis, type II or unspecified type, uncontrolled | Diagnosis | ICD-9-CM |
| 250.13 | Diabetes with ketoacidosis, type I [juvenile type], uncontrolled | Diagnosis | ICD-9-CM |
| 250.2 | Diabetes with hyperosmolarity | Diagnosis | ICD-9-CM |
| 250.20 | Diabetes with hyperosmolarity, type II or unspecified type, not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.21 | Diabetes with hyperosmolarity, type I [juvenile type], not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.22 | Diabetes with hyperosmolarity, type II or unspecified type, uncontrolled | Diagnosis | ICD-9-CM |
| 250.23 | Diabetes with hyperosmolarity, type I [juvenile type], uncontrolled | Diagnosis | ICD-9-CM |
| 250.3 | Diabetes with other coma | Diagnosis | ICD-9-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| 250.30 | Diabetes with other coma, type II or unspecified type, not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.31 | Diabetes with other coma, type I [juvenile type], not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.32 | Diabetes with other coma, type II or unspecified type, uncontrolled | Diagnosis | ICD-9-CM |
| 250.33 | Diabetes with other coma, type I [juvenile type], uncontrolled | Diagnosis | ICD-9-CM |
| 250.4 | Diabetes with renal manifestations | Diagnosis | ICD-9-CM |
| 250.40 | Diabetes with renal manifestations, type II or unspecified type, not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.41 | Diabetes with renal manifestations, type I [juvenile type], not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.42 | Diabetes with renal manifestations, type II or unspecified type, uncontrolled | Diagnosis | ICD-9-CM |
| 250.43 | Diabetes with renal manifestations, type I [juvenile type], uncontrolled | Diagnosis | ICD-9-CM |
| 250.5 | Diabetes with ophthalmic manifestations | Diagnosis | ICD-9-CM |
| 250.50 | Diabetes with ophthalmic manifestations, type II or unspecified type, not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.51 | Diabetes with ophthalmic manifestations, type I [juvenile type], not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.52 | Diabetes with ophthalmic manifestations, type II or unspecified type, uncontrolled | Diagnosis | ICD-9-CM |
| 250.53 | Diabetes with ophthalmic manifestations, type I [juvenile type], uncontrolled | Diagnosis | ICD-9-CM |
| 250.6 | Diabetes with neurological manifestations | Diagnosis | ICD-9-CM |
| 250.60 | Diabetes with neurological manifestations, type II or unspecified type, not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.61 | Diabetes with neurological manifestations, type I [juvenile type], not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.62 | Diabetes with neurological manifestations, type II or unspecified type, uncontrolled | Diagnosis | ICD-9-CM |
| 250.63 | Diabetes with neurological manifestations, type I [juvenile type], uncontrolled | Diagnosis | ICD-9-CM |
| 250.7 | Diabetes with peripheral circulatory disorders | Diagnosis | ICD-9-CM |
| 250.70 | Diabetes with peripheral circulatory disorders, type II or unspecified type, not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.71 | Diabetes with peripheral circulatory disorders, type I [juvenile type], not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.72 | Diabetes with peripheral circulatory disorders, type II or unspecified type, uncontrolled | Diagnosis | ICD-9-CM |
| 250.73 | Diabetes with peripheral circulatory disorders, type I [juvenile type], uncontrolled | Diagnosis | ICD-9-CM |
| 250.8 | Diabetes with other specified manifestations | Diagnosis | ICD-9-CM |
| 250.80 | Diabetes with other specified manifestations, type II or unspecified type, not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.81 | Diabetes with other specified manifestations, type I [juvenile type], not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.82 | Diabetes with other specified manifestations, type II or unspecified type, uncontrolled | Diagnosis | ICD-9-CM |
| 250.83 | Diabetes with other specified manifestations, type I [juvenile type], uncontrolled | Diagnosis | ICD-9-CM |
| 250.9 | Diabetes with unspecified complication | Diagnosis | ICD-9-CM |
| 250.90 | Diabetes with unspecified complication, type II or unspecified type, not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.91 | Diabetes with unspecified complication, type I [juvenile type], not stated as uncontrolled | Diagnosis | ICD-9-CM |
| 250.92 | Diabetes with unspecified complication, type II or unspecified type, uncontrolled | Diagnosis | ICD-9-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| 250.93 | Diabetes with unspecified complication, type I [juvenile type], uncontrolled | Diagnosis | ICD-9-CM |
| A5500 | For diabetics only, fitting (including follow-up), custom preparation and supply of off-the-shelf depth-inlay shoe manufactured to accommodate multidensity insert(s), per shoe | Procedure | HCPCS |
| A5501 | For diabetics only, fitting (including follow-up), custom preparation and supply of shoe molded from cast(s) of patient's foot (custom molded shoe), per shoe | Procedure | HCPCS |
| A5503 | For diabetics only, modification (including fitting) of off-the-shelf depth-inlay shoe or custom molded shoe with roller or rigid rocker bottom, per shoe | Procedure | HCPCS |
| A5504 | For diabetics only, modification (including fitting) of off-the-shelf depth-inlay shoe or custom molded shoe with wedge(s), per shoe | Procedure | HCPCS |
| A5505 | For diabetics only, modification (including fitting) of off-the-shelf depth-inlay shoe or custom molded shoe with metatarsal bar, per shoe | Procedure | HCPCS |
| A5506 | For diabetics only, modification (including fitting) of off-the-shelf depth-inlay shoe or custom molded shoe with off-set heel(s), per shoe | Procedure | HCPCS |
| A5507 | For diabetics only, not otherwise specified modification (including fitting) of off-the-shelf depth-inlay shoe or custom molded shoe, per shoe | Procedure | HCPCS |
| A5508 | For diabetics only, deluxe feature of off-the-shelf depth-inlay shoe or custom molded shoe, per shoe | Procedure | HCPCS |
| A5510 | For diabetics only, direct formed, compression molded to patient's foot without external heat source, multiple-density insert(s) prefabricated, per shoe | Procedure | HCPCS |
| A5512 | For diabetics only, multiple density insert, direct formed, molded to foot after external heat source of 230 degrees Fahrenheit or higher, total contact with patient's foot, including arch, base layer minimum of 1/4 inch material of shore a 35 durome | Procedure | HCPCS |
| A5513 | For diabetics only, multiple density insert, custom molded from model of patient's foot, total contact with patient's foot, including arch, base layer minimum of 3/16 inch material of shore a 35 durometer or higher), includes arch filler and other sh | Procedure | HCPCS |
| E10.10 | Type 1 diabetes mellitus with ketoacidosis without coma | Diagnosis | ICD-10-CM |
| E10.11 | Type 1 diabetes mellitus with ketoacidosis with coma | Diagnosis | ICD-10-CM |
| E10.21 | Type 1 diabetes mellitus with diabetic nephropathy | Diagnosis | ICD-10-CM |
| E10.22 | Type 1 diabetes mellitus with diabetic chronic kidney disease | Diagnosis | ICD-10-CM |
| E10.29 | Type 1 diabetes mellitus with other diabetic kidney complication | Diagnosis | ICD-10-CM |
| E10.311 | Type 1 diabetes mellitus with unspecified diabetic retinopathy with macular edema | Diagnosis | ICD-10-CM |
| E10.319 | Type 1 diabetes mellitus with unspecified diabetic retinopathy without macular edema | Diagnosis | ICD-10-CM |
| E10.3211 | Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| E10.3212 | Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye | Diagnosis | ICD-10-CM |
| E10.3213 | Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral | Diagnosis | ICD-10-CM |
| E10.3219 | Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E10.3291 | Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, right eye | Diagnosis | ICD-10-CM |
| E10.3292 | Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, left eye | Diagnosis | ICD-10-CM |
| E10.3293 | Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, bilateral | Diagnosis | ICD-10-CM |
| E10.3299 | Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E10.3311 | Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye | Diagnosis | ICD-10-CM |
| E10.3312 | Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye | Diagnosis | ICD-10-CM |
| E10.3313 | Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral | Diagnosis | ICD-10-CM |
| E10.3319 | Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E10.3391 | Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, right eye | Diagnosis | ICD-10-CM |
| E10.3392 | Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, left eye | Diagnosis | ICD-10-CM |
| E10.3393 | Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, bilateral | Diagnosis | ICD-10-CM |
| E10.3399 | Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E10.3411 | Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye | Diagnosis | ICD-10-CM |
| E10.3412 | Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye | Diagnosis | ICD-10-CM |
| E10.3413 | Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral | Diagnosis | ICD-10-CM |
| E10.3419 | Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E10.3491 | Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, right eye | Diagnosis | ICD-10-CM |
| E10.3492 | Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, left eye | Diagnosis | ICD-10-CM |
| E10.3493 | Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, bilateral | Diagnosis | ICD-10-CM |
| E10.3499 | Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, unspecified eye | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| E10.3511 | Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye | Diagnosis | ICD-10-CM |
| E10.3512 | Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye | Diagnosis | ICD-10-CM |
| E10.3513 | Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral | Diagnosis | ICD-10-CM |
| E10.3519 | Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E10.3521 | Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye | Diagnosis | ICD-10-CM |
| E10.3522 | Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye | Diagnosis | ICD-10-CM |
| E10.3523 | Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral | Diagnosis | ICD-10-CM |
| E10.3529 | Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, unspecified eye | Diagnosis | ICD-10-CM |
| E10.3531 | Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye | Diagnosis | ICD-10-CM |
| E10.3532 | Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye | Diagnosis | ICD-10-CM |
| E10.3533 | Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral | Diagnosis | ICD-10-CM |
| E10.3539 | Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, unspecified eye | Diagnosis | ICD-10-CM |
| E10.3541 | Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye | Diagnosis | ICD-10-CM |
| E10.3542 | Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye | Diagnosis | ICD-10-CM |
| E10.3543 | Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral | Diagnosis | ICD-10-CM |
| E10.3549 | Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, unspecified eye | Diagnosis | ICD-10-CM |
| E10.3551 | Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, right eye | Diagnosis | ICD-10-CM |
| E10.3552 | Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, left eye | Diagnosis | ICD-10-CM |
| E10.3553 | Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, bilateral | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| E10.3559 | Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, unspecified eye | Diagnosis | ICD-10-CM |
| E10.3591 | Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye | Diagnosis | ICD-10-CM |
| E10.3592 | Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye | Diagnosis | ICD-10-CM |
| E10.3593 | Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral | Diagnosis | ICD-10-CM |
| E10.3599 | Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E10.36 | Type 1 diabetes mellitus with diabetic cataract | Diagnosis | ICD-10-CM |
| E10.37X1 | Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, right eye | Diagnosis | ICD-10-CM |
| E10.37X2 | Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, left eye | Diagnosis | ICD-10-CM |
| E10.37X3 | Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, bilateral | Diagnosis | ICD-10-CM |
| E10.37X9 | Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, unspecified eye | Diagnosis | ICD-10-CM |
| E10.39 | Type 1 diabetes mellitus with other diabetic ophthalmic complication | Diagnosis | ICD-10-CM |
| E10.40 | Type 1 diabetes mellitus with diabetic neuropathy, unspecified | Diagnosis | ICD-10-CM |
| E10.41 | Type 1 diabetes mellitus with diabetic mononeuropathy | Diagnosis | ICD-10-CM |
| E10.42 | Type 1 diabetes mellitus with diabetic polyneuropathy | Diagnosis | ICD-10-CM |
| E10.43 | Type 1 diabetes mellitus with diabetic autonomic (poly)neuropathy | Diagnosis | ICD-10-CM |
| E10.44 | Type 1 diabetes mellitus with diabetic amyotrophy | Diagnosis | ICD-10-CM |
| E10.49 | Type 1 diabetes mellitus with other diabetic neurological complication | Diagnosis | ICD-10-CM |
| E10.51 | Type 1 diabetes mellitus with diabetic peripheral angiopathy without gangrene | Diagnosis | ICD-10-CM |
| E10.52 | Type 1 diabetes mellitus with diabetic peripheral angiopathy with gangrene | Diagnosis | ICD-10-CM |
| E10.59 | Type 1 diabetes mellitus with other circulatory complications | Diagnosis | ICD-10-CM |
| E10.610 | Type 1 diabetes mellitus with diabetic neuropathic arthropathy | Diagnosis | ICD-10-CM |
| E10.618 | Type 1 diabetes mellitus with other diabetic arthropathy | Diagnosis | ICD-10-CM |
| E10.620 | Type 1 diabetes mellitus with diabetic dermatitis | Diagnosis | ICD-10-CM |
| E10.621 | Type 1 diabetes mellitus with foot ulcer | Diagnosis | ICD-10-CM |
| E10.622 | Type 1 diabetes mellitus with other skin ulcer | Diagnosis | ICD-10-CM |
| E10.628 | Type 1 diabetes mellitus with other skin complications | Diagnosis | ICD-10-CM |
| E10.630 | Type 1 diabetes mellitus with periodontal disease | Diagnosis | ICD-10-CM |
| E10.638 | Type 1 diabetes mellitus with other oral complications | Diagnosis | ICD-10-CM |
| E10.641 | Type 1 diabetes mellitus with hypoglycemia with coma | Diagnosis | ICD-10-CM |
| E10.649 | Type 1 diabetes mellitus with hypoglycemia without coma | Diagnosis | ICD-10-CM |
| E10.65 | Type 1 diabetes mellitus with hyperglycemia | Diagnosis | ICD-10-CM |
| E10.69 | Type 1 diabetes mellitus with other specified complication | Diagnosis | ICD-10-CM |
| E10.8 | Type 1 diabetes mellitus with unspecified complications | Diagnosis | ICD-10-CM |
| E10.9 | Type 1 diabetes mellitus without complications | Diagnosis | ICD-10-CM |
| E11.00 | Type 2 diabetes mellitus with hyperosmolarity without nonketotic hyperglycemic-hyperosmolar coma (NKHHC) | Diagnosis | ICD-10-CM |
| E11.01 | Type 2 diabetes mellitus with hyperosmolarity with coma | Diagnosis | ICD-10-CM |
| E11.21 | Type 2 diabetes mellitus with diabetic nephropathy | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| E11.22 | Type 2 diabetes mellitus with diabetic chronic kidney disease | Diagnosis | ICD-10-CM |
| E11.29 | Type 2 diabetes mellitus with other diabetic kidney complication | Diagnosis | ICD-10-CM |
| E11.311 | Type 2 diabetes mellitus with unspecified diabetic retinopathy with macular edema | Diagnosis | ICD-10-CM |
| E11.319 | Type 2 diabetes mellitus with unspecified diabetic retinopathy without macular edema | Diagnosis | ICD-10-CM |
| E11.3211 | Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye | Diagnosis | ICD-10-CM |
| E11.3212 | Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye | Diagnosis | ICD-10-CM |
| E11.3213 | Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral | Diagnosis | ICD-10-CM |
| E11.3219 | Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E11.3291 | Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, right eye | Diagnosis | ICD-10-CM |
| E11.3292 | Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, left eye | Diagnosis | ICD-10-CM |
| E11.3293 | Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, bilateral | Diagnosis | ICD-10-CM |
| E11.3299 | Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E11.3311 | Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye | Diagnosis | ICD-10-CM |
| E11.3312 | Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye | Diagnosis | ICD-10-CM |
| E11.3313 | Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral | Diagnosis | ICD-10-CM |
| E11.3319 | Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E11.3391 | Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, right eye | Diagnosis | ICD-10-CM |
| E11.3392 | Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, left eye | Diagnosis | ICD-10-CM |
| E11.3393 | Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, bilateral | Diagnosis | ICD-10-CM |
| E11.3399 | Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E11.3411 | Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye | Diagnosis | ICD-10-CM |
| E11.3412 | Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye | Diagnosis | ICD-10-CM |
| E11.3413 | Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral | Diagnosis | ICD-10-CM |
| E11.3419 | Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E11.3491 | Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, right eye | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| E11.3492 | Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, left eye | Diagnosis | ICD-10-CM |
| E11.3493 | Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, bilateral | Diagnosis | ICD-10-CM |
| E11.3499 | Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E11.3511 | Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye | Diagnosis | ICD-10-CM |
| E11.3512 | Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye | Diagnosis | ICD-10-CM |
| E11.3513 | Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral | Diagnosis | ICD-10-CM |
| E11.3519 | Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E11.3521 | Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye | Diagnosis | ICD-10-CM |
| E11.3522 | Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye | Diagnosis | ICD-10-CM |
| E11.3523 | Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral | Diagnosis | ICD-10-CM |
| E11.3529 | Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, unspecified eye | Diagnosis | ICD-10-CM |
| E11.3531 | Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye | Diagnosis | ICD-10-CM |
| E11.3532 | Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye | Diagnosis | ICD-10-CM |
| E11.3533 | Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral | Diagnosis | ICD-10-CM |
| E11.3539 | Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, unspecified eye | Diagnosis | ICD-10-CM |
| E11.3541 | Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye | Diagnosis | ICD-10-CM |
| E11.3542 | Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye | Diagnosis | ICD-10-CM |
| E11.3543 | Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| E11.3549 | Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, unspecified eye | Diagnosis | ICD-10-CM |
| E11.3551 | Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, right eye | Diagnosis | ICD-10-CM |
| E11.3552 | Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, left eye | Diagnosis | ICD-10-CM |
| E11.3553 | Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, bilateral | Diagnosis | ICD-10-CM |
| E11.3559 | Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, unspecified eye | Diagnosis | ICD-10-CM |
| E11.3591 | Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye | Diagnosis | ICD-10-CM |
| E11.3592 | Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye | Diagnosis | ICD-10-CM |
| E11.3593 | Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral | Diagnosis | ICD-10-CM |
| E11.3599 | Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E11.36 | Type 2 diabetes mellitus with diabetic cataract | Diagnosis | ICD-10-CM |
| E11.37X1 | Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, right eye | Diagnosis | ICD-10-CM |
| E11.37X2 | Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, left eye | Diagnosis | ICD-10-CM |
| E11.37X3 | Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, bilateral | Diagnosis | ICD-10-CM |
| E11.37X9 | Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, unspecified eye | Diagnosis | ICD-10-CM |
| E11.39 | Type 2 diabetes mellitus with other diabetic ophthalmic complication | Diagnosis | ICD-10-CM |
| E11.40 | Type 2 diabetes mellitus with diabetic neuropathy, unspecified | Diagnosis | ICD-10-CM |
| E11.41 | Type 2 diabetes mellitus with diabetic mononeuropathy | Diagnosis | ICD-10-CM |
| E11.42 | Type 2 diabetes mellitus with diabetic polyneuropathy | Diagnosis | ICD-10-CM |
| E11.43 | Type 2 diabetes mellitus with diabetic autonomic (poly)neuropathy | Diagnosis | ICD-10-CM |
| E11.44 | Type 2 diabetes mellitus with diabetic amyotrophy | Diagnosis | ICD-10-CM |
| E11.49 | Type 2 diabetes mellitus with other diabetic neurological complication | Diagnosis | ICD-10-CM |
| E11.51 | Type 2 diabetes mellitus with diabetic peripheral angiopathy without gangrene | Diagnosis | ICD-10-CM |
| E11.52 | Type 2 diabetes mellitus with diabetic peripheral angiopathy with gangrene | Diagnosis | ICD-10-CM |
| E11.59 | Type 2 diabetes mellitus with other circulatory complications | Diagnosis | ICD-10-CM |
| E11.610 | Type 2 diabetes mellitus with diabetic neuropathic arthropathy | Diagnosis | ICD-10-CM |
| E11.618 | Type 2 diabetes mellitus with other diabetic arthropathy | Diagnosis | ICD-10-CM |
| E11.620 | Type 2 diabetes mellitus with diabetic dermatitis | Diagnosis | ICD-10-CM |
| E11.621 | Type 2 diabetes mellitus with foot ulcer | Diagnosis | ICD-10-CM |
| E11.622 | Type 2 diabetes mellitus with other skin ulcer | Diagnosis | ICD-10-CM |
| E11.628 | Type 2 diabetes mellitus with other skin complications | Diagnosis | ICD-10-CM |
| E11.630 | Type 2 diabetes mellitus with periodontal disease | Diagnosis | ICD-10-CM |
| E11.638 | Type 2 diabetes mellitus with other oral complications | Diagnosis | ICD-10-CM |
| E11.641 | Type 2 diabetes mellitus with hypoglycemia with coma | Diagnosis | ICD-10-CM |
| E11.649 | Type 2 diabetes mellitus with hypoglycemia without coma | Diagnosis | ICD-10-CM |
| E11.65 | Type 2 diabetes mellitus with hyperglycemia | Diagnosis | ICD-10-CM |
| E11.69 | Type 2 diabetes mellitus with other specified complication | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| E11.8 | Type 2 diabetes mellitus with unspecified complications | Diagnosis | ICD-10-CM |
| E11.9 | Type 2 diabetes mellitus without complications | Diagnosis | ICD-10-CM |
| E13.00 | Other specified diabetes mellitus with hyperosmolarity without nonketotic hyperglycemic-hyperosmolar coma (NKHHC) | Diagnosis | ICD-10-CM |
| E13.01 | Other specified diabetes mellitus with hyperosmolarity with coma | Diagnosis | ICD-10-CM |
| E13.10 | Other specified diabetes mellitus with ketoacidosis without coma | Diagnosis | ICD-10-CM |
| E13.11 | Other specified diabetes mellitus with ketoacidosis with coma | Diagnosis | ICD-10-CM |
| E13.21 | Other specified diabetes mellitus with diabetic nephropathy | Diagnosis | ICD-10-CM |
| E13.22 | Other specified diabetes mellitus with diabetic chronic kidney disease | Diagnosis | ICD-10-CM |
| E13.29 | Other specified diabetes mellitus with other diabetic kidney complication | Diagnosis | ICD-10-CM |
| E13.311 | Other specified diabetes mellitus with unspecified diabetic retinopathy with macular edema | Diagnosis | ICD-10-CM |
| E13.319 | Other specified diabetes mellitus with unspecified diabetic retinopathy without macular edema | Diagnosis | ICD-10-CM |
| E13.3211 | Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye | Diagnosis | ICD-10-CM |
| E13.3212 | Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye | Diagnosis | ICD-10-CM |
| E13.3213 | Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral | Diagnosis | ICD-10-CM |
| E13.3219 | Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E13.3291 | Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, right eye | Diagnosis | ICD-10-CM |
| E13.3292 | Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, left eye | Diagnosis | ICD-10-CM |
| E13.3293 | Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, bilateral | Diagnosis | ICD-10-CM |
| E13.3299 | Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E13.3311 | Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye | Diagnosis | ICD-10-CM |
| E13.3312 | Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye | Diagnosis | ICD-10-CM |
| E13.3313 | Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral | Diagnosis | ICD-10-CM |
| E13.3319 | Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E13.3391 | Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, right eye | Diagnosis | ICD-10-CM |
| E13.3392 | Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, left eye | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| E13.3393 | Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, bilateral | Diagnosis | ICD-10-CM |
| E13.3399 | Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E13.3411 | Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye | Diagnosis | ICD-10-CM |
| E13.3412 | Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye | Diagnosis | ICD-10-CM |
| E13.3413 | Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral | Diagnosis | ICD-10-CM |
| E13.3419 | Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E13.3491 | Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, right eye | Diagnosis | ICD-10-CM |
| E13.3492 | Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, left eye | Diagnosis | ICD-10-CM |
| E13.3493 | Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, bilateral | Diagnosis | ICD-10-CM |
| E13.3499 | Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E13.3511 | Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye | Diagnosis | ICD-10-CM |
| E13.3512 | Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye | Diagnosis | ICD-10-CM |
| E13.3513 | Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral | Diagnosis | ICD-10-CM |
| E13.3519 | Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E13.3521 | Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye | Diagnosis | ICD-10-CM |
| E13.3522 | Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye | Diagnosis | ICD-10-CM |
| E13.3523 | Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral | Diagnosis | ICD-10-CM |
| E13.3529 | Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, unspecified eye | Diagnosis | ICD-10-CM |
| E13.3531 | Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| E13.3532 | Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye | Diagnosis | ICD-10-CM |
| E13.3533 | Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral | Diagnosis | ICD-10-CM |
| E13.3539 | Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, unspecified eye | Diagnosis | ICD-10-CM |
| E13.3541 | Other specified diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye | Diagnosis | ICD-10-CM |
| E13.3542 | Other specified diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye | Diagnosis | ICD-10-CM |
| E13.3543 | Other specified diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral | Diagnosis | ICD-10-CM |
| E13.3549 | Other specified diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, unspecified eye | Diagnosis | ICD-10-CM |
| E13.3551 | Other specified diabetes mellitus with stable proliferative diabetic retinopathy, right eye | Diagnosis | ICD-10-CM |
| E13.3552 | Other specified diabetes mellitus with stable proliferative diabetic retinopathy, left eye | Diagnosis | ICD-10-CM |
| | Other specified diabetes mellitus with stable proliferative diabetic retinopathy, bilateral | Diagnosis | ICD-10-CM |
| E13.3553 | Other specified diabetes mellitus with stable proliferative diabetic retinopathy, unspecified eye | Diagnosis | ICD-10-CM |
| E13.3559 | Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye | Diagnosis | ICD-10-CM |
| E13.3591 | Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye | Diagnosis | ICD-10-CM |
| E13.3592 | Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral | Diagnosis | ICD-10-CM |
| E13.3593 | Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema, unspecified eye | Diagnosis | ICD-10-CM |
| E13.3599 | Other specified diabetes mellitus with diabetic cataract | Diagnosis | ICD-10-CM |
| E13.36 | Other specified diabetes mellitus with diabetic macular edema, resolved following treatment, right eye | Diagnosis | ICD-10-CM |
| E13.37X1 | Other specified diabetes mellitus with diabetic macular edema, resolved following treatment, left eye | Diagnosis | ICD-10-CM |
| E13.37X2 | Other specified diabetes mellitus with diabetic macular edema, resolved following treatment, bilateral | Diagnosis | ICD-10-CM |
| E13.37X3 | Other specified diabetes mellitus with diabetic macular edema, resolved following treatment, unspecified eye | Diagnosis | ICD-10-CM |
| E13.37X9 | Other specified diabetes mellitus with other diabetic ophthalmic complication | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| E13.39 | Other specified diabetes mellitus with diabetic neuropathy, unspecified | Diagnosis | ICD-10-CM |
| E13.40 | Other specified diabetes mellitus with diabetic mononeuropathy | Diagnosis | ICD-10-CM |
| E13.41 | Other specified diabetes mellitus with diabetic polyneuropathy | Diagnosis | ICD-10-CM |
| E13.42 | Other specified diabetes mellitus with diabetic autonomic (poly)neuropathy | Diagnosis | ICD-10-CM |
| E13.43 | Other specified diabetes mellitus with diabetic amyotrophy | Diagnosis | ICD-10-CM |
| E13.44 | Other specified diabetes mellitus with other diabetic neurological complication | Diagnosis | ICD-10-CM |
| E13.49 | Other specified diabetes mellitus with diabetic peripheral angiopathy without gangrene | Diagnosis | ICD-10-CM |
| E13.51 | Other specified diabetes mellitus with diabetic peripheral angiopathy with gangrene | Diagnosis | ICD-10-CM |
| E13.52 | Other specified diabetes mellitus with other circulatory complications | Diagnosis | ICD-10-CM |
| E13.59 | Other specified diabetes mellitus with diabetic neuropathic arthropathy | Diagnosis | ICD-10-CM |
| E13.610 | Other specified diabetes mellitus with other diabetic arthropathy | Diagnosis | ICD-10-CM |
| E13.618 | Other specified diabetes mellitus with diabetic dermatitis | Diagnosis | ICD-10-CM |
| E13.620 | Other specified diabetes mellitus with foot ulcer | Diagnosis | ICD-10-CM |
| E13.621 | Other specified diabetes mellitus with other skin ulcer | Diagnosis | ICD-10-CM |
| E13.622 | Other specified diabetes mellitus with other skin complications | Diagnosis | ICD-10-CM |
| E13.628 | Other specified diabetes mellitus with periodontal disease | Diagnosis | ICD-10-CM |
| E13.630 | Other specified diabetes mellitus with other oral complications | Diagnosis | ICD-10-CM |
| E13.638 | Other specified diabetes mellitus with hypoglycemia with coma | Diagnosis | ICD-10-CM |
| E13.641 | Other specified diabetes mellitus with hypoglycemia without coma | Diagnosis | ICD-10-CM |
| E13.649 | Other specified diabetes mellitus with hyperglycemia | Diagnosis | ICD-10-CM |
| E13.65 | Other specified diabetes mellitus with other specified complication | Diagnosis | ICD-10-CM |
| E13.69 | Other specified diabetes mellitus with unspecified complications | Diagnosis | ICD-10-CM |
| E13.8 | Other specified diabetes mellitus without complications | Diagnosis | ICD-10-CM |
| E13.9 | Diabetes outpatient self-management training services, individual, per 30 minutes | Procedure | HCPCS |
| G0108 | Diabetes outpatient self-management training services, group session (2 or more), per 30 minutes | Procedure | HCPCS |
| G0109 | Initial physician evaluation and management of a diabetic patient with diabetic sensory neuropathy resulting in a loss of protective sensation (LOPS) which must include: (1) the diagnosis of LOPS, (2) a patient history, (3) a physical examination tha | Procedure | HCPCS |
| G0245 | Follow-up physician evaluation and management of a diabetic patient with diabetic sensory neuropathy resulting in a loss of protective sensation (LOPS) to include at least the following: (1) a patient history, (2) a physical examination that includes | Procedure | HCPCS |
| G0246 | Routine foot care by a physician of a diabetic patient with diabetic sensory neuropathy resulting in a loss of protective sensation (LOPS) to include the local care of superficial wounds (i.e., superficial to muscle and fascia) and at least the follo | Procedure | HCPCS |
| G0247 | Diabetic patient with most recent hemoglobin A1c level (within the last 6 months) documented as greater than 9% | Procedure | HCPCS |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| G8015 | Diabetic patient with most recent hemoglobin A1c level (within the last 6 months) documented as less than or equal to 9% | Procedure | HCPCS |
| G8016 | Clinician documented that diabetic patient was not eligible candidate for hemoglobin A1c measure | Procedure | HCPCS |
| G8017 | Clinician has not provided care for the diabetic patient for the required time for hemoglobin A1c measure (6 months) | Procedure | HCPCS |
| G8018 | Diabetic patient with most recent low-density lipoprotein (within the last 12 months) documented as greater than or equal to 100 mg/dl | Procedure | HCPCS |
| G8019 | Diabetic patient with most recent low-density lipoprotein (within the last 12 months) documented as less than 100 mg/dl | Procedure | HCPCS |
| G8020 | Clinician documented that diabetic patient was not eligible candidate for low-density lipoprotein measure | Procedure | HCPCS |
| G8021 | Clinician has not provided care for the diabetic patient for the required time for low-density lipoprotein measure (12 months) | Procedure | HCPCS |
| G8022 | Diabetic patient with most recent blood pressure (within the last 6 months) documented as equal to or greater than 140 systolic or equal to or greater than 80 mm Hg diastolic | Procedure | HCPCS |
| G8023 | Diabetic patient with most recent blood pressure (within the last 6 months) documented as less than 140 systolic and less than 80 diastolic | Procedure | HCPCS |
| G8024 | Clinician documented that the diabetic patient was not eligible candidate for blood pressure measure | Procedure | HCPCS |
| G8025 | Clinician has not provided care for the diabetic patient for the required time for blood pressure measure (within the last 6 months) | Procedure | HCPCS |
| G8026 | Clinician has not provided care for the diabetic retinopathy patient for the required time for macular edema and retinopathy measurement | Procedure | HCPCS |
| G8332 | Patient documented to have had findings of macular or fundus exam communicated to the physician managing the diabetes care | Procedure | HCPCS |
| G8333 | Documentation of findings of macular or fundus exam not communicated to the physician managing the patient's ongoing diabetes care | Procedure | HCPCS |
| G8334 | Clinician documentation that patient was not an eligible candidate for the findings of their macular or fundus exam being communicated to the physician managing their diabetes care during the reporting year | Procedure | HCPCS |
| G8335 | Clinician has not provided care for the diabetic retinopathy patient for the required time for physician communication measurement | Procedure | HCPCS |
| G8336 | Diabetic patients with no documentation of hemoglobin A1c level (within the last 12 months) | Procedure | HCPCS |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| G8385 | Diabetic patients with no documentation of low-density lipoprotein (within the last 12 months) | Procedure | HCPCS |
| G8386 | Diabetic patients with no documentation of blood pressure measurement (within the last 12 months) | Procedure | HCPCS |
| | **Ischemic Heart Disease** | | |
| 411 | Other acute and subacute forms of ischemic heart disease | Diagnosis | ICD-9-CM |
| 411.0 | Postmyocardial infarction syndrome | Diagnosis | ICD-9-CM |
| 411.1 | Intermediate coronary syndrome | Diagnosis | ICD-9-CM |
| 411.8 | Other acute and subacute forms of ischemic heart disease | Diagnosis | ICD-9-CM |
| 411.81 | Acute coronary occlusion without myocardial infarction | Diagnosis | ICD-9-CM |
| 411.89 | Other acute and subacute form of ischemic heart disease | Diagnosis | ICD-9-CM |
| 413 | Angina pectoris | Diagnosis | ICD-9-CM |
| 413.0 | Angina decubitus | Diagnosis | ICD-9-CM |
| 413.1 | Prinzmetal angina | Diagnosis | ICD-9-CM |
| 413.9 | Other and unspecified angina pectoris | Diagnosis | ICD-9-CM |
| 414 | Other forms of chronic ischemic heart disease | Diagnosis | ICD-9-CM |
| 414.0 | Coronary atherosclerosis | Diagnosis | ICD-9-CM |
| 414.00 | Coronary atherosclerosis of unspecified type of vessel, native or graft | Diagnosis | ICD-9-CM |
| 414.01 | Coronary atherosclerosis of native coronary artery | Diagnosis | ICD-9-CM |
| 414.02 | Coronary atherosclerosis of autologous vein bypass graft | Diagnosis | ICD-9-CM |
| 414.03 | Coronary atherosclerosis of nonautologous biological bypass graft | Diagnosis | ICD-9-CM |
| 414.04 | Coronary atherosclerosis of artery bypass graft | Diagnosis | ICD-9-CM |
| 414.05 | Coronary atherosclerosis of unspecified type of bypass graft | Diagnosis | ICD-9-CM |
| 414.06 | Coronary atherosclerosis, of native coronary artery of transplanted heart | Diagnosis | ICD-9-CM |
| 414.07 | Coronary atherosclerosis, of bypass graft (artery) (vein) of transplanted heart | Diagnosis | ICD-9-CM |
| 414.1 | Aneurysm and dissection of heart | Diagnosis | ICD-9-CM |
| 414.10 | Aneurysm of heart | Diagnosis | ICD-9-CM |
| 414.11 | Aneurysm of coronary vessels | Diagnosis | ICD-9-CM |
| 414.12 | Dissection of coronary artery | Diagnosis | ICD-9-CM |
| 414.19 | Other aneurysm of heart | Diagnosis | ICD-9-CM |
| 414.2 | Chronic total occlusion of coronary artery | Diagnosis | ICD-9-CM |
| 414.3 | Coronary atherosclerosis due to lipid rich plaque | Diagnosis | ICD-9-CM |
| 414.4 | Coronary atherosclerosis due to calcified coronary lesion | Diagnosis | ICD-9-CM |
| 414.8 | Other specified forms of chronic ischemic heart disease | Diagnosis | ICD-9-CM |
| 414.9 | Unspecified chronic ischemic heart disease | Diagnosis | ICD-9-CM |
| 429.2 | Unspecified cardiovascular disease | Diagnosis | ICD-9-CM |
| 429.5 | Rupture of chordae tendineae | Diagnosis | ICD-9-CM |
| 429.6 | Rupture of papillary muscle | Diagnosis | ICD-9-CM |
| 429.7 | Certain sequelae of myocardial infarction, not elsewhere classified | Diagnosis | ICD-9-CM |
| 429.71 | Acquired cardiac septal defect | Diagnosis | ICD-9-CM |
| 429.79 | Other certain sequelae of myocardial infarction, not elsewhere classified | Diagnosis | ICD-9-CM |
| 429.9 | Unspecified heart disease | Diagnosis | ICD-9-CM |
| G8033 | Prior myocardial infarction, coronary artery disease patient documented to be on beta-blocker therapy | Procedure | HCPCS |
| G8034 | Prior myocardial infarction, coronary artery disease patient not documented to be on beta-blocker therapy | Procedure | HCPCS |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| G8035 | Clinician documented that prior myocardial infarction, coronary artery disease patient was not eligible candidate for beta-blocker therapy measure | Procedure | HCPCS |
| G8036 | Coronary artery disease patient documented to be on antiplatelet therapy | Procedure | HCPCS |
| G8037 | Coronary artery disease patient not documented to be on antiplatelet therapy | Procedure | HCPCS |
| G8038 | Clinician documented that coronary artery disease patient was not eligible candidate for antiplatelet therapy measure | Procedure | HCPCS |
| G8039 | Coronary artery disease patient with low-density lipoprotein documented to be greater than 100 mg/dl | Procedure | HCPCS |
| G8040 | Coronary artery disease patient with low-density lipoprotein documented to be less than or equal to 100 mg/dl | Procedure | HCPCS |
| G8041 | Clinician documented that coronary artery disease patient was not eligible candidate for low-density lipoprotein measure | Procedure | HCPCS |
| I20.0 | Unstable angina | Diagnosis | ICD-10-CM |
| I20.1 | Angina pectoris with documented spasm | Diagnosis | ICD-10-CM |
| I20.8 | Other forms of angina pectoris | Diagnosis | ICD-10-CM |
| I20.9 | Angina pectoris, unspecified | Diagnosis | ICD-10-CM |
| I23.0 | Hemopericardium as current complication following acute myocardial infarction | Diagnosis | ICD-10-CM |
| I23.1 | Atrial septal defect as current complication following acute myocardial infarction | Diagnosis | ICD-10-CM |
| I23.2 | Ventricular septal defect as current complication following acute myocardial infarction | Diagnosis | ICD-10-CM |
| I23.3 | Rupture of cardiac wall without hemopericardium as current complication following acute myocardial infarction | Diagnosis | ICD-10-CM |
| I23.4 | Rupture of chordae tendineae as current complication following acute myocardial infarction | Diagnosis | ICD-10-CM |
| I23.5 | Rupture of papillary muscle as current complication following acute myocardial infarction | Diagnosis | ICD-10-CM |
| I23.6 | Thrombosis of atrium, auricular appendage, and ventricle as current complications following acute myocardial infarction | Diagnosis | ICD-10-CM |
| I23.7 | Postinfarction angina | Diagnosis | ICD-10-CM |
| I23.8 | Other current complications following acute myocardial infarction | Diagnosis | ICD-10-CM |
| I24.0 | Acute coronary thrombosis not resulting in myocardial infarction | Diagnosis | ICD-10-CM |
| I24.1 | Dressler's syndrome | Diagnosis | ICD-10-CM |
| I24.8 | Other forms of acute ischemic heart disease | Diagnosis | ICD-10-CM |
| I24.9 | Acute ischemic heart disease, unspecified | Diagnosis | ICD-10-CM |
| I25.10 | Atherosclerotic heart disease of native coronary artery without angina pectoris | Diagnosis | ICD-10-CM |
| I25.110 | Atherosclerotic heart disease of native coronary artery with unstable angina pectoris | Diagnosis | ICD-10-CM |
| I25.111 | Atherosclerotic heart disease of native coronary artery with angina pectoris with documented spasm | Diagnosis | ICD-10-CM |
| I25.118 | Atherosclerotic heart disease of native coronary artery with other forms of angina pectoris | Diagnosis | ICD-10-CM |
| I25.119 | Atherosclerotic heart disease of native coronary artery with unspecified angina pectoris | Diagnosis | ICD-10-CM |
| I25.3 | Aneurysm of heart | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| I25.41 | Coronary artery aneurysm | Diagnosis | ICD-10-CM |
| I25.42 | Coronary artery dissection | Diagnosis | ICD-10-CM |
| I25.5 | Ischemic cardiomyopathy | Diagnosis | ICD-10-CM |
| I25.6 | Silent myocardial ischemia | Diagnosis | ICD-10-CM |
| I25.700 | Atherosclerosis of coronary artery bypass graft(s), unspecified, with unstable angina pectoris | Diagnosis | ICD-10-CM |
| I25.701 | Atherosclerosis of coronary artery bypass graft(s), unspecified, with angina pectoris with documented spasm | Diagnosis | ICD-10-CM |
| I25.708 | Atherosclerosis of coronary artery bypass graft(s), unspecified, with other forms of angina pectoris | Diagnosis | ICD-10-CM |
| I25.709 | Atherosclerosis of coronary artery bypass graft(s), unspecified, with unspecified angina pectoris | Diagnosis | ICD-10-CM |
| I25.710 | Atherosclerosis of autologous vein coronary artery bypass graft(s) with unstable angina pectoris | Diagnosis | ICD-10-CM |
| I25.711 | Atherosclerosis of autologous vein coronary artery bypass graft(s) with angina pectoris with documented spasm | Diagnosis | ICD-10-CM |
| I25.718 | Atherosclerosis of autologous vein coronary artery bypass graft(s) with other forms of angina pectoris | Diagnosis | ICD-10-CM |
| I25.719 | Atherosclerosis of autologous vein coronary artery bypass graft(s) with unspecified angina pectoris | Diagnosis | ICD-10-CM |
| I25.720 | Atherosclerosis of autologous artery coronary artery bypass graft(s) with unstable angina pectoris | Diagnosis | ICD-10-CM |
| I25.721 | Atherosclerosis of autologous artery coronary artery bypass graft(s) with angina pectoris with documented spasm | Diagnosis | ICD-10-CM |
| I25.728 | Atherosclerosis of autologous artery coronary artery bypass graft(s) with other forms of angina pectoris | Diagnosis | ICD-10-CM |
| I25.729 | Atherosclerosis of autologous artery coronary artery bypass graft(s) with unspecified angina pectoris | Diagnosis | ICD-10-CM |
| I25.730 | Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unstable angina pectoris | Diagnosis | ICD-10-CM |
| I25.731 | Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with angina pectoris with documented spasm | Diagnosis | ICD-10-CM |
| I25.738 | Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with other forms of angina pectoris | Diagnosis | ICD-10-CM |
| I25.739 | Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unspecified angina pectoris | Diagnosis | ICD-10-CM |
| I25.750 | Atherosclerosis of native coronary artery of transplanted heart with unstable angina | Diagnosis | ICD-10-CM |
| I25.751 | Atherosclerosis of native coronary artery of transplanted heart with angina pectoris with documented spasm | Diagnosis | ICD-10-CM |
| I25.758 | Atherosclerosis of native coronary artery of transplanted heart with other forms of angina pectoris | Diagnosis | ICD-10-CM |
| I25.759 | Atherosclerosis of native coronary artery of transplanted heart with unspecified angina pectoris | Diagnosis | ICD-10-CM |
| I25.760 | Atherosclerosis of bypass graft of coronary artery of transplanted heart with unstable angina | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| I25.761 | Atherosclerosis of bypass graft of coronary artery of transplanted heart with angina pectoris with documented spasm | Diagnosis | ICD-10-CM |
| I25.768 | Atherosclerosis of bypass graft of coronary artery of transplanted heart with other forms of angina pectoris | Diagnosis | ICD-10-CM |
| I25.769 | Atherosclerosis of bypass graft of coronary artery of transplanted heart with unspecified angina pectoris | Diagnosis | ICD-10-CM |
| I25.790 | Atherosclerosis of other coronary artery bypass graft(s) with unstable angina pectoris | Diagnosis | ICD-10-CM |
| I25.791 | Atherosclerosis of other coronary artery bypass graft(s) with angina pectoris with documented spasm | Diagnosis | ICD-10-CM |
| I25.798 | Atherosclerosis of other coronary artery bypass graft(s) with other forms of angina pectoris | Diagnosis | ICD-10-CM |
| I25.799 | Atherosclerosis of other coronary artery bypass graft(s) with unspecified angina pectoris | Diagnosis | ICD-10-CM |
| I25.810 | Atherosclerosis of coronary artery bypass graft(s) without angina pectoris | Diagnosis | ICD-10-CM |
| I25.811 | Atherosclerosis of native coronary artery of transplanted heart without angina pectoris | Diagnosis | ICD-10-CM |
| I25.812 | Atherosclerosis of bypass graft of coronary artery of transplanted heart without angina pectoris | Diagnosis | ICD-10-CM |
| I25.82 | Chronic total occlusion of coronary artery | Diagnosis | ICD-10-CM |
| I25.83 | Coronary atherosclerosis due to lipid rich plaque | Diagnosis | ICD-10-CM |
| I25.84 | Coronary atherosclerosis due to calcified coronary lesion | Diagnosis | ICD-10-CM |
| I25.89 | Other forms of chronic ischemic heart disease | Diagnosis | ICD-10-CM |
| I25.9 | Chronic ischemic heart disease, unspecified | Diagnosis | ICD-10-CM |
| I51.0 | Cardiac septal defect, acquired | Diagnosis | ICD-10-CM |
| I51.1 | Rupture of chordae tendineae, not elsewhere classified | Diagnosis | ICD-10-CM |
| I51.2 | Rupture of papillary muscle, not elsewhere classified | Diagnosis | ICD-10-CM |
| I51.9 | Heart disease, unspecified | Diagnosis | ICD-10-CM |
| I52 | Other heart disorders in diseases classified elsewhere | Diagnosis | ICD-10-CM |
| | **Renal Disorders** | | |
| 584 | Acute kidney failure | Diagnosis | ICD-9-CM |
| 584.5 | Acute kidney failure with lesion of tubular necrosis | Diagnosis | ICD-9-CM |
| 584.6 | Acute kidney failure with lesion of renal cortical necrosis | Diagnosis | ICD-9-CM |
| 584.7 | Acute kidney failure with lesion of medullary [papillary] necrosis | Diagnosis | ICD-9-CM |
| 584.8 | Acute kidney failure with other specified pathological lesion in kidney | Diagnosis | ICD-9-CM |
| 584.9 | Acute kidney failure, unspecified | Diagnosis | ICD-9-CM |
| 585 | Chronic kidney disease (CKD) | Diagnosis | ICD-9-CM |
| 585.1 | Chronic kidney disease, Stage I | Diagnosis | ICD-9-CM |
| 585.2 | Chronic kidney disease, Stage II (mild) | Diagnosis | ICD-9-CM |
| 585.3 | Chronic kidney disease, Stage III (moderate) | Diagnosis | ICD-9-CM |
| 585.4 | Chronic kidney disease, Stage IV (severe) | Diagnosis | ICD-9-CM |
| 585.5 | Chronic kidney disease, Stage V | Diagnosis | ICD-9-CM |
| 585.6 | End stage renal disease | Diagnosis | ICD-9-CM |
| 585.9 | Chronic kidney disease, unspecified | Diagnosis | ICD-9-CM |
| 586 | Unspecified renal failure | Diagnosis | ICD-9-CM |
| 587 | Unspecified renal sclerosis | Diagnosis | ICD-9-CM |
| N17.0 | Acute kidney failure with tubular necrosis | Diagnosis | ICD-10-CM |

**Appendix F. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System, Level II (HCPCS) Codes Used to Define Covariates in this Request**

| Code | Description | Code Category | Code Type |
|---|---|---|---|
| N17.1 | Acute kidney failure with acute cortical necrosis | Diagnosis | ICD-10-CM |
| N17.2 | Acute kidney failure with medullary necrosis | Diagnosis | ICD-10-CM |
| N17.8 | Other acute kidney failure | Diagnosis | ICD-10-CM |
| N17.9 | Acute kidney failure, unspecified | Diagnosis | ICD-10-CM |
| N18.1 | Chronic kidney disease, stage 1 | Diagnosis | ICD-10-CM |
| N18.2 | Chronic kidney disease, stage 2 (mild) | Diagnosis | ICD-10-CM |
| N18.3 | Chronic kidney disease, stage 3 (moderate) | Diagnosis | ICD-10-CM |
| N18.4 | Chronic kidney disease, stage 4 (severe) | Diagnosis | ICD-10-CM |
| N18.5 | Chronic kidney disease, stage 5 | Diagnosis | ICD-10-CM |
| N18.6 | End stage renal disease | Diagnosis | ICD-10-CM |
| N18.9 | Chronic kidney disease, unspecified | Diagnosis | ICD-10-CM |
| N19 | Unspecified kidney failure | Diagnosis | ICD-10-CM |
| N26.1 | Atrophy of kidney (terminal) | Diagnosis | ICD-10-CM |
| N26.9 | Renal sclerosis, unspecified | Diagnosis | ICD-10-CM |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| **Allergy Treatments** | |
| Chlorpheniramine Maleate/Codeine Phosphate/Acetaminophen | Cotabflu |
| DIPHENHYDRAMINE HCL | Dicopanol |
| acetaminophen/dextromethorphan HBr | Child Cough and Sore Throat |
| aclidinium bromide | Tudorza Pressair |
| albuterol sulfate | ProAir HFA |
| albuterol sulfate | ProAir RespiClick |
| albuterol sulfate | Proventil HFA |
| albuterol sulfate | Ventolin HFA |
| albuterol sulfate | Vospire ER |
| albuterol sulfate | albuterol sulfate |
| alcaftadine | Lastacaft |
| aldosterone | aldosterone (bulk) |
| aminophylline | aminophylline |
| aminophylline | aminophylline (bulk) |
| arformoterol tartrate | Brovana |
| azelastine HCl | Astelin |
| azelastine HCl | Astepro |
| azelastine HCl | Optivar |
| azelastine HCl | azelastine |
| azelastine HCl/fluticasone propionate | Dymista |
| azelastine/fluticasone/sodium chloride/sodium bicarbonate | Ticalast |
| beclomethasone dipropionate | Beconase AQ |
| beclomethasone dipropionate | QNASL |
| beclomethasone dipropionate | Qvar |
| beclomethasone dipropionate | Qvar RediHaler |
| benralizumab | Fasenra |
| bepotastine besilate | Bepreve |
| betamethasone acetate and sodium phos in sterile water/PF | betameth ac,sodphos(PF)-water |
| betamethasone acetate and sodium phosph/norflurane/HFC 245fa | Betaloan SUIK |
| betamethasone acetate and sodium phosph/norflurane/HFC 245fa | Pod-Care 100CG |
| betamethasone acetate/betamethasone sodium phosphate | Beta-1 |
| betamethasone acetate/betamethasone sodium phosphate | Celestone Soluspan |
| betamethasone acetate/betamethasone sodium phosphate | Pod-Care 100C |
| betamethasone acetate/betamethasone sodium phosphate | ReadySharp Betamethasone |
| betamethasone acetate/betamethasone sodium phosphate | betamethasone acet,sod phos |
| betamethasone acetate/betamethasone sodium phosphate/water | betamethasone ace,sodphos-wtr |
| betamethasone sodium phosph in sterile water for injection | betamethasone sodphosph-water |
| brompheniramine maleate | J-TAN PD |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| brompheniramine maleate | brompheniramine maleate(bulk) |
| brompheniramine maleate/phenylephrine HCl | Children's Cold-Allergy (PE) |
| brompheniramine maleate/phenylephrine HCl | Dimaphen (PE) |
| brompheniramine maleate/phenylephrine HCl | Glenmax PEB |
| brompheniramine maleate/phenylephrine HCl | Relhist BP |
| brompheniramine maleate/phenylephrine HCl/chlophedianol HCl | Trexbrom |
| brompheniramine maleate/phenylephrine HCl/codeine phosphate | M-END PE |
| brompheniramine maleate/phenylephrine HCl/codeine phosphate | Poly-Tussin AC |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | AP-Hist DM |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Ala-Hist DM |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Altipres-B |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Bio T Pres-B |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | BroveX PEB DM |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Children's Cold and Cough(PE) |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Children's Cold and CoughDM |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Children's Dibromm DMCold-Cou |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Cold and Cough DM |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Cold and Cough Elixir |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Dimaphen DM |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Dimetapp DM Cold-Cough(PE) |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | EndaCof - DM |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Glenmax PEB DM |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Glenmax PEB DM Forte |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | LoHist PEB DM |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | LoHist-DM |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | M-Hist DM |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Niva-Hist DM |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Presgen B |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | RelCof DM |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Rynex DM |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Tussi Pres-B |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | Wal-tap DM |
| brompheniramine maleate/phenylephrine HCl/dextromethorphan | brompheniramin-phenylephrin-DM |
| brompheniramine maleate/pseudoephedrine HCl/chlophedianol | Atuss DA |
| brompheniramine maleate/pseudoephedrine HCl/dextromethorphan | brompheniramine-pseudoeph-DM |
| budesonide | Pulmicort |
| budesonide | Pulmicort Flexhaler |
| budesonide | Rhinocort Allergy |
| budesonide | Rhinocort Aqua |
| budesonide | budesonide |
| budesonide, micronized | budesonide, micronized (bulk) |
| budesonide/formoterol fumarate | Symbicort |
| carbinoxamine maleate | Arbinoxa |
| carbinoxamine maleate | Karbinal ER |
| carbinoxamine maleate | PALGIC |
| carbinoxamine maleate | RyVent |
| carbinoxamine maleate | carbinoxamine maleate |
| cetirizine HCl | 24Hour Allergy |
| cetirizine HCl | All Day Allergy (cetirizine) |
| cetirizine HCl | All Day Allergy Relief(cetir) |
| cetirizine HCl | Aller-Tec |
| cetirizine HCl | Allergy Relief (cetirizine) |
| cetirizine HCl | Child Allergy Relf(cetirizine) |
| cetirizine HCl | Child's All Day Allergy(cetir) |
| cetirizine HCl | Children's Aller-Tec |
| cetirizine HCl | Children's Allergy Complete |
| cetirizine HCl | Children's Allergy(cetirizine) |
| cetirizine HCl | Children's Cetirizine |
| cetirizine HCl | Children's Wal-Zyr |
| cetirizine HCl | Children's Zyrtec Allergy |
| cetirizine HCl | Wal-Zyr (cetirizine) |
| cetirizine HCl | Zyrtec |
| cetirizine HCl | cetirizine |
| cetirizine HCl/pseudoephedrine HCl | All Day Allergy-D |
| cetirizine HCl/pseudoephedrine HCl | Aller-Tec D |
| cetirizine HCl/pseudoephedrine HCl | Allergy Complete-D |
| cetirizine HCl/pseudoephedrine HCl | Allergy D-12 |
| cetirizine HCl/pseudoephedrine HCl | Allergy Relief-D (cetirizine) |
| cetirizine HCl/pseudoephedrine HCl | Allergy-Congest Relief-D (cet) |
| cetirizine HCl/pseudoephedrine HCl | Cetiri-D |
| cetirizine HCl/pseudoephedrine HCl | Wal-Zyr D |
| cetirizine HCl/pseudoephedrine HCl | Zyrtec-D |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| cetirizine HCl/pseudoephedrine HCl | cetirizine-pseudoephedrine |
| chlophedianol HCl/guaifenesin | Chlo Tuss EX |
| chlophedianol HCl/guaifenesin | Vanacof G |
| chlophedianol HCl/guaifenesin | chlophedianol-guaifenesin |
| chlorcyclizine HCl | Ahist (chlorcyclizine) |
| chlorcyclizine HCl/codeine phosphate | Poly-Tussin |
| chlorcyclizine HCl/phenylephrine HCl | Dallergy (chlorcyclizine-PE) |
| chlorcyclizine HCl/pseudoephedrine HCl | Nasopen |
| chlorcyclizine HCl/pseudoephedrine HCl | Stahist AD |
| chlorcyclizine HCl/pseudoephedrine HCl/chlophedianol HCl | Biclora-D |
| chlorcyclizine HCl/pseudoephedrine HCl/codeine phosphate | Poly-Tussin D |
| chlorcyclizine hydrochloride/chlophedianol hydrochloride | Biclora |
| chlorpheniram/phenyleph/dextromethorphn /acetaminophen/guaifn | Cold-Flu M-SymptomDay-Night |
| chlorpheniram/phenyleph/dextromethorphn /acetaminophen/guaifn | Tylenol Cold-Flu SevereDay-Nt |
| chlorpheniramine maleate | Aller-Chlor |
| chlorpheniramine maleate | Allergy (chlorpheniramine) |
| chlorpheniramine maleate | Allergy 4-Hour |
| chlorpheniramine maleate | Allergy Relief(chlorpheniramn) |
| chlorpheniramine maleate | Allergy-Time |
| chlorpheniramine maleate | Chlor-Trimeton |
| chlorpheniramine maleate | Chlorphen SR |
| chlorpheniramine maleate | ED Chlorped Jr |
| chlorpheniramine maleate | Ed-ChlorPed |
| chlorpheniramine maleate | Ed-Chlortan |
| chlorpheniramine maleate | Pharbechlor |
| chlorpheniramine maleate | Wal-Finate |
| chlorpheniramine maleate | chlorpheniramine maleate |
| chlorpheniramine maleate/codeine phosphate | Codar AR |
| chlorpheniramine maleate/codeine phosphate | EndaCof-C |
| chlorpheniramine maleate/codeine phosphate | Tuxarin ER |
| chlorpheniramine maleate/codeine phosphate | Z-Tuss AC |
| chlorpheniramine maleate/codeine phosphate | Zodryl AC 25 |
| chlorpheniramine maleate/codeine phosphate | Zodryl AC 30 |
| chlorpheniramine maleate/codeine phosphate | Zodryl AC 35 |
| chlorpheniramine maleate/codeine phosphate | Zodryl AC 40 |
| chlorpheniramine maleate/codeine phosphate | Zodryl AC 50 |
| chlorpheniramine maleate/codeine phosphate | Zodryl AC 60 |
| chlorpheniramine maleate/codeine phosphate | Zodryl AC 80 |
| chlorpheniramine maleate/dextromethorphan HBr | Chld Robitussin Night CoughDM |
| chlorpheniramine maleate/dextromethorphan HBr | Cough and Cold(chlorphen-DM) |
| chlorpheniramine maleate/dextromethorphan HBr | Cough-Cold Relief HBP |
| chlorpheniramine maleate/dextromethorphan HBr | Maxi-TussDM(chlorpheniramine) |
| chlorpheniramine maleate/dextromethorphan HBr | Scot-Tussin DM |
| chlorpheniramine maleate/phenylephrine HCl | Cold and Allergy |
| chlorpheniramine maleate/phenylephrine HCl | Sinus and Allergy PE |
| chlorpheniramine maleate/phenylephrine HCl | Sinus-Allergy (phenylephrine) |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| chlorpheniramine maleate/phenylephrine HCl/chlophedianol HCl | Carbaphen CH |
| chlorpheniramine maleate/phenylephrine HCl/chlophedianol HCl | Carbaphen Ped CH |
| chlorpheniramine maleate/phenylephrine HCl/chlophedianol HCl | ExaPhen CH |
| chlorpheniramine maleate/phenylephrine HCl/chlophedianol HCl | Phenagil CH |
| chlorpheniramine maleate/phenylephrine HCl/codeine phosphate | CapCof |
| chlorpheniramine maleate/phenylephrine HCl/codeine phosphate | Maxi-Tuss CD |
| chlorpheniramine maleate/phenylephrine HCl/dextromethorphan | Bio-Rytuss |
| chlorpheniramine maleate/phenylephrine HCl/dextromethorphan | Maxichlor PEH DM |
| chlorpheniramine maleate/phenylephrine HCl/ibuprofen | Advil Allergy-Congestion Rlf |
| chlorpheniramine maleate/phenylephrine bitartrate/aspirin | Cold Relief |
| chlorpheniramine maleate/phenylephrine bitartrate/aspirin | Cold Relief Plus |
| chlorpheniramine maleate/pseudoephedrine HCl/codeine | Tricode AR |
| chlorpheniramine maleate/pseudoephedrine HCl/codeine | Zodryl DAC 25 |
| chlorpheniramine maleate/pseudoephedrine HCl/codeine | Zodryl DAC 30 |
| chlorpheniramine maleate/pseudoephedrine HCl/codeine | Zodryl DAC 35 |
| chlorpheniramine maleate/pseudoephedrine HCl/codeine | Zodryl DAC 40 |
| chlorpheniramine maleate/pseudoephedrine HCl/codeine | Zodryl DAC 50 |
| chlorpheniramine maleate/pseudoephedrine HCl/codeine | Zodryl DAC 60 |
| chlorpheniramine maleate/pseudoephedrine HCl/codeine | Zodryl DAC 80 |
| chlorpheniramine maleate/pseudoephedrine HCl/ibuprofen | Advil Allergy Sinus |
| ciclesonide | Alvesco |
| ciclesonide | Omnaris |
| ciclesonide | Zetonna |
| clemastine fumarate | Allergy Relief (clemastine) |
| clemastine fumarate | Allerhist (clemastine) |
| clemastine fumarate | Allerhist-1 |
| clemastine fumarate | Dayhist Allergy |
| clemastine fumarate | Tavist-1 |
| clemastine fumarate | clemastine |
| clemizole HCl | clemizole HCl (bulk) |
| codeine phosphate/guaifenesin | G Tussin AC |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| codeine phosphate/guaifenesin | Robafen AC |
| codeine phosphate/guaifenesin | Virtussin AC |
| codeine phosphate/guaifenesin | codeine-guaifenesin |
| codeine phosphate/pyrilamine maleate | Pro-Clear AC |
| codeine polistirex/chlorpheniramine polistirex | Tuzistra XR |
| cortisone acetate | cortisone |
| cromolyn sodium | Nasal Allergy SymptomControl |
| cromolyn sodium | cromolyn |
| cyproheptadine HCl | cyproheptadine |
| cyproheptadine HCl | cyproheptadine (bulk) |
| deflazacort | Emflaza |
| desloratadine | Clarinex |
| desloratadine | desloratadine |
| desloratadine/pseudoephedrine sulfate | Clarinex-D 12 HOUR |
| desloratadine/pseudoephedrine sulfate | Clarinex-D 24 HOUR |
| desoxycorticosterone acetate | desoxycorticosterone ac(bulk) |
| dexamethasone | Decadron |
| dexamethasone | DexPak 10 day |
| dexamethasone | DexPak 13 Day |
| dexamethasone | DexPak 6 Day |
| dexamethasone | Dexamethasone Intensol |
| dexamethasone | Dxevo |
| dexamethasone | HiDex |
| dexamethasone | LoCort |
| dexamethasone | TaperDex |
| dexamethasone | ZoDex |
| dexamethasone | ZonaCort |
| dexamethasone | dexamethasone |
| dexamethasone acetate and sodium phosphate in sterile water | dexamethasone ac, sodph-water |
| dexamethasone acetate in sodium chloride, iso-osmotic | dexamethasoneace-NaCl,iso-osm |
| dexamethasone acetate, micronized | dexamethasone ac, micro(bulk) |
| dexamethasone sodium phosphate | Dexonto |
| dexamethasone sodium phosphate | dexamethasone sod phos(bulk) |
| dexamethasone sodium phosphate in 0.9 % sodium chloride | dexamethasone-0.9 % sod.chlor |
| dexamethasone sodium phosphate/PF | Active Injection Kit D (PF) |
| dexamethasone sodium phosphate/PF | DoubleDex (PF) |
| dexamethasone sodium phosphate/PF | MAS Care-Pak (PF) |
| dexamethasone sodium phosphate/PF | dexamethasone sodium phos(PF) |
| dexamethasone sodium phosphate/lidocaine HCl | Lidocidex-I |
| dexamethasone, micronized | dexamethasone,micronized(bulk) |
| dexamethasone/PF/norflurane/pentafluoropropane (HFC 245fa) | DMT SUIK |
| dexbromphen-pseudoephedrine -dextromethorphan | M-End DMX |
| dexbrompheniramine maleate | Ala-Hist IR |
| dexbrompheniramine maleate | Pediavent |
| dexbrompheniramine maleate/chlophedianol HCl | Chlo Hist |
| dexbrompheniramine maleate/phenylephrine HCl | Ala-Hist PE |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| dexbrompheniramine maleate/phenylephrine HCl | Dallergy(dexbrompheniramn-PE) |
| dexbrompheniramine maleate/phenylephrine HCl | dexbrompheniramine-phenyleph |
| dexbrompheniramine maleate/pseudoephedrine HCl | Acticon (dexbromph-pse) |
| dexbrompheniramine maleate/pseudoephedrine HCl/codeine phos | M-End Max D |
| dexchlorpheniramine maleate | Ryclora |
| dexchlorpheniramine maleate | dexchlorpheniramine maleate |
| dexchlorpheniramine maleate/phenylephrine HCl | Rymed(dexchlorpheniramine-PE) |
| dexchlorpheniramine maleate/phenylephrine HCl | Stahist (dexchlorpheniramine) |
| dexchlorpheniramine maleate/phenylephrine HCl/codeine | Pro-Red AC (w/dexchlorphenir) |
| dexchlorpheniramine maleate/phenylephrine/dextromethorphan | Polytussin DM |
| dextromethorphan | Child Plus Cough andRunnyNose |
| HBr/acetaminophen/chlorpheniramine maleate dextromethorphan | Child's TylenolplusCough,RNos |
| HBr/acetaminophen/chlorpheniramine maleate dextromethorphan | Coricidin HBP Flu |
| HBr/acetaminophen/chlorpheniramine maleate dextromethorphan | Flu BP |
| HBr/acetaminophen/chlorpheniramine maleate dextromethorphan | Flu HBP |
| HBr/acetaminophen/chlorpheniramine maleate dextromethorphan | Maximum Strength Flu |
| HBr/acetaminophen/chlorpheniramine maleate dextromethorphan | Vicks NyQuil Cold/Flu (cpm) |
| HBr/acetaminophen/chlorpheniramine maleate dextromethorphan | Diabetic Tussin Night Time |
| HBr/acetaminophen/diphenhydramine HCl dextromethorphan | All-Nite Cold-Flu |
| HBr/acetaminophen/doxylamine dextromethorphan | Cold-Flu Relief |
| HBr/acetaminophen/doxylamine dextromethorphan | Contac Cold-Flu Night |
| HBr/acetaminophen/doxylamine dextromethorphan | Coricidin HBP Cold-MultiSympt |
| HBr/acetaminophen/doxylamine dextromethorphan | Cough-Sore Throat Night |
| HBr/acetaminophen/doxylamine dextromethorphan | Night Time |
| HBr/acetaminophen/doxylamine dextromethorphan | Night Time Cold |
| HBr/acetaminophen/doxylamine dextromethorphan | Night Time Cold and FluRelief |
| HBr/acetaminophen/doxylamine dextromethorphan | Night Time Cold-Flu |
| HBr/acetaminophen/doxylamine dextromethorphan | Night Time Cold-Flu Relief |
| HBr/acetaminophen/doxylamine | |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| dextromethorphan HBr/acetaminophen/doxylamine | Nighttime Cold-Flu |
| dextromethorphan HBr/acetaminophen/doxylamine | Nighttime Cold-Flu Relief |
| dextromethorphan HBr/acetaminophen/doxylamine | Nite Time Cold-Flu |
| dextromethorphan HBr/acetaminophen/doxylamine | Nite Time Cold-Flu Relief |
| dextromethorphan HBr/acetaminophen/doxylamine | Nite-Time Cold-Flu |
| dextromethorphan HBr/acetaminophen/doxylamine | Nitetime Multi-Symptom |
| dextromethorphan HBr/acetaminophen/doxylamine | Robitussin Cold-Flu Night |
| dextromethorphan HBr/acetaminophen/doxylamine | Vicks Nature Fusion Cold-Flu |
| dextromethorphan HBr/acetaminophen/doxylamine | Vicks NyQuil Cold/FluLiquicap |
| dextromethorphan HBr/acetaminophen/doxylamine | Vicks Nyquil Nighttime Relief |
| dextromethorphan HBr/doxylamine succinate | Daytime-Nighttime Cough |
| dextromethorphan HBr/doxylamine succinate | NightTime Cough |
| dextromethorphan HBr/doxylamine succinate | Nite Time Cough |
| dextromethorphan HBr/doxylamine succinate | Nitetime Cough |
| dextromethorphan HBr/doxylamine succinate | Robitussin Nighttime CoughDM |
| dextromethorphan HBr/doxylamine succinate | SafeTussin PM |
| dextromethorphan HBr/doxylamine succinate | Tussin Nighttime Cough DM |
| dextromethorphan HBr/doxylamine succinate | Vicks NyQuil Cough |
| dextromethorphan HBr/phenylephrine HCl | Children's Cold-CoughDaytime |
| dextromethorphan HBr/phenylephrine HCl | Children's Sudafed PE Cough |
| dextromethorphan HBr/phenylephrine HCl | Cold and Cough (pe-dm) |
| dextromethorphan HBr/phenylephrine HCl | Triaminic Cold and Cough(PE) |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Cold Head CongestionDaytime |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Cold Multi-Symptom |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Cold-Flu Relief |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Day Multi-Symp Flu-SevereCold |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Day Time PE |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | DayTime |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Daytime Cold |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Daytime Cold-Flu |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Daytime Cold-Flu Relief (PE) |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Flu Relief Therapy Daytime |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Flu-Severe Cold-CoughDaytime |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | HerbioMed Body Aches-SinusM-S |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Mapap Cold Formula |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Mucinex Fast-MaxCongest-Head |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Mucinex Fast-MaxSevCold-Sinus |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Robitussin Cold-Flu Day |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Sudafed PEPressure-Pain-Cough |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Theraflu ExpressMax ColdDay |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Theraflu Multi-Symptom Cold |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Tylenol Cold Max Day |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Tylenol Cold Multi-SymptomDay |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Vicks DayQuil Cold-Flu Relief |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Vicks Nature Fusion |
| dextromethorphan HBr/phenylephrine HCl/acetaminophen | Wal-Flu Severe Cold-Cough |
| dextromethorphan HBr/phenylephrine HCl/dexbrompheniramine | Alahist CF |
| dextromethorphan HBr/phenylephrine HCl/dexbrompheniramine | Alahist DM |
| dextromethorphan HBr/phenylephrine HCl/dexbrompheniramine | Bionatuss DXP |
| dextromethorphan HBr/phenylephrine HCl/dexbrompheniramine | G-P-Tuss DXP |
| dextromethorphan HBr/phenylephrine HCl/dexbrompheniramine | Supress A |
| dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine | Alka-Seltzer PlusSin-Allg-Cgh |
| dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine | Cold Multi-SymptomNightTime |
| dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine | Cold and Flu Relief Plus (D/N) |
| dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine | Cold-Flu Relief, Day/Night |
| dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine | Daytime-Nighttime |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine | Daytime-Nighttime Cold-Flu |
| dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine | Mucinex Fast-Max Nite (doxyl) |
| dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine | Nite Time Cold-Flu Relief (PE) |
| dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine | Severe Cold and FluNighttime |
| dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine | Severe Sinus CongestAlrgy-Cgh |
| dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine | Tylenol Cold Max Night |
| dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine | Tylenol Cold Multi-SymptNight |
| dextromethorphan HBr/phenylephrine/acetaminophen/doxylamine | Vicks NyQuil Severe Cold-Flu |
| dextromethorphan HBr/pseudoephedrine HCl/acetaminophen | DAY-TIME |
| dextromethorphan HBr/pseudoephedrine HCl/acetaminophen | Daytime Cold and Flu Relief |
| dextromethorphan/phenylephrine/acetaminophen /diphenhydramine | HerbioMed Deep Cold-FluNight |
| dextromethorphan/phenylephrine/acetaminophen /diphenhydramine | Multi-Symptom SevereCold-Nt |
| dextromethorphan/pseudoephrine HCl/acetaminophen/doxylamine | Alka-Seltzer Plus Cold+Flu |
| dextromethorphan/pseudoephrine HCl/acetaminophen/doxylamine | Night Time Cold Medicine |
| dextromethorphan/pseudoephrine HCl/acetaminophen/doxylamine | Night Time Cold-Flu |
| dextromethorphan/pseudoephrine HCl/acetaminophen/doxylamine | Night Time Cold-Flu Relief |
| dextromethorphan/pseudoephrine HCl/acetaminophen/doxylamine | Nite Time |
| diclofenac sodium | diclofenac sodium |
| diphenhydramine HCl | Alka-Seltzer Plus Allergy |
| diphenhydramine HCl | Aller-G-Time |
| diphenhydramine HCl | Allergy |
| diphenhydramine HCl | Allergy (diphenhydramine) |
| diphenhydramine HCl | Allergy Medication |
| diphenhydramine HCl | Allergy Medicine |
| diphenhydramine HCl | AllergyRelief(diphenhydramin) |
| diphenhydramine HCl | Banophen |
| diphenhydramine HCl | Banophen Allergy |
| diphenhydramine HCl | Benadryl |
| diphenhydramine HCl | Benadryl Allergy |
| diphenhydramine HCl | Child Allergy Relief (diphen) |
| diphenhydramine HCl | Children's Allergy (diphenhyd) |
| diphenhydramine HCl | Children's Allergy Medicine |
| diphenhydramine HCl | Children's Benadryl Allergy |
| diphenhydramine HCl | Children's Diphenhydramine |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| diphenhydramine HCl | Children's Wal-Dryl Allergy |
| diphenhydramine HCl | Complete Allergy |
| diphenhydramine HCl | Complete Allergy Medicine |
| diphenhydramine HCl | Compoz |
| diphenhydramine HCl | Diphedryl |
| diphenhydramine HCl | Diphen |
| diphenhydramine HCl | Diphenhist |
| diphenhydramine HCl | EZ Nite Sleep |
| diphenhydramine HCl | Geri-Dryl |
| diphenhydramine HCl | Medi-Phedryl |
| diphenhydramine HCl | Naramin |
| diphenhydramine HCl | NightTime Sleep Aid (diphen) |
| diphenhydramine HCl | Nighttime Allergy Relief |
| diphenhydramine HCl | Ormir |
| diphenhydramine HCl | Pharbedryl |
| diphenhydramine HCl | Q-Dryl |
| diphenhydramine HCl | Quenalin |
| diphenhydramine HCl | Rest Simply Nighttime Sleep |
| diphenhydramine HCl | Restfully Sleep |
| diphenhydramine HCl | Siladryl SA |
| diphenhydramine HCl | Silphen Cough |
| diphenhydramine HCl | Simply Sleep |
| diphenhydramine HCl | Sleep |
| diphenhydramine HCl | Sleep Aid (diphenhydramine) |
| diphenhydramine HCl | Sleep Aid Max Str(diphenhydr) |
| diphenhydramine HCl | Sleep II |
| diphenhydramine HCl | Sleep Time |
| diphenhydramine HCl | Sleep-Tabs |
| diphenhydramine HCl | Sleeping |
| diphenhydramine HCl | Total Allergy Medicine |
| diphenhydramine HCl | Unisom SleepGels |
| diphenhydramine HCl | Unisom SleepMelts |
| diphenhydramine HCl | Valu-Dryl Allergy |
| diphenhydramine HCl | Vanamine PD |
| diphenhydramine HCl | Vicks QlearQuil Nighttime Rlf |
| diphenhydramine HCl | Wal-Dryl Allergy |
| diphenhydramine HCl | Wal-Sleep Z |
| diphenhydramine HCl | Wal-Som (diphenhydramine) |
| diphenhydramine HCl | Z-Sleep |
| diphenhydramine HCl | ZzzQuil |
| diphenhydramine HCl | diphenhydramine HCl |
| diphenhydramine HCl in 0.9 % sodium chloride | diphenhydramine-0.9 %sod.chlr |
| diphenhydramine HCl/hydrocortisone | HC Derma-Pax |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Adult Robitussin Night M-SCld |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Allergy M-S Nighttime |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Allergy Plus Severe Sinus HA |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Allergy Sinus Headache (PE) |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Allergy and Cold PE |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Child Delsym Cough+Cold |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Children Dimetapp M-SCold-Flu |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Children's Mucinex NightTime |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Cold and FluRelief(diphen-pe) |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Cough and Severe Cold |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Delsym Cough-ColdNightTime |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Flu Relief Therapy Nighttime |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Flu and Sore Throat Relief |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Flu-Severe Cold-Cough Night |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Herbiomed Allergy Cold-Sinus |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Mucinex Fast-Max NiteCold-Flu |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Mucinex Sinus-Max NiteCongest |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Severe Allergy-SinusHeadache |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Severe Cold Cough-Flu |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Severe Cold PE |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Theraflu ExpressMax ColdNight |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Theraflu Night SevereCold-Cgh |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Theraflu Nighttime PowerPod |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Wal-Dryl Severe Allergy-Sinus |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Wal-Flu Severe Cold andCough |
| diphenhydramine HCl/phenylephrine HCl/acetaminophen | Wal-phed PE Severe Cold |
| diphenhydramine HCl/phenylephrine HCl/dextromethorphan HBr | Child Cold-Cough Day-Night |
| diphenhydramine HCl/phenylephrine/acetaminophen/guaifenesin | Sinus Relief Max StrDay-Night |
| diphenhydramine/phenylephrin/dextromethorph/acetaminophen/GG | Children's M-S ColdDay-Night |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| diphenhydramine/phenylephrin/dextromethorph /acetaminophen/GG | Daytime-ColdNighttime-Cld-Flu |
| diphenhydramine/phenylephrin/dextromethorph /acetaminophen/GG | Mucinex Fast-Max Day-NiteCold |
| diphenhydramine/phenylephrin/dextromethorph /acetaminophen/GG | Mucinex Fast-Max Day-NiteCong |
| doxylamine succ/pseudoephedrine HCl/dextromethorphan Hbr | Glentuss |
| doxylamine succ/pseudoephedrine HCl/dextromethorphan Hbr | Lortuss DM |
| doxylamine succinate/phenylephrine HCl | Poly Hist Forte |
| doxylamine succinate/phenylephrine HCl | Poly Hist Forte (doxylamine) |
| doxylamine succinate/phenylephrine HCl | doxylamine-phenylephrine |
| doxylamine succinate/pseudoephedrine HCl | Lortuss LQ |
| doxylamine/phenylephrine/dextromethorphan /acetaminophen/GG | Day-Nite Severe Cold-Flu |
| doxylamine/phenylephrine/dextromethorphan /acetaminophen/GG | Mucinex Fast-MaxDay-Nt(doxyl) |
| doxylamine/phenylephrine/dextromethorphan /acetaminophen/GG | Mucinex Sinus-Max Dy-Nt(dxyl) |
| doxylamine/phenylephrine/dextromethorphan /acetaminophen/GG | Severe Cold andFlu(Day/Night) |
| dupilumab | Dupixent |
| dyphylline | Lufyllin |
| dyphylline | dyphylline (bulk) |
| emedastine difumarate | Emadine |
| ephedrine sulfate | ephedrine sulfate |
| ephedrine sulfate/guaifenesin | Bronkaid Dual Action |
| epinastine HCl | Elestat |
| epinastine HCl | epinastine |
| epinephrine | Adrenaclick |
| epinephrine | Adrenalin |
| epinephrine | Adyphren |
| epinephrine | Adyphren Amp |
| epinephrine | Adyphren Amp II |
| epinephrine | Adyphren II |
| epinephrine | Auvi-Q |
| epinephrine | Bronchial Mist |
| epinephrine | Bronchial Mist Refill |
| epinephrine | EPIsnap |
| epinephrine | EpiPen |
| epinephrine | EpiPen 2-Pak |
| epinephrine | EpiPen Jr |
| epinephrine | EpiPen Jr 2-Pak |
| epinephrine | EpinephrineSnap-EMS |
| epinephrine | EpinephrineSnap-V |
| epinephrine | Epy |
| epinephrine | Primatene Mist |
| epinephrine | Symjepi |
| epinephrine | epinephrine |
| epinephrine HCl/PF | epinephrine HCl (PF) |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| fexofenadine HCl | Allegra Allergy |
| fexofenadine HCl | Aller-Fex |
| fexofenadine HCl | Aller-ease |
| fexofenadine HCl | Allergy Relief (fexofenadine) |
| fexofenadine HCl | Children's Allegra Allergy |
| fexofenadine HCl | Children's Allergy Relief(fex) |
| fexofenadine HCl | Children's Wal-Fex |
| fexofenadine HCl | Mucinex Allergy |
| fexofenadine HCl | Wal-Fex Allergy |
| fexofenadine HCl | fexofenadine |
| fexofenadine HCl | fexofenadine (bulk) |
| fexofenadine HCl/pseudoephedrine HCl | Allegra-D 12 Hour |
| fexofenadine HCl/pseudoephedrine HCl | Allegra-D 24 Hour |
| fexofenadine HCl/pseudoephedrine HCl | Allergy Relief D |
| fexofenadine HCl/pseudoephedrine HCl | Allergy Relief-D(fexofenadine) |
| fexofenadine HCl/pseudoephedrine HCl | Allergy-CongestRelief-D(fexo) |
| fexofenadine HCl/pseudoephedrine HCl | Wal-Fex D 12 Hour |
| fexofenadine HCl/pseudoephedrine HCl | Wal-Fex D 24 Hour |
| fexofenadine HCl/pseudoephedrine HCl | fexofenadine-pseudoephedrine |
| fludrocortisone acetate | fludrocortisone |
| flunisolide | Aerospan |
| flunisolide | flunisolide |
| fluocinolone acetonide/emollient combination no.65 | Synalar Cream Kit |
| fluocinolone acetonide/emollient combination no.65 | Synalar Ointment Kit |
| fluocinolone acetonide/skin cleanser comb no.28 | Synalar TS |
| fluocinolone acetonide/skin cleanser no.10/silicone, tape | Xilapak |
| fluocinolone acetonide/urea/silicone, adhesive | Noxipak |
| flurbiprofen | flurbiprofen |
| fluticasone furoate | Arnuity Ellipta |
| fluticasone furoate | Children's Flonase Sensimist |
| fluticasone furoate | Flonase Sensimist |
| fluticasone furoate | Veramyst |
| fluticasone furoate/umeclidinium bromide/vilanterol trifenat | Trelegy Ellipta |
| fluticasone furoate/vilanterol trifenatate | Breo Ellipta |
| fluticasone propionate | 24 Hour Allergy Relief |
| fluticasone propionate | Aller-Flo |
| fluticasone propionate | Allergy Relief (fluticasone) |
| fluticasone propionate | ArmonAir RespiClick |
| fluticasone propionate | Children's Flonase Allergy Rlf |
| fluticasone propionate | Childrens 24 Hr Allergy Relief |
| fluticasone propionate | ClariSpray |
| fluticasone propionate | Flonase |
| fluticasone propionate | Flonase Allergy Relief |
| fluticasone propionate | Flovent Diskus |
| fluticasone propionate | Flovent HFA |
| fluticasone propionate | Xhance |
| fluticasone propionate | fluticasone propionate |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| fluticasone propionate | fluticasone propionate (bulk) |
| fluticasone propionate, micronized | fluticasone prop, micro (bulk) |
| fluticasone propionate/emollient combination no.65 | Beser Kit |
| fluticasone propionate/salmeterol xinafoate | Advair Diskus |
| fluticasone propionate/salmeterol xinafoate | Advair HFA |
| fluticasone propionate/salmeterol xinafoate | AirDuo RespiClick |
| fluticasone propionate/salmeterol xinafoate | Wixela Inhub |
| fluticasone propionate/salmeterol xinafoate | fluticasone propion-salmeterol |
| fluticasone propionate/sodium chloride/sodium bicarbonate | Ticanase |
| fluticasone propionate/sodium chloride/sodium bicarbonate | Ticaspray |
| formoterol fumarate | Foradil Aerolizer |
| formoterol fumarate | Perforomist |
| formoterol fumarate | formoterol fumarate (bulk) |
| formoterol fumarate dihydrate, micronized | formoterol fum dihyd,mic(bulk) |
| glycopyrrolate | Seebri Neohaler |
| glycopyrrolate/formoterol fumarate | Bevespi Aerosphere |
| glycopyrrolate/nebulizer accessories | Lonhala Magnair Refill |
| glycopyrrolate/nebulizer and accessories | Lonhala Magnair Starter |
| guaifenesin/acetaminophen | Chest Congestion |
| guaifenesin/dextromethorphan HBr | Adt Robitussin Peak Cld DMMax |
| guaifenesin/dextromethorphan HBr | Adult Cough Formula DM Max |
| guaifenesin/dextromethorphan HBr | Adult Robitussin Peak ColdDM |
| guaifenesin/dextromethorphan HBr | Adult Tussin Cough CongestDM |
| guaifenesin/dextromethorphan HBr | Adult Tussin DM |
| guaifenesin/dextromethorphan HBr | Adult Wal-Tussin DM Max |
| guaifenesin/dextromethorphan HBr | Allfen DM |
| guaifenesin/dextromethorphan HBr | Biocotron |
| guaifenesin/dextromethorphan HBr | Biospec DMX |
| guaifenesin/dextromethorphan HBr | Chest Congestion Relief DM |
| guaifenesin/dextromethorphan HBr | Chest Congestion-CoughRelief |
| guaifenesin/dextromethorphan HBr | Child ChestCongestion-Cough |
| guaifenesin/dextromethorphan HBr | Child Cough-Chest CongestDM |
| guaifenesin/dextromethorphan HBr | Child Delsym Cough+ChestDM |
| guaifenesin/dextromethorphan HBr | Child Mucinex CoughMini-Melts |
| guaifenesin/dextromethorphan HBr | Child Mucus Relief Cough |
| guaifenesin/dextromethorphan HBr | Child TriaminicCough-Congest |
| guaifenesin/dextromethorphan HBr | Children's Cough |
| guaifenesin/dextromethorphan HBr | Children's Mucinex Cough |
| guaifenesin/dextromethorphan HBr | Chld Robitussin Cough-ChestDM |
| guaifenesin/dextromethorphan HBr | Coricidin HBP ChestCong-Cough |
| guaifenesin/dextromethorphan HBr | Cough Control DM |
| guaifenesin/dextromethorphan HBr | Cough Control DM Max |
| guaifenesin/dextromethorphan HBr | CoughSuppressant-Expectorant |
| guaifenesin/dextromethorphan HBr | Cough Syrup DM |
| guaifenesin/dextromethorphan HBr | Cough-Chest Congestion DM |
| guaifenesin/dextromethorphan HBr | DM Max |
| guaifenesin/dextromethorphan HBr | Daytime Mucus Relief DM |
| guaifenesin/dextromethorphan HBr | Delsym Cough-ChestCongest DM |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| guaifenesin/dextromethorphan HBr | Diabetic Siltussin-DM |
| guaifenesin/dextromethorphan HBr | Diabetic Siltussin-DM Max Str |
| guaifenesin/dextromethorphan HBr | Diabetic Tussin DM |
| guaifenesin/dextromethorphan HBr | Diabetic Tussin Max St |
| guaifenesin/dextromethorphan HBr | Double-Tussin DM |
| guaifenesin/dextromethorphan HBr | Expectorant DM |
| guaifenesin/dextromethorphan HBr | Fenesin DM IR |
| guaifenesin/dextromethorphan HBr | G-Fenesin DM |
| guaifenesin/dextromethorphan HBr | G-Tron |
| guaifenesin/dextromethorphan HBr | G-Zyncof |
| guaifenesin/dextromethorphan HBr | Geri-Tussin DM |
| guaifenesin/dextromethorphan HBr | Guaiasorb DM |
| guaifenesin/dextromethorphan HBr | Guaicon DMS |
| guaifenesin/dextromethorphan HBr | Guaifenesin-DM |
| guaifenesin/dextromethorphan HBr | Intense Cough |
| guaifenesin/dextromethorphan HBr | Intense Cough Reliever |
| guaifenesin/dextromethorphan HBr | Iophen DM-NR |
| guaifenesin/dextromethorphan HBr | Medi-Tussin DM |
| guaifenesin/dextromethorphan HBr | Medi-Tussin DM Diabetic |
| guaifenesin/dextromethorphan HBr | Mucinex DM |
| guaifenesin/dextromethorphan HBr | Mucinex Fast-Max DM Max |
| guaifenesin/dextromethorphan HBr | Mucosa DM |
| guaifenesin/dextromethorphan HBr | Mucus DM |
| guaifenesin/dextromethorphan HBr | Mucus DM Max ER |
| guaifenesin/dextromethorphan HBr | Mucus Relief Cough |
| guaifenesin/dextromethorphan HBr | Mucus Relief DM |
| guaifenesin/dextromethorphan HBr | Mucus Relief DM Cough |
| guaifenesin/dextromethorphan HBr | Mucus Relief DM Max |
| guaifenesin/dextromethorphan HBr | Mucus Relief ER DM-MAX |
| guaifenesin/dextromethorphan HBr | Mucus and Cough Relief |
| guaifenesin/dextromethorphan HBr | Neo-Tuss |
| guaifenesin/dextromethorphan HBr | Q-Tussin DM |
| guaifenesin/dextromethorphan HBr | Refenesen DM |
| guaifenesin/dextromethorphan HBr | Ri-Tussin DM |
| guaifenesin/dextromethorphan HBr | Robafen DM |
| guaifenesin/dextromethorphan HBr | Robafen DM Cough |
| guaifenesin/dextromethorphan HBr | Robafen DM Cough-ChestCongest |
| guaifenesin/dextromethorphan HBr | Robitussin Cough-ChestCong DM |
| guaifenesin/dextromethorphan HBr | Safe Tussin DM |
| guaifenesin/dextromethorphan HBr | Scot-Tussin Senior |
| guaifenesin/dextromethorphan HBr | Siltussin DM DAS |
| guaifenesin/dextromethorphan HBr | Siltussin-DM |
| guaifenesin/dextromethorphan HBr | Sorbugen NR |
| guaifenesin/dextromethorphan HBr | Supress DM |
| guaifenesin/dextromethorphan HBr | TRISPEC DMX |
| guaifenesin/dextromethorphan HBr | Tab Tussin DM |
| guaifenesin/dextromethorphan HBr | Tusnel Diabetic |
| guaifenesin/dextromethorphan HBr | Tussin Cough DM |
| guaifenesin/dextromethorphan HBr | Tussin Cough-ChestCongestion |
| guaifenesin/dextromethorphan HBr | Tussin DM |
| guaifenesin/dextromethorphan HBr | Tussin DM Clear |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| guaifenesin/dextromethorphan HBr | Tussin DM Cough |
| guaifenesin/dextromethorphan HBr | Tussin DM Cough and Chest |
| guaifenesin/dextromethorphan HBr | Tussin DM Max |
| guaifenesin/dextromethorphan HBr | Ultra DM Free and Clear |
| guaifenesin/dextromethorphan HBr | Ultra Tuss Safe |
| guaifenesin/dextromethorphan HBr | Wal-Tussin DM |
| guaifenesin/dextromethorphan HBr | Zyncof |
| guaifenesin/dextromethorphan HBr | dextromethorphan-guaifenesin |
| guaifenesin/dextromethorphan HBr/phenylephrine | Actidom DMX |
| guaifenesin/dextromethorphan HBr/phenylephrine | Adult Robitussin M-S Cold |
| guaifenesin/dextromethorphan HBr/phenylephrine | Adult Robitussin Peak ColdM-S |
| guaifenesin/dextromethorphan HBr/phenylephrine | Adult Tussin Multi-Symp Cold |
| guaifenesin/dextromethorphan HBr/phenylephrine | Altipres |
| guaifenesin/dextromethorphan HBr/phenylephrine | Altipres Pediatric |
| guaifenesin/dextromethorphan HBr/phenylephrine | Aquanaz |
| guaifenesin/dextromethorphan HBr/phenylephrine | Bio T Pres |
| guaifenesin/dextromethorphan HBr/phenylephrine | Bio T Pres Pediatric |
| guaifenesin/dextromethorphan HBr/phenylephrine | Bio-S-Pres Dx |
| guaifenesin/dextromethorphan HBr/phenylephrine | BioGtuss NF |
| guaifenesin/dextromethorphan HBr/phenylephrine | Biobron DX |
| guaifenesin/dextromethorphan HBr/phenylephrine | Biobron SF |
| guaifenesin/dextromethorphan HBr/phenylephrine | Biocotron-D |
| guaifenesin/dextromethorphan HBr/phenylephrine | Biodesp DM |
| guaifenesin/dextromethorphan HBr/phenylephrine | Biogil |
| guaifenesin/dextromethorphan HBr/phenylephrine | Broncotron PED |
| guaifenesin/dextromethorphan HBr/phenylephrine | Brontuss SF |
| guaifenesin/dextromethorphan HBr/phenylephrine | Child MucinexCongestion-Cough |
| guaifenesin/dextromethorphan HBr/phenylephrine | Child Multi-SymptomCold/Cough |
| guaifenesin/dextromethorphan HBr/phenylephrine | Child's Mucus Relief M-S Cold |
| guaifenesin/dextromethorphan HBr/phenylephrine | Children's MucinexMulti-Symp |
| guaifenesin/dextromethorphan HBr/phenylephrine | Cough Control CF (PE) |
| guaifenesin/dextromethorphan HBr/phenylephrine | Cough and Cold |
| guaifenesin/dextromethorphan HBr/phenylephrine | Cough and Cold Mucus ReliefCF |
| guaifenesin/dextromethorphan HBr/phenylephrine | Deconex DMX |
| guaifenesin/dextromethorphan HBr/phenylephrine | Desgen |
| guaifenesin/dextromethorphan HBr/phenylephrine | Desgen DM |
| guaifenesin/dextromethorphan HBr/phenylephrine | Despec DM-G |
| guaifenesin/dextromethorphan HBr/phenylephrine | Despec EDA Cough-ColdDrops |
| guaifenesin/dextromethorphan HBr/phenylephrine | Despec-DM(phenyleph-DM-guaif) |
| guaifenesin/dextromethorphan HBr/phenylephrine | Dometuss-DMX |
| guaifenesin/dextromethorphan HBr/phenylephrine | Duravent DM |
| guaifenesin/dextromethorphan HBr/phenylephrine | Endacon |
| guaifenesin/dextromethorphan HBr/phenylephrine | Exactuss |
| guaifenesin/dextromethorphan HBr/phenylephrine | Exactuss TR |
| guaifenesin/dextromethorphan HBr/phenylephrine | Fast Mucus RlfCongest-Cough |
| guaifenesin/dextromethorphan HBr/phenylephrine | G-Supress DX |
| guaifenesin/dextromethorphan HBr/phenylephrine | G-Tron PED |
| guaifenesin/dextromethorphan HBr/phenylephrine | G-Tusicof |
| guaifenesin/dextromethorphan HBr/phenylephrine | Giltuss |
| guaifenesin/dextromethorphan HBr/phenylephrine | Giltuss Cough-Cold |
| guaifenesin/dextromethorphan HBr/phenylephrine | Giltuss Pediatric |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| guaifenesin/dextromethorphan HBr/phenylephrine | Giltuss TR |
| guaifenesin/dextromethorphan HBr/phenylephrine | Maxiphen DM |
| guaifenesin/dextromethorphan HBr/phenylephrine | Mucinex Fast-MaxCongest-Cough |
| guaifenesin/dextromethorphan HBr/phenylephrine | Mucus ReliefCongestion-Cough |
| guaifenesin/dextromethorphan HBr/phenylephrine | NeoTuss-D (ImprovedFormula) |
| guaifenesin/dextromethorphan HBr/phenylephrine | Nivanex DMX |
| guaifenesin/dextromethorphan HBr/phenylephrine | Pres Gen |
| guaifenesin/dextromethorphan HBr/phenylephrine | Pres Gen Pediatric |
| guaifenesin/dextromethorphan HBr/phenylephrine | Relhist DMX |
| guaifenesin/dextromethorphan HBr/phenylephrine | Robafen CF (phenylephrine) |
| guaifenesin/dextromethorphan HBr/phenylephrine | Robitussin Cough and ColdCF |
| guaifenesin/dextromethorphan HBr/phenylephrine | Robitussin M-S Cold CF Max |
| guaifenesin/dextromethorphan HBr/phenylephrine | Severe Congestion andCoughMax |
| guaifenesin/dextromethorphan HBr/phenylephrine | Supress DX |
| guaifenesin/dextromethorphan HBr/phenylephrine | Tusicof |
| guaifenesin/dextromethorphan HBr/phenylephrine | Tusnel DM |
| guaifenesin/dextromethorphan HBr/phenylephrine | Tusnel DMPediatric(phenyleph) |
| guaifenesin/dextromethorphan HBr/phenylephrine | Tussi-Pres |
| guaifenesin/dextromethorphan HBr/phenylephrine | Tussi-Pres Pediatric |
| guaifenesin/dextromethorphan HBr/phenylephrine | Tussin CF (PE-DM-guaif) |
| guaifenesin/dextromethorphan HBr/phenylephrine | Tussin CF Cough-Cold |
| guaifenesin/dextromethorphan HBr/phenylephrine | Tussin CF MAX |
| guaifenesin/dextromethorphan HBr/phenylephrine | Tusslin |
| guaifenesin/dextromethorphan HBr/phenylephrine | VanaTab DM |
| guaifenesin/dextromethorphan HBr/phenylephrine | Vanacof DM |
| guaifenesin/dextromethorphan HBr/phenylephrine | Wal-Tussin Cough and ColdCF |
| guaifenesin/dextromethorphan HBr/phenylephrine | phenylephrine-DM-guaifenesin |
| guaifenesin/dextromethorphan HBr/potassium citrate | Sorbutuss |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Actinel |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Actinel Pediatric |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Ambi 40PSE-400GFN-20DM |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Bionel |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Bionel Pediatric |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Capmist DM |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Desgen DM(pseudoephedrine) |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Despec-DM(pseudoeph-DM-guaif) |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Entex PAC |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Entre-Cough |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | ExeFen DMX |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Pecgen PSE |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Poly-Vent DM |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Robafen CF |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | TRISPEC PSE |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Tusnel DMPediatric(pseudoeph) |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Tusnel New Formula |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Tusnel Pediatric |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Tussin CF |
| guaifenesin/dextromethorphan HBr/pseudoephedrine HCl | Z-Cof 12 DM |
| guaifenesin/dyphylline | Difil-G 400 |
| guaifenesin/ephedrine HCl | Primatene Asthma |
| guaifenesin/hydrocodone bitartrate | Flowtuss |
| guaifenesin/hydrocodone bitartrate | Obredon |
| guaifenesin/hydrocodone bitartrate | hydrocodone-guaifenesin |
| guaifenesin/phenylephrine HCl | Chest Congestion Relief PE |
| guaifenesin/phenylephrine HCl | Chest-Sinus CongestionRelief |
| guaifenesin/phenylephrine HCl | Child Mucinex StuffyNose-Chst |
| guaifenesin/phenylephrine HCl | Child Mucinex StuffyNose-Cold |
| guaifenesin/phenylephrine HCl | Children's Stuffy Nose-Cold |
| guaifenesin/phenylephrine HCl | Congest-Eze PE |
| guaifenesin/phenylephrine HCl | Deconex IR |
| guaifenesin/phenylephrine HCl | Despec |
| guaifenesin/phenylephrine HCl | Duravent PE |
| guaifenesin/phenylephrine HCl | ED Bron GP |
| guaifenesin/phenylephrine HCl | Entex LQ |
| guaifenesin/phenylephrine HCl | ExaPhex TR |
| guaifenesin/phenylephrine HCl | Fenesin PE IR |
| guaifenesin/phenylephrine HCl | Gilphex TR |
| guaifenesin/phenylephrine HCl | J-MAX |
| guaifenesin/phenylephrine HCl | Liquibid D-R |
| guaifenesin/phenylephrine HCl | Liquibid PD-R |
| guaifenesin/phenylephrine HCl | Maxiphen |
| guaifenesin/phenylephrine HCl | MucaphEd |
| guaifenesin/phenylephrine HCl | Mucus Relief D(phenylephrine) |
| guaifenesin/phenylephrine HCl | Mucus Relief PE |
| guaifenesin/phenylephrine HCl | Mucus Relief Sinus |
| guaifenesin/phenylephrine HCl | Refenesen PE |
| guaifenesin/phenylephrine HCl | RelCof IR |
| guaifenesin/phenylephrine HCl | Rescon-GG |
| guaifenesin/phenylephrine HCl | Supress-PE |
| guaifenesin/phenylephrine HCl | TL-DMX |
| guaifenesin/phenylephrine HCl/acetaminophen | Cold HeadCongest(gg-pe-acetm) |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| guaifenesin/phenylephrine HCl/acetaminophen | Mucinex Cold and Sinus |
| guaifenesin/phenylephrine HCl/acetaminophen | Mucinex Fast-Max Cold-Sinus |
| guaifenesin/phenylephrine HCl/acetaminophen | Mucinex Sinus-MaxPressur-Pain |
| guaifenesin/phenylephrine HCl/acetaminophen | Mucinex Sinus-Max SevCongestn |
| guaifenesin/phenylephrine HCl/acetaminophen | Mucus Relief Cold and Sinus |
| guaifenesin/phenylephrine HCl/acetaminophen | Mucus ReliefSinusPressur-Pain |
| guaifenesin/phenylephrine HCl/acetaminophen | Mucus Rlf Severe SinusCongest |
| guaifenesin/phenylephrine HCl/acetaminophen | Pressure-Pain PE Plus Mucus |
| guaifenesin/phenylephrine HCl/acetaminophen | Severe Congestion Relief |
| guaifenesin/phenylephrine HCl/acetaminophen | Severe Sinus |
| guaifenesin/phenylephrine HCl/acetaminophen | Sinus Congestion-Pain(guaif) |
| guaifenesin/phenylephrine HCl/acetaminophen | Sinus Relief Pressure andPain |
| guaifenesin/phenylephrine HCl/acetaminophen | Sinus Relief SevereCongestion |
| guaifenesin/phenylephrine HCl/acetaminophen | Sudafed PEPressure-Pain-Mucus |
| guaifenesin/phenylephrine HCl/acetaminophen | Tylenol Cold Head CongestSevr |
| guaifenesin/phenylephrine HCl/acetaminophen | Tylenol Sinus CongestionPain |
| guaifenesin/phenylephrine HCl/acetaminophen | Tylenol Sinus Severe |
| guaifenesin/pseudoephedrine HCl | Ambi 60PSE-400GFN |
| guaifenesin/pseudoephedrine HCl | Chest Congestion Relief D |
| guaifenesin/pseudoephedrine HCl | Congest-Eze |
| guaifenesin/pseudoephedrine HCl | Congestac |
| guaifenesin/pseudoephedrine HCl | Despec-Tab |
| guaifenesin/pseudoephedrine HCl | Entex T |
| guaifenesin/pseudoephedrine HCl | ExeFen-IR |
| guaifenesin/pseudoephedrine HCl | Maxifed |
| guaifenesin/pseudoephedrine HCl | Mucinex D |
| guaifenesin/pseudoephedrine HCl | Mucinex D Maximum Strength |
| guaifenesin/pseudoephedrine HCl | Mucus D |
| guaifenesin/pseudoephedrine HCl | Mucus Relief D(pseudoephed) |
| guaifenesin/pseudoephedrine HCl | Poly-Vent IR |
| guaifenesin/pseudoephedrine HCl | Respaire-30 |
| guaifenesin/pseudoephedrine HCl | Triacting Expectorant |
| guaifenesin/pseudoephedrine HCl | Tusnel Pediatric |
| guaifenesin/pseudoephedrine HCl | pseudoephedrine-guaifenesin |
| halobetasol propionate/ammonium lactate | Halonate |
| halobetasol propionate/ammonium lactate | Halonate Pac |
| halobetasol propionate/ammonium lactate | Ultravate PAC |
| halobetasol propionate/lactic acid | Ultravate X |
| hydrocodone bitartrate/chlorpheniramine maleate | Vituz |
| hydrocodone bitartrate/homatropine methylbromide | Hydrocodone Compound |
| hydrocodone bitartrate/homatropine methylbromide | Hydromet |
| hydrocodone bitartrate/homatropine methylbromide | Tussigon |
| hydrocodone bitartrate/homatropine methylbromide | hydrocodone-homatropine |
| hydrocodone bitartrate/pseudoephedrine HCl/guaifenesin | Hycofenix |
| hydrocodone polistirex/chlorpheniramine polistirex | TussiCaps |
| hydrocodone polistirex/chlorpheniramine polistirex | Tussionex Pennkinetic ER |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| hydrocodone polistirex/chlorpheniramine polistirex | hydrocodone-chlorpheniramine |
| hydrocortisone | Cortef |
| hydrocortisone | hydrocortisone |
| hydrocortisone acetate/aloe vera | Nucort |
| hydrocortisone acetate/aloe vera | hydrocortisone acet-aloe vera |
| hydrocortisone acetate/pramoxine HCl | Analpram-HC |
| hydrocortisone acetate/pramoxine HCl | Epifoam |
| hydrocortisone acetate/pramoxine HCl | Mezparox-HC |
| hydrocortisone acetate/pramoxine HCl | Novacort |
| hydrocortisone acetate/pramoxine HCl | Pramosone |
| hydrocortisone acetate/pramoxine HCl | hydrocortisone-pramoxine |
| hydrocortisone acetate/pramoxine HCl/aloe polysaccharide | Novacort (with aloe) |
| hydrocortisone acetate/pramoxine HCl/emollient base | Pramosone E |
| hydrocortisone acetate/urea | U-Cort |
| hydrocortisone sod succinate | A-Hydrocort |
| hydrocortisone sod succinate | Solu-Cortef |
| hydrocortisone sodium succinate/PF | Solu-Cortef Act-O-Vial (PF) |
| hydrocortisone/aloe vera | Anti-Itch(hydrocortisone)-Aloe |
| hydrocortisone/aloe vera | Cortisone with Aloe |
| hydrocortisone/aloe vera | Cortizone-10 with aloe |
| hydrocortisone/aloe vera | Hydrocortisone Plus |
| hydrocortisone/aloe vera | Hydroskin with Aloe |
| hydrocortisone/aloe vera | hydrocortisone-aloe vera |
| hydrocortisone/aloe vera/vitamin E acetate/vitamins A and D | Anti-Itch (HC) with Aloe-Vit E |
| hydrocortisone/aloe vera/vitamin E acetate/vitamins A and D | Anti-Itch Plus |
| hydrocortisone/emollient combination no.45 | Pediaderm HC |
| hydrocortisone/mineral oil/petrolatum,white | hydrocortisone-min oil-wht pet |
| hydrocortisone/skin cleanser combination no.25 | Aqua Glycolic HC |
| hydrocortisone/skin cleanser combination no.35 | Dermasorb HC Complete Kit |
| ibuprofen | Addaprin |
| ibuprofen | Children's Ibu-Drops |
| ibuprofen | Children's Ibuprofen |
| ibuprofen | Ibuprofen IB |
| ibuprofen | Ibuprofen Jr Strength |
| ibuprofen | Infant's Ibuprofen |
| ibuprofen | Infants Ibu-Drops |
| ibuprofen | Medi-Profen |
| ibuprofen | Wal-Profen |
| ibuprofen | ibuprofen |
| ibuprofen/diphenhydramine HCl | Ibuprofen PM |
| ibuprofen/diphenhydramine HCl | ibuprofen-diphenhydramineHCl |
| ibuprofen/diphenhydramine citrate | Ibuprofen PM |
| ibuprofen/phenylephrine HCl | Advil Congestion Relief |
| ibuprofen/phenylephrine HCl | Congestion Relief(ibuprof-PE) |
| ibuprofen/pseudoephedrine HCl | Advil Cold and Sinus |
| ibuprofen/pseudoephedrine HCl | Cold and Sinus Pain Relief |
| ibuprofen/pseudoephedrine HCl | Cold-Sinus Relief |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| ibuprofen/pseudoephedrine HCl | Ibuprofen Cold |
| ibuprofen/pseudoephedrine HCl | Ibuprofen Cold-Sinus(withPSE) |
| ibuprofen/pseudoephedrine HCl | Wal-Profen Cold-Sinus |
| ibuprofen/pseudoephedrine HCl | Wal-Profen D Cold and Sinus |
| indacaterol maleate | Arcapta Neohaler |
| indacaterol maleate/glycopyrrolate | Utibron Neohaler |
| ipratropium bromide | Atrovent HFA |
| ipratropium bromide | ipratropium bromide |
| ipratropium bromide/albuterol sulfate | Combivent Respimat |
| ipratropium bromide/albuterol sulfate | DuoNeb |
| ipratropium bromide/albuterol sulfate | ipratropium-albuterol |
| ketotifen fumarate | Alaway |
| ketotifen fumarate | Allergy Eye (ketotifen) |
| ketotifen fumarate | Antihistamine Eye Drops |
| ketotifen fumarate | Children's Alaway |
| ketotifen fumarate | Eye Itch Relief |
| ketotifen fumarate | Itchy Eye Drops |
| ketotifen fumarate | Wal-Zyr (ketotifen) |
| ketotifen fumarate | Zaditor |
| ketotifen fumarate | ketotifen fumarate |
| levalbuterol HCl | Xopenex |
| levalbuterol HCl | Xopenex Concentrate |
| levalbuterol HCl | levalbuterol HCl |
| levalbuterol HCl | levalbuterol HCl (bulk) |
| levalbuterol tartrate | Xopenex HFA |
| levalbuterol tartrate | levalbuterol tartrate |
| levocetirizine dihydrochloride | 24HR Allergy Relief |
| levocetirizine dihydrochloride | Xyzal |
| levocetirizine dihydrochloride | levocetirizine |
| levocetirizine dihydrochloride | levocetirizine (bulk) |
| lodoxamide tromethamine | Alomide |
| loratadine | Alavert |
| loratadine | Allerclear |
| loratadine | Allergy Relief (loratadine) |
| loratadine | Children's Allergy Relief(lor) |
| loratadine | Children's Claritin |
| loratadine | Children's Loratadine |
| loratadine | Claritin |
| loratadine | Claritin Liqui-Gel |
| loratadine | Claritin RediTabs |
| loratadine | Loradamed |
| loratadine | Non-Drowsy Allergy |
| loratadine | Vicks QlearQuil Allergy |
| loratadine | Wal-itin |
| loratadine | loratadine |
| loratadine | loratadine (bulk) |
| loratadine, micronized | loratadine, micronized (bulk) |
| loratadine/pseudoephedrine sulfate | Alavert D-12 Allergy-Sinus |
| loratadine/pseudoephedrine sulfate | AllerClear D-12hr |
| loratadine/pseudoephedrine sulfate | AllerClear D-24hr |
| loratadine/pseudoephedrine sulfate | Allergy Relief D-24hr |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| loratadine/pseudoephedrine sulfate | Allergy Relief D12 |
| loratadine/pseudoephedrine sulfate | Allergy Relief,NasalDecongest |
| loratadine/pseudoephedrine sulfate | Allergy Relief-D (loratadine) |
| loratadine/pseudoephedrine sulfate | Allergy and Congestion Relief |
| loratadine/pseudoephedrine sulfate | Allergy-Congestion Relief-D |
| loratadine/pseudoephedrine sulfate | Claritin-D 12 Hour |
| loratadine/pseudoephedrine sulfate | Claritin-D 24 Hour |
| loratadine/pseudoephedrine sulfate | Lorata-D |
| loratadine/pseudoephedrine sulfate | Loratadine-D |
| loratadine/pseudoephedrine sulfate | Wal-Itin D 12 Hour |
| loratadine/pseudoephedrine sulfate | Wal-itin D |
| loratadine/pseudoephedrine sulfate | lorata-dine D |
| loratadine/pseudoephedrine sulfate | loratadine-pseudoephedrine |
| meloxicam | Mobic |
| meloxicam | meloxicam |
| mepolizumab | Nucala |
| metaproterenol sulfate | metaproterenol |
| methylprednisolone | Medrol |
| methylprednisolone | Medrol (Pak) |
| methylprednisolone | Methylpred DP |
| methylprednisolone | methylprednisolone |
| methylprednisolone acetate | Depo-Medrol |
| methylprednisolone acetate | P-Care D40 |
| methylprednisolone acetate | P-Care D80 |
| methylprednisolone acetate | ReadySharpMethylprednisolone |
| methylprednisolone acetate | methylprednisolone acetate |
| methylprednisolone acetate in sodium chloride,iso-osmotic/PF | methylpredac(PF)-NaCl,iso-osm |
| methylprednisolone acetate in sterile water for injection | methylprednisoloneacet-water |
| methylprednisolone acetate/bupivacaine HCl | Physicians EZ Use M-Pred |
| methylprednisolone acetate/bupivacaine HCl in sterile water | methylprednisolac-bupivac-wat |
| methylprednisolone acetate/norflurane/HFC 245fa | Medroloan II SUIK |
| methylprednisolone acetate/norflurane/HFC 245fa | Medroloan SUIK |
| methylprednisolone acetate/norflurane/HFC 245fa | P-Care D40G |
| methylprednisolone acetate/norflurane/HFC 245fa | P-Care D80G |
| methylprednisolone sodium succinate | Solu-Medrol |
| methylprednisolone sodium succinate | methylprednisolone sodiumsucc |
| methylprednisolone sodium succinate/PF | Solu-Medrol (PF) |
| methylprednisolone, micronized | methylprednisolone, mic(bulk) |
| mometasone furoate | Asmanex HFA |
| mometasone furoate | Asmanex Twisthaler |
| mometasone furoate | Nasonex |
| mometasone furoate | mometasone |
| mometasone furoate | mometasone furoate (bulk) |
| mometasone furoate/ammonium lactate | Momexin |
| mometasone furoate/formoterol fumarate | Dulera |
| montelukast sodium | Singulair |
| montelukast sodium | montelukast |
| montelukast sodium | montelukast (bulk) |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| naproxen | naproxen |
| naproxen sodium | All Day Pain Relief |
| naproxen sodium | All Day Relief |
| naproxen sodium | Flanax (naproxen) |
| naproxen sodium | Midol (naproxen) |
| naproxen sodium | Wal-Proxen |
| naproxen sodium | naproxen sodium |
| naproxen sodium/pseudoephedrine HCl | Aleve Cold and Sinus |
| naproxen sodium/pseudoephedrine HCl | Aleve Sinus and Headache |
| naproxen sodium/pseudoephedrine HCl | All Day Pain Relief Sinus,Cold |
| naproxen sodium/pseudoephedrine HCl | Sinus and Cold-D |
| nedocromil sodium | Alocril |
| olodaterol HCl | Striverdi Respimat |
| olopatadine HCl | Pataday |
| olopatadine HCl | Patanase |
| olopatadine HCl | Patanol |
| olopatadine HCl | Pazeo |
| olopatadine HCl | olopatadine |
| omalizumab | Xolair |
| phenylephrine HCl/acetaminophen | AcetaminophenCongestion-Pain |
| phenylephrine HCl/acetaminophen | Contac Cold-Flu Day |
| phenylephrine HCl/acetaminophen | DayTime Sinus |
| phenylephrine HCl/acetaminophen | Daytime Sinus-Congestion |
| phenylephrine HCl/acetaminophen | Mapap Sinus Max Strength(PE) |
| phenylephrine HCl/acetaminophen | Non-Aspirin Sinus |
| phenylephrine HCl/acetaminophen | Pain Relief Sinus PE |
| phenylephrine HCl/acetaminophen | Pyrroxate Cold andCongestion |
| phenylephrine HCl/acetaminophen | Sinus Congestion and Pain |
| phenylephrine HCl/acetaminophen | Sinus Headache PE |
| phenylephrine HCl/acetaminophen | Sinus Maximum Strength |
| phenylephrine HCl/acetaminophen | Sinus Pain-Pressure (PE) |
| phenylephrine HCl/acetaminophen | Sinus Relief (Non-Drowsy) |
| phenylephrine HCl/acetaminophen | Sudafed PE Pressure-Pain |
| phenylephrine HCl/acetaminophen | Suphedrine PE SinusHeadache |
| phenylephrine HCl/acetaminophen | Tylenol Sinus CongestionPain |
| phenylephrine HCl/acetaminophen | Vicks Dayquil Sinex |
| phenylephrine HCl/acetaminophen | Vicks QlearQuil DaytimeSinus |
| phenylephrine HCl/acetaminophen | Vicks Sinex Daytime |
| phenylephrine HCl/acetaminophen | Wal-Phed PE SinusHeadache |
| phenylephrine HCl/acetaminophen/chlorpheniramine | Allergy Multi-Symptom |
| phenylephrine HCl/acetaminophen/chlorpheniramine | Allergy Relief Multi-Symptom |
| phenylephrine HCl/acetaminophen/chlorpheniramine | Allergy Relief(chlorphen-acet) |
| phenylephrine HCl/acetaminophen/chlorpheniramine | Allergy Sinus PE |
| phenylephrine HCl/acetaminophen/chlorpheniramine | Contac Cold-Flu Day andNight |
| phenylephrine HCl/acetaminophen/chlorpheniramine | Contac Cold-Flu Max Strength |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| phenylephrine HCl/acetaminophen/chlorpheniramine | Dristan Cold |
| phenylephrine HCl/acetaminophen/chlorpheniramine | Effervescent Cold Relief Plus |
| phenylephrine HCl/acetaminophen/chlorpheniramine | Medicidin-D |
| phenylephrine HCl/acetaminophen/chlorpheniramine | Norel AD |
| phenylephrine HCl/acetaminophen/chlorpheniramine | Sinus Congest-PainDay-Night |
| phenylephrine HCl/acetaminophen/chlorpheniramine | SinusCongestion-Pain(chlorph) |
| phenylephrine HCl/acetaminophen/chlorpheniramine | Sinutrol PE |
| phenylephrine HCl/acetaminophen/doxylamine succinate | DayTime and NiteTime Sinus |
| phenylephrine HCl/acetaminophen/doxylamine succinate | NightTime Sinus |
| phenylephrine HCl/acetaminophen/doxylamine succinate | Nighttime Sinus-Congestion |
| phenylephrine HCl/acetaminophen/doxylamine succinate | Sinus Daytime-Nightime |
| phenylephrine HCl/acetaminophen/doxylamine succinate | Vicks Nyquil Sinex |
| phenylephrine HCl/acetaminophen/doxylamine succinate | Vicks QlearQuil NightimeSinus |
| phenylephrine HCl/chlophedianol HCl/guaifenesin | Donatussin Pediatric |
| phenylephrine HCl/chlophedianol HCl/guaifenesin | Vanacof GPE |
| phenylephrine HCl/chlophedianol HCl/guaifenesin | phenylephrine-chlophedianol-GG |
| phenylephrine HCl/codeine phosphate/acetaminophen/guaifen | Phenflu CD |
| phenylephrine HCl/codeine phosphate/acetaminophen/guaifen | Phenflu CDX |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Children's Cold-Cough-Sore |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Children's MucinexCold-Fever |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Cold Head Congestion SeverDay |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Cold Severe Congestion |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Cold and Flu Severe |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Cold-Cough Sinus Relief PE |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Decorel Forte Plus |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Delsym Cough-Cold Daytime |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Dometuss G |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Fast Mucus Relief SevereCold |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Head Congestion Cold Relief |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Herbiomed Severe Cold-FluM-S |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Mucinex Cold,Flu,Sore Throat |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Mucinex Fast-MaxCold-Flu-Thrt |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Mucinex Fast-Max SevereCold |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Mucinex Sinus-MaxPressure-Cgh |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Mucinex Sinus-Max SevCong(DM) |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Mucus Relief Cold-Flu-SoreThr |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Mucus Relief Plus |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Mucus Relief SevCongest-Cold |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Mucus Relief Severe Cold |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Multi-Symptom Cold (PE) |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Non-Pseudo Cold Relief |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Pain Relief Cold |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Pressure-Pain PE Plus Cold |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Pressure-Pain-Cold |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Rompe Pecho Max MultiSymptoms |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Severe Cold |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Severe Cold Multi-Symptom |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Severe Cold and Flu (PE) |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Sudafed PEPressure-Pain-Cold |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Tussin CF Max Severe M-SCold |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Tylenol Cold and Flu Severe |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Vicks DayQuil SevereCold-Flu |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Wal-Phed PE Cold-Cough |
| phenylephrine HCl/dextromethorphan HBr/acetaminophen/guaifen | Wal-Phed PEPressure+Pain+Cold |
| phenylephrine HCl/diphenhydramine HCl | Aldex-CT |
| phenylephrine HCl/diphenhydramine HCl | Allergy and Sinus Relief |
| phenylephrine HCl/diphenhydramine HCl | Child Allergy Plus Congestion |
| phenylephrine HCl/diphenhydramine HCl | Child Benadryl PlusCongestion |
| phenylephrine HCl/diphenhydramine HCl | Child's Benadryl-D Allergy-Sin |
| phenylephrine HCl/diphenhydramine HCl | Children Night TimeCold-Cough |
| phenylephrine HCl/diphenhydramine HCl | Childs Triacting Cold-Cough |
| phenylephrine HCl/diphenhydramine HCl | Cold and Cough(diphenhydr-pe) |
| phenylephrine HCl/diphenhydramine HCl | Dimetapp Cold-Congestion |
| phenylephrine HCl/diphenhydramine HCl | Nighttime Cough-Cold |
| phenylephrine HCl/diphenhydramine HCl | Triaminic Cold andCoughNT(PE) |
| phenylephrine HCl/diphenhydramine HCl | diphenhydramine-phenylephrine |
| phenylephrine HCl/promethazine HCl | Promethazine VC |
| phenylephrine HCl/promethazine HCl | promethazine-phenylephrine |
| phenylephrine HCl/pyrilamine maleate | Aldex D |
| phenylephrine HCl/pyrilamine maleate | Glen PE |
| phenylephrine HCl/pyrilamine maleate | Poly Hist Forte (pyrilamine) |
| phenylephrine HCl/pyrilamine maleate | Pyril D |
| phenylephrine HCl/pyrilamine maleate | Vazotab (pyrilamine) |
| phenylephrine HCl/pyrilamine maleate | pyrilamine-phenylephrine |
| phenylephrine HCl/triprolidine HCl | Histex PE |
| phenylephrine HCl/triprolidine HCl | Sinus Nighttime |
| prednisolone | Millipred |
| prednisolone | Millipred DP |
| prednisolone | Prelone |
| prednisolone | prednisolone |
| prednisolone acetate | Flo-Pred |
| prednisolone acetate, micronized | prednisolone ac, micro (bulk) |
| prednisolone, micronized | prednisolone, micro (bulk) |
| prednisone | Deltasone |
| prednisone | Prednisone Intensol |
| prednisone | Rayos |
| prednisone | prednisone |
| prednisone micronized | prednisone micronized (bulk) |
| promethazine HCl | Phenadoz |
| promethazine HCl | Phenergan |
| promethazine HCl | Promethegan |
| promethazine HCl | promethazine |
| promethazine HCl | promethazine (bulk) |
| promethazine HCl in 0.9 % sodium chloride | promethazine in 0.9 % NaCl |
| promethazine HCl/codeine | promethazine-codeine |
| promethazine HCl/dextromethorphan HBr | promethazine-DM |
| promethazine/phenylephrine HCl/codeine | Promethazine VC-Codeine |
| promethazine/phenylephrine HCl/codeine | promethazine-phenyleph-codeine |
| pseudoephedrine HCl/acetaminophen | Nexafed Sinus Pressure-Pain |
| pseudoephedrine HCl/acetaminophen | Sinus HeadacheDegongestant |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| pseudoephedrine HCl/acetaminophen/chlorpheniramine | Allergy Sinus-D |
| pseudoephedrine HCl/acetaminophen/chlorpheniramine | Non-Aspirin Allergy Sinus |
| pseudoephedrine HCl/acetaminophen/chlorpheniramine | Non-Aspirin Child's Cold |
| pseudoephedrine HCl/acetaminophen/chlorpheniramine | Pain Reliever Allergy Sinus |
| pseudoephedrine HCl/acrivastine | Semprex-D |
| pseudoephedrine HCl/chlophedianol HCl | Rondec-D |
| pseudoephedrine HCl/chlophedianol HCl/guaifenesin | Certuss-D |
| pseudoephedrine HCl/chlophedianol HCl/guaifenesin | Vanacof DX |
| pseudoephedrine HCl/chlophedianol HCl/guaifenesin | Vanatab DX |
| pseudoephedrine HCl/chlorpheniramine maleate/bellad alk | Respa-AR |
| pseudoephedrine HCl/codeine phosphate | Codar D |
| pseudoephedrine HCl/codeine phosphate/acetaminophen/guaifen | Maxiflu CD |
| pseudoephedrine HCl/codeine phosphate/acetaminophen/guaifen | Maxiflu CDX |
| pseudoephedrine HCl/codeine phosphate/guaifenesin | Cheratussin DAC |
| pseudoephedrine HCl/codeine phosphate/guaifenesin | Coditussin DAC |
| pseudoephedrine HCl/codeine phosphate/guaifenesin | Guaifenesin DAC |
| pseudoephedrine HCl/codeine phosphate/guaifenesin | Lortuss EX |
| pseudoephedrine HCl/codeine phosphate/guaifenesin | Phenylhistine |
| pseudoephedrine HCl/codeine phosphate/guaifenesin | Tricode GF |
| pseudoephedrine HCl/codeine phosphate/guaifenesin | Tusnel C |
| pseudoephedrine HCl/codeine phosphate/guaifenesin | Virtussin DAC |
| pseudoephedrine HCl/codeine phosphate/guaifenesin | Zodryl DEC 25 |
| pseudoephedrine HCl/codeine phosphate/guaifenesin | Zodryl DEC 30 |
| pseudoephedrine HCl/codeine phosphate/guaifenesin | Zodryl DEC 35 |
| pseudoephedrine HCl/codeine phosphate/guaifenesin | Zodryl DEC 40 |
| pseudoephedrine HCl/codeine phosphate/guaifenesin | Zodryl DEC 50 |
| pseudoephedrine HCl/codeine phosphate/guaifenesin | Zodryl DEC 60 |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| pseudoephedrine HCl/codeine phosphate/guaifenesin | Zodryl DEC 80 |
| pseudoephedrine HCl/codeine/chlorpheniramine | Phenylhistine DH |
| pseudoephedrine HCl/hydrocodone bitartrate | Rezira |
| pyrilamine maleate | pyrilamine maleate (bulk) |
| pyrilamine maleate/chlophedianol HCl | DayClear Allergy Relief |
| pyrilamine maleate/chlophedianol HCl | Ninjacof |
| pyrilamine maleate/chlophedianol HCl | VanaCof AC |
| pyrilamine maleate/chlophedianol HCl | VanaTab AC |
| pyrilamine maleate/chlophedianol HCl | Vanacof-8 |
| pyrilamine maleate/chlophedianol HCl/acetaminophen | Ninjacof-A |
| pyrilamine maleate/dextromethorphan HBr | Capron DM |
| pyrilamine maleate/dextromethorphan HBr | Capron DMT |
| pyrilamine maleate/phenylephrine HCl/chlophedianol HCl | Pro-Chlo |
| pyrilamine maleate/phenylephrine HCl/dextromethorphan HBr | Codituss DM |
| pyrilamine maleate/pseudoephedrine HCl/chlophedianol HCl | Ninjacof-D |
| racepinephrine HCl | Asthmanefrin Refill |
| racepinephrine HCl | Asthmanefrin Starter Kit |
| racepinephrine HCl | S2 Racepinephrine |
| racepinephrine HCl | racepinephrine |
| racepinephrine HCl | racepinephrine (bulk) |
| reslizumab | Cinqair |
| revefenacin | Yupelri |
| roflumilast | Daliresp |
| salmeterol xinafoate | Serevent Diskus |
| terbutaline sulfate | terbutaline |
| theophylline anhydrous | Elixophyllin |
| theophylline anhydrous | Theo-24 |
| theophylline anhydrous | Theochron |
| theophylline anhydrous | theophylline |
| thonzylamine HCl/chlophedianol HCl | POLY HIST PD |
| thonzylamine HCl/phenylephrine HCl | Nasopen PE |
| thonzylamine HCl/phenylephrine HCl/chlophedianol HCl | Vanacof APE |
| thonzylamine HCl/phenylephrine HCl/dextromethorphan HBr | Poly-Hist DM (thonzylamine) |
| tiotropium bromide | Spiriva Respimat |
| tiotropium bromide | Spiriva with HandiHaler |
| tiotropium bromide/olodaterol HCl | Stiolto Respimat |
| tranilast | tranilast (bulk) |
| triamcinolone acetonide | 24 Hour Nasal Allergy |
| triamcinolone acetonide | Arze-Ject-A |
| triamcinolone acetonide | Children's Nasacort |
| triamcinolone acetonide | Kenalog |
| triamcinolone acetonide | Kenalog-80 |
| triamcinolone acetonide | Nasacort |
| triamcinolone acetonide | Nasacort AQ |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| triamcinolone acetonide | Nasal Allergy |
| triamcinolone acetonide | P-Care K40 |
| triamcinolone acetonide | P-Care K80 |
| triamcinolone acetonide | Pod-Care 100K |
| triamcinolone acetonide | Pro-C-Dure 5 |
| triamcinolone acetonide | Pro-C-Dure 6 |
| triamcinolone acetonide | ReadySharp Triamcinolone |
| triamcinolone acetonide | Zilretta |
| triamcinolone acetonide | triamcinolone acetonide |
| triamcinolone acetonide | triamcinolone acetonide (bulk) |
| triamcinolone acetonide in 0.9 % sodium chloride | triamcinolone aceton-0.9%NaCl |
| triamcinolone acetonide/0.9% sodium chloride/PF | triamcinol ac (PF) in0.9%NaCl |
| triamcinolone acetonide/dimethicone | Ellzia Pak |
| triamcinolone acetonide/dimethicone/silicone, adhesive | DermaSilkRx SDS |
| triamcinolone acetonide/dimethicone/silicone, adhesive | DermaWerx SDS |
| triamcinolone acetonide/dimethicone/silicone, adhesive | DermacinRx SilaPak |
| triamcinolone acetonide/dimethicone/silicone, adhesive | NuTriaRx |
| triamcinolone acetonide/dimethicone/silicone, adhesive | SanaDermRx |
| triamcinolone acetonide/dimethicone/silicone, adhesive | Sure Result Tac Pak |
| triamcinolone acetonide/dimethicone/silicone, adhesive | Tri-Sila |
| triamcinolone acetonide/dimethicone/silicone, adhesive | Whytederm TDPak |
| triamcinolone acetonide/dimethicone/silicone, adhesive | Whytederm Trilasil Pak |
| triamcinolone acetonide/emollient combination no.45 | Pediaderm TA |
| triamcinolone acetonide/emollient combination no.86 | Dermasorb TA Complete Kit |
| triamcinolone acetonide/lidocaine HCl | EZ Use Joint-Tunnel-Trigger |
| triamcinolone acetonide/lidocaine HCl | Lidocilone I |
| triamcinolone acetonide/lidocaine/prilocaine | DermacinRx Cinlone-I CPI |
| triamcinolone diacetate in 0.9 % sodium chloride | triamcinolone diacet-0.9%NaCl |
| triamcinolone diacetate in 0.9 % sodium chloride/PF | triamcinolonedia(PF)-0.9%NaCl |
| triamcinolone hexacetonide | Aristospan Intra-Articular |
| triamcinolone hexacetonide | Aristospan Intralesional |
| triamcinolone hexacetonide | triamcinolone hexaceton(bulk) |
| triamcinolone hexacetonide, micronized | triamcin hexacet, micro (bulk) |
| triamcinolone/norflurane and pentafluoropropane (HFC 245fa) | P-Care K40G |
| triamcinolone/norflurane and pentafluoropropane (HFC 245fa) | P-Care K80G |
| triamcinolone/norflurane and pentafluoropropane (HFC 245fa) | Pod-Care 100KG |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| triamcinolone/norflurane and pentafluoropropane (HFC 245fa) | Triloan II SUIK |
| triamcinolone/norflurane and pentafluoropropane (HFC 245fa) | Triloan SUIK |
| trimeprazine tartrate | trimeprazine tartrate (bulk) |
| tripelennamine HCl | tripelennamine (bulk) |
| triprolidine HCl | Histex (triprolidine) |
| triprolidine HCl | Histex PD |
| triprolidine HCl | Histex PDX |
| triprolidine HCl | M-Hist PD |
| triprolidine HCl | VanaClear PD |
| triprolidine HCl | Vanahist PD |
| triprolidine HCl | triprolidine HCl |
| triprolidine HCl | triprolidine HCl (bulk) |
| triprolidine HCl/phenylephrine HCl/codeine phosphate | Histex-AC |
| triprolidine HCl/phenylephrine HCl/dextromethorphan HBr | Histex DM |
| triprolidine HCl/pseudoephedrine HCl | Aprodine |
| triprolidine HCl/pseudoephedrine HCl/chlophedianol HCl | Trymine CD |
| umeclidinium bromide | Incruse Ellipta |
| umeclidinium bromide/vilanterol trifenatate | Anoro Ellipta |
| zafirlukast | Accolate |
| zafirlukast | zafirlukast |
| zileuton | Zyflo |
| zileuton | Zyflo CR |
| zileuton | zileuton |
| **Nonsteroidal Anti-Inflammatory Drugs** | |
| CHLORPHENIRAMINE MALEATE/PHENYLEPHRINE HCL/IBUPROFEN | Advil Allergy-Congestion Rlf |
| CHLORPHENIRAMINE MALEATE/PSEUDOEPHEDRINE HCL/IBUPROFEN | Advil Allergy Sinus |
| HYDROCODONE/IBUPROFEN | Ibudone |
| HYDROCODONE/IBUPROFEN | Reprexain |
| HYDROCODONE/IBUPROFEN | Vicoprofen |
| HYDROCODONE/IBUPROFEN | Xylon 10 |
| HYDROCODONE/IBUPROFEN | hydrocodone-ibuprofen |
| IBUPROFEN | Children's Ibuprofen |
| IBUPROFEN | ibuprofen |
| IBUPROFEN/OXYCODONE HCL | ibuprofen-oxycodone |
| IBUPROFEN/PHENYLEPHRINE HCL | Advil Congestion Relief |
| IBUPROFEN/PHENYLEPHRINE HCL | Congestion Relief(ibuprof-PE) |
| IBUPROFEN/PSEUDOEPHEDRINE HCL | Advil Cold and Sinus |
| IBUPROFEN/PSEUDOEPHEDRINE HCL | Cold and Sinus Pain Relief |
| IBUPROFEN/PSEUDOEPHEDRINE HCL | Cold-Sinus Relief |
| IBUPROFEN/PSEUDOEPHEDRINE HCL | Ibuprofen Cold |
| IBUPROFEN/PSEUDOEPHEDRINE HCL | Ibuprofen Cold-Sinus(withPSE) |
| IBUPROFEN/PSEUDOEPHEDRINE HCL | Wal-Profen Cold-Sinus |
| IBUPROFEN/PSEUDOEPHEDRINE HCL | Wal-Profen D Cold and Sinus |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| INDOMETHACIN | indomethacin |
| NAPROXEN SODIUM | naproxen sodium |
| NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL | Aleve Cold and Sinus |
| NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL | Aleve Sinus and Headache |
| NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL | Aleve-D Sinus and Cold |
| NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL | Aleve-D Sinus and Headache |
| NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL | All Day Pain Relief Sinus,Cold |
| NAPROXEN SODIUM/PSEUDOEPHEDRINE HCL | Sinus and Cold-D |
| OXAPROZIN | oxaprozin |
| PIROXICAM | piroxicam |
| SUMATRIPTAN SUCCINATE/NAPROXEN SODIUM | Treximet |
| celecoxib | Celebrex |
| celecoxib | celecoxib |
| diclofenac potassium | Cambia |
| diclofenac potassium | Cataflam |
| diclofenac potassium | Zipsor |
| diclofenac potassium | diclofenac potassium |
| diclofenac sodium | Voltaren-XR |
| diclofenac sodium/misoprostol | Arthrotec 50 |
| diclofenac sodium/misoprostol | Arthrotec 75 |
| diclofenac sodium/misoprostol | diclofenac-misoprostol |
| diclofenac submicronized | Zorvolex |
| etodolac | Lodine |
| etodolac | etodolac |
| fenoprofen calcium | Fenortho |
| fenoprofen calcium | Nalfon |
| fenoprofen calcium | ProFeno |
| fenoprofen calcium | fenoprofen |
| flurbiprofen | Ansaid |
| ibuprofen | Advil |
| ibuprofen | Advil Liqui-Gel |
| ibuprofen | Advil Migraine |
| ibuprofen | Child Ibuprofen |
| ibuprofen | Children's Advil |
| ibuprofen | Children's Medi-Profen |
| ibuprofen | Children's Motrin |
| ibuprofen | Children's Profen IB |
| ibuprofen | I-Prin |
| ibuprofen | IBU |
| ibuprofen | IBU-200 |
| ibuprofen | Ibu-Drops |
| ibuprofen | Infant's Advil |
| ibuprofen | Infant's Medi-Profen |
| ibuprofen | Infant's Motrin |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| ibuprofen | Infants ProfenIB |
| ibuprofen | Motrin IB |
| ibuprofen | Provil |
| ibuprofen/diphenhydramine HCl | Advil PM Liqui-Gels |
| ibuprofen/diphenhydramine citrate | Advil PM |
| ibuprofen/diphenhydramine citrate | Motrin PM |
| ibuprofen/diphenhydramine citrate | ibuprofen-diphenhydramine cit |
| ibuprofen/famotidine | Duexis |
| indomethacin | Indocin |
| indomethacin | indomethacin |
| indomethacin, submicronized | Tivorbex |
| ketoprofen | ketoprofen |
| ketorolac tromethamine | ketorolac |
| meclofenamate sodium | meclofenamate |
| mefenamic acid | Ponstel |
| mefenamic acid | mefenamic acid |
| meloxicam | Qmiiz ODT |
| meloxicam, submicronized | Vivlodex |
| nabumetone | nabumetone |
| naproxen | EC-Naprosyn |
| naproxen | EC-Naproxen |
| naproxen | Naprosyn |
| naproxen sodium | Aleve |
| naproxen sodium | Anaprox |
| naproxen sodium | Anaprox DS |
| naproxen sodium | Mediproxen |
| naproxen sodium | Naprelan CR |
| naproxen sodium/diphenhydramine HCl | Aleve PM |
| naproxen/esomeprazole magnesium | Vimovo |
| oxaprozin | Daypro |
| oxaprozin | oxaprozin |
| piroxicam | Feldene |
| piroxicam | piroxicam |
| sulindac | sulindac |
| tolmetin sodium | tolmetin |
| **Diuretics (Thiazides, Potassium Sparing, Loop Diuretics)** | |
| amiloride HCl | amiloride |
| amiloride HCl/hydrochlorothiazide | amiloride-hydrochlorothiazide |
| bumetanide | bumetanide |
| chlorothiazide | Diuril |
| chlorothiazide | chlorothiazide |
| chlorothiazide sodium | Diuril IV |
| chlorothiazide sodium | chlorothiazide sodium |
| chlorthalidone | chlorthalidone |
| eplerenone | Inspra |
| eplerenone | eplerenone |
| ethacrynate sodium | Sodium Edecrin |
| ethacrynate sodium | ethacrynate sodium |
| ethacrynic acid | Edecrin |
| ethacrynic acid | ethacrynic acid |
| furosemide | Lasix |

**Appendix G. Generic and Brand Names of Medical Products Used to Define Covariates in this Request**

| Generic Name | Brand Name |
|---|---|
| furosemide | furosemide |
| furosemide | furosemide (bulk) |
| furosemide in 0.9 % sodium chloride | furosemide in 0.9 % NaCl |
| furosemide/dextrose 5 % in water | furosemide in dextrose 5 % |
| hydrochlorothiazide | Microzide |
| hydrochlorothiazide | hydrochlorothiazide |
| hydrochlorothiazide | hydrochlorothiazide (bulk) |
| indapamide | indapamide |
| methyclothiazide | methyclothiazide |
| metolazone | Zaroxolyn |
| metolazone | metolazone |
| spironolactone | Aldactone |
| spironolactone | CaroSpir |
| spironolactone | spironolactone |
| spironolactone | spironolactone (bulk) |
| spironolactone, micronized | spironolactone micro (bulk) |
| spironolactone/hydrochlorothiazide | Aldactazide |
| spironolactone/hydrochlorothiazide | spironolacton-hydrochlorothiaz |
| torsemide | Demadex |
| torsemide | torsemide |
| triamterene | Dyrenium |
| triamterene | triamterene |
| triamterene | triamterene (bulk) |
| triamterene/hydrochlorothiazide | Dyazide |
| triamterene/hydrochlorothiazide | Maxzide |
| triamterene/hydrochlorothiazide | Maxzide-25mg |
| triamterene/hydrochlorothiazide | triamterene-hydrochlorothiazid |
| trichlormethiazide | trichlormethiazide (bulk) |
| **Everolimus** | |
| everolimus | Afinitor |
| everolimus | Afinitor Disperz |
| everolimus | Zortress |
| **Sirolimus** | |
| sirolimus | Rapamune |
| sirolimus | sirolimus |

**Appendix H. Specifications Defining Parameters for this Request**

This request executed the Cohort Identification and Descriptive Analysis (CIDA) and Propensity Score Analysis (PSA) modules within the Query Request Package, version 9.7.0, with custom programming to assess the risk for angioedema associated with sacubitril/valsartan (SV) compared to angiotensin-converting enzyme inhibitors (ACEIs) or to angiotensin II receptor blockers (ARBs, excluding SV) among heart failure patients in the Sentinel Distributed Database (SDD).

**Query Period:** 7/7/2015 - data completeness
**Coverage Requirement:** Medical and drug coverage
**Enrollment Requirement:** 183 days
**Enrollment Gap:** 45 days
**Age Groups:** 18-44, 45-54, 55-64, 65+ years
**Output Requested:** Attrition table, Kaplan–Meier curves
**Additional Programming Needed:** Allow SV switchers to re-enter comparisons requiring prior comparator use by altering PSA pre-processing rules
**Notes:** Ran against the same ETLs of the SCDM as cder_mpl2r_wp016

| | Prior comparator use (183 days); angioedema SV users allowed to be in primary exposure group AND comparator group | | | | Prior comparator use (14 days); angioedema SV users allowed to be in primary exposure group AND comparator group | | | |
|---|---|---|---|---|---|---|---|---|
| | Comparison 1 | | Comparison 2 | | Comparison 3 | | Comparison 4 | |
| **Drug/Exposure** | | | | | | | | |
| **Exposure/Comparator** | SV | ACEI | SV | ARBs | SV | ACEI | SV | ARBs |
| **Incident with Respect to:** | SV, ARBs | ACEI, ARBs, SV | SV, ACEI | ACEI, ARBs, SV | SV, ARBs | ACEI, ARBs, SV | SV, ACEI | ACEI, ARBs, SV |
| **Incidence Assessment** | Dispensing date or days supply | | Dispensing date or days supply | | Dispensing date or days supply | | Dispensing date or days supply | |
| **Washout (days)** | 183 | | 183 | | 183 | | 183 | |
| **Cohort Definition** | First valid incident exposure episode | | First valid incident exposure episode | | First valid incident exposure episode | | First valid incident exposure episode | |
| **Stockpiling Overlapping Claims** | Default | | Default | | Default | | Default | |
| **Episode Gap (days)** | 14 | | 14 | | 14 | | 14 | |
| **Episode Extension Period (days)** | 14 | | 14 | | 14 | | 14 | |
| **Maximum Episode Duration (days)** | 365 | | 365 | | 365 | | 365 | |
| **Censor Criteria** | ACEI | SV | ARBs | SV | ACEI | SV | ARBs | SV |
| | ARBs, end of treatment, outcome occurrence, disenrollment, recorded death, data end date | | ACEI, end of treatment, outcome occurrence, disenrollment, recorded death, data end date | | ARBs, end of treatment, outcome occurrence, disenrollment, recorded death, data end date | | ACEI, end of treatment, outcome occurrence, disenrollment, recorded death, data end date | |
| **Inclusion/Exclusion*** | | | | | | | | |
| **Pre-Existing Condition** | Heart failure | | Heart failure | | Heart failure | | Heart failure | |
| **Include/Exclude** | Include | | Include | | Include | | Include | |
| **Lookback Period (days)** | -183, 0 | | -183, 0 | | -183, 0 | | -183, 0 | |

**Appendix H. Specifications Defining Parameters for this Request**

| | Prior comparator use (183 days); angioedema SV users allowed to be in primary exposure group AND comparator group | | | | Prior comparator use (14 days); angioedema SV users allowed to be in primary exposure group AND comparator group | | | |
|---|---|---|---|---|---|---|---|---|
| | Comparison 1 | | Comparison 2 | | Comparison 3 | | Comparison 4 | |
| **Pre-Existing Condition** | ACEI | -- | ARBs | -- | ACEI | -- | ARBs | -- |
| **Include/Exclude** | Include | -- | Include | -- | Include | -- | Include | -- |
| **Care Setting/PDX** | Any | -- | Any | -- | Any | -- | Any | -- |
| **Lookback Period (days)** | -183, 0 | -- | -183, 0 | -- | -14, 0 | -- | -14, 0 | -- |
| **Inclusion Assessment** | Dispensing date or days supply | -- | Dispensing date or days supply | -- | Dispensing date or days supply | -- | Dispensing date or days supply | -- |
| **Pre-Existing Condition** | ACEI, ARBs | SV, ARBs | ARBs, ACEI | SV, ACEI | ACEI, ARBs | SV, ARBs | ARBs, ACEI | SV, ACEI |
| **Include/Exclude** | Exclude | Exclude | Exclude | Exclude | Exclude | Exclude | Exclude | Exclude |
| **Care Setting/PDX** | Any | Any | Any | Any | Any | Any | Any | Any |
| **Lookback Period** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Inclusion Assessment** | Dispensing date | Dispensing date | Dispensing date | Dispensing date | Dispensing date | Dispensing date | Dispensing date | Dispensing date |
| **Event/Outcome** | | | | | | | | |
| **Event/Outcome** | Angioedema | | Angioedema | | Angioedema | | Angioedema | |
| **Care Setting/PDX** | Inpatient, emergency department or outpatient | | Inpatient, emergency department or outpatient | | Inpatient, emergency department or outpatient | | Inpatient, emergency department or outpatient | |
| **Washout (days)** | 0 | | 0 | | 0 | | 0 | |
| **Blackout Period (days)** | 0 | | 0 | | 0 | | 0 | |
| **Propensity Score Matching** | | | | | | | | |
| **Covariates** | See Covar_Categories tab | | See Covar_Categories tab | | See Covar_Categories tab | | See Covar_Categories tab | |
| **Matching Ratio** | 1:1 | | 1:1 | | 1:1 | | 1:1 | |
| **Matching Caliper Settings** | 0.05 | | 0.05 | | 0.05 | | 0.05 | |
| **Analysis Type** | Conditional and unconditional | | Conditional and unconditional | | Conditional and unconditional | | Conditional and unconditional | |
| **Sensitivity Analysis** | PS stratification with deciles | | PS stratification with deciles | | -- | | -- | |
| **Subgroup Analyses** | | | | | | | | |
| **Stratifying variable** | Angioedema | | Angioedema | | Angioedema | | Angioedema | |
| **Evaluation Window (days)** | -183, -1 | | -183, -1 | | -183, -1 | | -183, -1 | |
| **Re-matching** | Re-matching should be done with the pre-matched cohort | | Re-matching should be done with the pre-matched cohort | | Re-matching should be done with the pre-matched cohort | | Re-matching should be done with the pre-matched cohort | |
| **Stratifying variable** | Angioedema | | Angioedema | | Angioedema | | Angioedema | |

**Appendix H. Specifications Defining Parameters for this Request**

| | Prior comparator use (183 days); angioedema SV users allowed to be in primary exposure group AND comparator group | | Prior comparator use (14 days); angioedema SV users allowed to be in primary exposure group AND comparator group | |
|---|---|---|---|---|
| | **Comparison 1** | **Comparison 2** | **Comparison 3** | **Comparison 4** |
| **Evaluation Window (days)**<br>**Re-matching** | Pre-index enrollment history, -1<br>Re-matching should be done with the pre-matched cohort | Pre-index enrollment history, -1<br>Re-matching should be done with the pre-matched cohort | Pre-index enrollment history, -1<br>Re-matching should be done with the pre-matched cohort | Pre-index enrollment history, -1<br>Re-matching should be done with the pre-matched cohort |
| **Stratifying variable**<br>**Evaluation Window (days)**<br>**Re-matching** | Serious allergies<br>-183, -1<br>Re-matching should be done with the pre-matched cohort | Serious allergies<br>-183, -1<br>Re-matching should be done with the pre-matched cohort | Serious allergies<br>-183, -1<br>Re-matching should be done with the pre-matched cohort | Serious allergies<br>-183, -1<br>Re-matching should be done with the pre-matched cohort |
| **Stratifying variable**<br>**Re-matching** | Age group<br>Re-matching should be done with the pre-matched cohort | Age group<br>Re-matching should be done with the pre-matched cohort | Age group<br>Re-matching should be done with the pre-matched cohort | Age group<br>Re-matching should be done with the pre-matched cohort |
| **Stratifying variable**<br>**Re-matching** | Sex<br>Re-matching should be done with the pre-matched cohort | Sex<br>Re-matching should be done with the pre-matched cohort | Sex<br>Re-matching should be done with the pre-matched cohort | Sex<br>Re-matching should be done with the pre-matched cohort |
| **Stratifying variable**<br>**Re-matching** | Race<br>Re-matching should be done with the pre-matched cohort | Race<br>Re-matching should be done with the pre-matched cohort | Race<br>Re-matching should be done with the pre-matched cohort | Race<br>Re-matching should be done with the pre-matched cohort |
| *** Day 0 EOI/REF dispensing exclusion were not created in input files, but instead achieved by PSA pre-processing.** | | | | |
| International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-9/10-CM), Healthcare Common Procedure Coding System (HCPCS), and Current Procedural Terminology (CPT) codes are provided by Optum360. National Drug Codes (NDC) are checked against First Data Bank's "National Drug Data File (NDDF®) Plus." | | | | |

Appendix H. Specifications Defining Parameters for this Request

| | Prior comparator use (183 days); angioedema<br>SV users allowed to be in primary exposure group AND comparator group<br>Gap sensitivity analysis | | | | Prior comparator use (183 days); serious angioedema<br>SV users allowed to be in primary exposure group AND comparator group | | | |
|---|---|---|---|---|---|---|---|---|
| | Comparison 5 | | Comparison 6 | | Comparison 7 | | Comparison 8 | |
| **Drug/Exposure** | | | | | | | | |
| **Exposure/Comparator** | SV | ACEI | SV | ARBs | SV | ACEI | SV | ARBs |
| **Incident with Respect to** | SV, ARBs | ACEI, ARBs, SV | SV, ACEI | ACEI, ARBs, SV | SV, ARBs | ACEI, ARBs, SV | SV, ACEI | ACEI, ARBs, SV |
| **Incidence Assessment** | Dispensing date or days supply | | Dispensing date or days supply | | Dispensing date or days supply | | Dispensing date or days supply | |
| **Washout (days)** | 183 | | 183 | | 183 | | 183 | |
| **Cohort Definition** | First valid incident exposure episode | | First valid incident exposure episode | | First valid incident exposure episode | | First valid incident exposure episode | |
| **Stockpiling Overlapping Claims** | Default | | Default | | Default | | Default | |
| **Episode Gap (days)** | 7 | | 7 | | 14 | | 14 | |
| **Episode Extension Period (days)** | 7 | | 7 | | 14 | | 14 | |
| **Maximum Episode Duration** | 365 | | 365 | | 365 | | 365 | |
| **Censor Criteria** | ACEI | SV | ARBs | SV | ACEI | SV | ARBs | SV |
| | ARBs, end of treatment, outcome occurrence, disenrollment, recorded death, data end date | | ACEI, end of treatment, outcome occurrence, disenrollment, recorded death, data end date | | ARBs, end of treatment, outcome occurrence, disenrollment, recorded death, data end date | | ACEI, end of treatment, outcome occurrence, disenrollment, recorded death, data end date | |
| **Inclusion/Exclusion*** | | | | | | | | |
| **Pre-Existing Condition** | Heart failure | | Heart failure | | Heart failure | | Heart failure | |
| **Include/Exclude** | Include | | Include | | Include | | Include | |
| **Lookback Period (days)** | -183, 0 | | -183, 0 | | -183, 0 | | -183, 0 | |
| **Pre-Existing Condition** | ACEI | -- | ARBs | -- | ACEI | -- | ARBs | -- |
| **Include/Exclude** | Include | -- | Include | -- | Include | -- | Include | -- |
| **Care Setting/PDX** | Any | -- | Any | -- | Any | -- | Any | -- |
| **Lookback Period (days)** | -183, 0 | -- | -183, 0 | -- | -183, 0 | -- | -183, 0 | -- |
| **Inclusion Assessment** | Dispensing date or days supply | -- | Dispensing date or days supply | -- | Dispensing date or days supply | -- | Dispensing date or days supply | -- |
| **Pre-Existing Condition** | ACEI, ARBs | SV, ARBs | ARBs, ACEI | SV, ACEI | ACEI, ARBs | SV, ARBs | ARBs, ACEI | SV, ACEI |
| **Include/Exclude** | Exclude | Exclude | Exclude | Exclude | Exclude | Exclude | Exclude | Exclude |
| **Care Setting/PDX** | Any | Any | Any | Any | Any | Any | Any | Any |
| **Lookback Period** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Inclusion Assessment** | Dispensing date | Dispensing date | Dispensing date | Dispensing date | Dispensing date | Dispensing date | Dispensing date | Dispensing date |
| **Event/Outcome** | | | | | | | | |

**Appendix H. Specifications Defining Parameters for this Request**

| | Prior comparator use (183 days); angioedema<br>SV users allowed to be in primary exposure group AND comparator group<br>Gap sensitivity analysis | | Prior comparator use (183 days); serious angioedema<br>SV users allowed to be in primary exposure group AND comparator group | |
|---|---|---|---|---|
| | **Comparison 5** | **Comparison 6** | **Comparison 7** | **Comparison 8** |
| **Event/Outcome** | Angioedema | Angioedema | Serious Angioedema | Serious Angioedema |
| **Care Setting/PDX** | Inpatient, emergency department or outpatient | Inpatient, emergency department or outpatient | Inpatient or emergency department (ED) angioedema diagnosis requiring an intensive care unit admission, intubation, tracheostomy, or laryngoscopy occurring within 2 days of the date of hospital admission or ED visit | Inpatient or emergency department (ED) angioedema diagnosis requiring an intensive care unit admission, intubation, tracheostomy, or laryngoscopy occurring within 2 days of the date of hospital admission or ED visit |
| **Washout (days)** | 0 | 0 | 0 | 0 |
| **Blackout Period (days)** | 0 | 0 | 0 | 0 |
| **Propensity Score Matching** | | | | |
| **Covariates** | See Covar_Categories tab | See Covar_Categories tab | See Covar_Categories tab | See Covar_Categories tab |
| **Matching Ratio** | 1:1 | 1:1 | 1:1 | 1:1 |
| **Matching Caliper Settings** | 0.05 | 0.05 | 0.05 | 0.05 |
| **Analysis Type** | Conditional and unconditional | Conditional and unconditional | Conditional and unconditional | Conditional and unconditional |
| **Sensitivity Analysis** | -- | -- | -- | -- |
| **Subgroup Analyses** | | | | |
| **Stratifying variable** | | | Angioedema | Angioedema |
| **Evaluation Window (days)** | | | -183, -1 | -183, -1 |
| **Re-matching** | | | Re-matching should be done with the pre-matched cohort | Re-matching should be done with the pre-matched cohort |
| **Stratifying variable** | | | Angioedema | Angioedema |
| **Evaluation Window (days)** | | | Pre-index enrollment history, -1 | Pre-index enrollment history, -1 |
| **Re-matching** | | | Re-matching should be done with the pre-matched cohort | Re-matching should be done with the pre-matched cohort |

**Appendix H. Specifications Defining Parameters for this Request**

| | Prior comparator use (183 days); angioedema<br>SV users allowed to be in primary exposure group AND comparator group<br>Gap sensitivity analysis | | Prior comparator use (183 days); serious angioedema<br>SV users allowed to be in primary exposure group AND comparator group | |
|---|---|---|---|---|
| | **Comparison 5** | **Comparison 6** | **Comparison 7** | **Comparison 8** |
| **Stratifying variable**<br>**Evaluation Window (days)**<br>**Re-matching** | | | Serious allergies<br>-183, -1<br>Re-matching should be done with the pre-matched cohort | Serious allergies<br>-183, -1<br>Re-matching should be done with the pre-matched cohort |
| **Stratifying variable**<br>**Re-matching** | | | Age group<br>Re-matching should be done with the pre-matched cohort | Age group<br>Re-matching should be done with the pre-matched cohort |
| **Stratifying variable**<br>**Re-matching** | | | Sex<br>Re-matching should be done with the pre-matched cohort | Sex<br>Re-matching should be done with the pre-matched cohort |
| **Stratifying variable**<br>**Re-matching** | | | Race<br>Re-matching should be done with the pre-matched cohort | Race<br>Re-matching should be done with the pre-matched cohort |
| *** Day 0 EOI/REF dispensing exclusion were not created in input files, but instead achieved by PSA pre-processing.** | | | | |
| International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-9/10-CM), Healthcare Common Procedure Coding System (HCPCS), and Current Procedural Terminology (CPT) codes are provided by Optum360. National Drug Codes (NDC) are checked against First Data Bank's "National Drug Data File (NDDF®) Plus." | | | | |

**Appendix I. Specifications Defining Parameters for Baseline Covariate Groups in this Request**

| Covariate | Covariate Evaluation Window (days) |
|---|---|
| **Demographic Characteristics** | |
| Age (years, continuous) | Index date |
| Age-group | |
| 18-44 years* | Index date |
| 45-54 years* | Index date |
| 55-64 years* | Index date |
| ≥65 years* | Index date |
| Sex | |
| Male | Index date |
| Female | Index date |
| Race/ethnicity | |
| American Indian or Alaska Native | Index date |
| Asian | Index date |
| Black or African American | Index date |
| Native Hawaiian or Other Pacific Islander | Index date |
| White | Index date |
| Unknown | Index date |
| Year | |
| 2015 | Index date |
| 2016 | Index date |
| 2017 | Index date |
| 2018 | Index date |
| 2019 | Index date |
| 2020 | Index date |
| **Combined Comorbidity Score** | |
| Combined comorbidity score | -183 to 0 |
| **Health Conditions** | |
| Angioedema | -183 to -1 |
| Angioedema* | Ever to -1 |
| Ambulatory allergies or allergy treatment* | -183 to -1 |
| Serious allergies (inpatient hospital stays or emergency department visits) | -183 to -1 |
| Ambulatory allergies or treatment and not serious allergies | -183 to -1 |
| Diabetes | -183 to 0 |
| Ischemic heart disease | -183 to 0 |
| Renal disorders | -183 to 0 |
| **Medications** | |
| Diuretics (thiazides, potassium sparing, loop diuretics) | -183 to 0 |
| Nonsteroidal anti-inflammatory drugs (NSAIDs) | -183 to 0 |
| Sirolimus | -183 to 0 |
| Everolimus | -183 to 0 |

**Appendix I. Specifications Defining Parameters for Baseline Covariate Groups in this Request**

| Covariate | Covariate Evaluation Window (days) |
|---|---|
| **Health care utilization** | |
| Number of inpatient hospital stays | -183 to 0 |
| Number of emergency department visits | -183 to 0 |
| Numer of institutional stay visits | -183 to 0 |
| Number of ambulatory visits | -183 to 0 |
| Number of other ambulatory visits | -183 to 0 |
| **Drug utilization** | |
| Number of unique dispensings* | -183 to 0 |
| Number of unique generics dispensed* | -183 to 0 |
| Number of unique drug classes dispensed | -183 to 0 |

* Covariates followed by an asterisk (*) were not included in the adjusted Propensity Score (PS) model; only those covariates not followed by an asterisk (*) were included in the adjusted PS model.