

## 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.

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\_iqp\_wp043

**Request ID:** cder\_iqp\_wp043\_tnx\_v01

**Request Description:** In this report, we aimed to list the most frequent diagnoses, procedures, medications and labs associated with use of atogepant, a new molecular entity (NME) approved by the FDA in 2021 using the TriNetX Live™ platform.

**Data Source:** We ran this query on May 29, 2024. This query contains data from 60 health care organizations (HCOs), provided through the TriNetX Live™ platform in their USA Network with Minimal Shift from December 18, 2020 to February 29, 2024.

TriNetX aggregates electronic health record (EHR) systems data from its partner HCOs to create queryable datasets. TriNetX datasets primarily comprise clinical patient data such as demographics, diagnoses, procedures, labs, and medications. The USA Network with Minimal Shift contains HCOs that date shift their data by 14 or fewer days (including 0). For more information on the TriNetX Live™ platform and the TriNetX data visit their website here: <https://trinetx.com/>

**Study Design:** In this retrospective cohort study, we identified patients with evidence of exposure to atogepant, an oral medication for migraine prevention, over the query period of December 18, 2020 to February 29, 2024. We used the Query Builder module in the TriNetX Live™ platform to create the aforementioned patient cohort. We used the Analytics module, specifically the Analyze Outcomes Analytics module with the Characteristics analysis type available on the TriNetX Live™ platform to generate the list of common diagnoses, procedures, medications and labs in time period between -365 days and -1 day from the index atogepant date (i.e., date of first atogepant prescription/dispensing in the query period).

**Note:** The usual lookback period for assessment of clinical characteristics in the Sentinel query series related to NMEs is six months or 183 days before index date. We extended the lookback period for the present study to 12 months or 365 days before index date. The reason for this is as follows:

- A previous study using the TriNetX Live™ platform (request id: cder\_iqp\_wp034\_tnx\_v02) showed atogepant users to be predominantly young to middle age adult females (~80% females with a mean age of 46 years).
- We wanted to ensure adequate capture of any comorbidities, prescribed medications, and any lab results, given the demographic characteristics, and the potentially low number of healthcare encounters of the users over a 6-month lookback period.

**Exposures of Interest:** We defined the exposure of interest, atogepant, using an RxNorm medication term in the Query Builder module. In order to be included in the cohort, we required evidence of at least one atogepant prescription or dispensing between December 18, 2020 and February 29, 2024. Please see Appendix A for the specific terms used to define atogepant in this request.

**Cohort Eligibility Criteria:** We created one cohort for atogepant users as detailed in the "Exposures of Interest" section. Patients of all ages were included in the cohort. Please see Appendix B for the specifications of the cohort parameters as included in the Query Builder.

**Baseline Characteristics:**

We utilized the Analyze Outcomes Analytics module with the Characteristics analysis type in the TriNetX Live™ platform to assess the most frequent diagnoses, procedures, medication classes prescribed/dispensed and lab terms (with values) in our atogepant cohort. The time period for the analysis was from 365 days before to the day before (i.e., -365 to -1 day) the index atogepant date. Please see Appendix C for the specifications defining analytic modules in this request.

### Overview for Request: cder\_iqp\_wp043

1. Most frequent diagnoses: We identified the most frequent baseline diagnoses/comorbid conditions defined as 3-digit International Classification of Diseases, 10th revision, Clinical Modification (ICD-10-CM) diagnoses codes using the relevant coding hierarchies in the TriNetX platform. For each 3-digit ICD-10-CM code, we included the most common 4-digit code within the hierarchy (i.e., 4-digit code ABC.X within 3-digit ABC code). Overall, we included up to 40 diagnoses codes using the outlined approach. The codes with the descriptions along with their prevalence in the cohort (over [-365, -1] days from index) are given in Table 1.

2. Most frequent procedures: We identified the most frequent procedures, using International Classification of Diseases, 10th Revision - Procedure Coding System (ICD-10-PCS), Healthcare Common Procedure Coding System (HCPCS), Current Procedural Terminology (CPT) and Systematized Nomenclature of Medicine (SNOMED) codes in the TriNetX platform. We used coding hierarchies, where applicable - the code chapter of the relevant system, followed by codes within, and included up to 40 procedure codes using the outlined approach. In certain situations, we focused on a level of the coding hierarchy that describe a procedure or set of similar procedures, rather than the detailed specific procedure code itself. See the note below for details. The codes with the descriptions along with their prevalence in the cohort are given in Table 2.

Note : TriNetX uses a hierarchical tree system within CPT codes using CPT subsets, which are developed for EHR systems and specific physician specialties for ease of data capture or data retrieval. These CPT subsets are 7-digit codes or parent terms, which encompasses child terms beneath, which could be other 7-digit subset or 5-digit CPT codes. *Additional details can be found at <https://cpt-international.ama-assn.org/implementation-framework>* . This is distinct from insurance claims databases (most of the Data Partners in the Sentinel Distributed Database), where only 5-digit CPT codes are used for billing purposes.

In the list of most frequent procedure codes, we included 7-digit CPT subset codes (parent terms) in addition to the 5-digit specific CPT codes, where relevant. Specifically, in situations where the procedure category or parent term was relevant to the index exposure and was frequent enough to be included in the list but the child terms were not.

3. Most frequent medication classes prescribed/dispensed: We identified the most frequent medication classes prescribed or dispensed using the Veterans Affairs (VA) Drug Classification System, which uses 5-character alphanumeric code to classify all medication products available in the United States. We listed the major classification system, followed by subcategories, and included up to 30 classes along with their prevalence in the cohort (Table 3).

Note : A specific generic ingredient can be listed in multiple classes, based on their route of administration or therapeutic category in the VA classification system.

4. Most common labs: We identified the most frequent lab terms (including vitals) using TriNetX aggregate lab terms (TNX:LAB) that group clinically relevant Logical Observation Identifiers Names and Codes (LOINC) together for each test. We listed the lab terms within the relevant lab categories curated by TriNetX (e.g., metabolic tests, lipid panel, etc.) with their description in Table 4. We also included the proportion of the cohort that had the test performed in the period of [-365, -1] days from index, and certain summary measures of the lab values closest to the index date (the mean and standard deviation, minimum and maximum value).

### Overview for Request: cder\_iqp\_wp043

**Limitations:** Algorithms used to define exposures, characteristics, and mapping of source data to the data model are imperfect and susceptible to misclassification. Additionally, EHR data in the United States lacks longitudinality. The information before or after patients' healthcare encounters could be missing, especially if patient care was administered across different HCOs that may or may not participate in the TriNetX USA network. We are unable to determine if absence of evidence of a condition implies a true absence of a condition or if the condition was not observed in the data. Furthermore, not all HCOs provide brand name or route information for RxNorm terms or laboratory data. Therefore, data should be interpreted with these limitations in mind.

The VA Classification System classifies medication products, rather than the generic ingredient. Hence, the same generic ingredient (e.g., sodium chloride, aspirin, etc.) can be classified in different drug classes, based on what route of administration or therapeutic category it belongs to. TriNetX uses two classification systems on their platform: the VA Classification System (classified available U.S. products) and the Anatomical Chemical and Therapeutic (ATC) Classification Systems (used globally), neither of which classifies drugs into mutually exclusive classes.

The units for lab tests in TriNetX are harmonized across labs when bringing new data onto the network. However, TriNetX does not remove outlier values so as not to bias the data. Hence, certain unexpected or implausible lab values may be observed in the database.

Additionally, lab values of 0 units could be observed in the database, but the interpretation of such a value could be different based on organization-specific practices for rounding, errors, or indicating inconclusive results.

All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. This rounding affects error, especially as sample sizes decrease. Error due to rounding can range from <0.09% when sample sizes are >10,000 to nearly 20% as sample sizes drop. Thus, all estimates should be interpreted as ranges, and small sample sizes should be interpreted with caution. Additionally, percentages are calculated based on these rounded numerators and denominators. Thus, due to rounding, the sum of each value in a category may not total to 100%.

A subset of HCOs that contribute to the TriNetX USA Minimal Shift network may implement date shifting between 1 and 14 days in either direction at the level of the patient record prior to data ingestion at TriNetX as a method to preserve patient privacy. When interpreting the results of an analysis, the impact of date shifting should be considered; readers should exercise caution when extrapolating information related to time.

**Notes:** We ran this query on May 29, 2024. A re-run of this query for the same query period in the future may not yield the same results owing to the dynamic nature of the TriNetX Live™ network.

Please contact the Sentinel Operations Center ([info@sentinelssystem.org](mailto:info@sentinelssystem.org)) for questions and to provide comments/suggestions for future enhancements to this document. For more information on Sentinel's querying in the TriNetX platform, please refer to the Sentinel Website (<https://www.sentinelinitiative.org/methods-data-tools/methods/trinetx-rapid-querying>).

**Table of Contents**

<b>Glossary</b>	List of Terms Found in this Report and their Definitions
<b>Table 1</b>	Most Frequent Diagnoses Among Patients with Atogepant Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024
<b>Table 2</b>	Most Frequent Procedures Among Patients with Atogepant Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024
<b>Table 3</b>	Most Frequent Prescribed Medication Classes Among Patients with Atogepant Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024
<b>Table 4</b>	Most Frequent Lab Terms Among Patients with Atogepant Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024
<b>Appendix A</b>	List of RxNorm Medication Terms Used to Define Exposure in this Request
<b>Appendix B</b>	Specifications Defining Query Builder Modules in this Request
<b>Appendix C</b>	Specifications Defining Analytic Modules in this Request

## Glossary of Terms for Analyses Using TriNetX Live™ Platform\*

**Characteristic** - A medical fact (e.g., diagnosis, procedure, lab result) that occurred on or before the cohort-defining index event.

**Explore Cohort** - A description module on the TriNetX platform that presents a clinical profile of patients in a given cohort. Patient counts are rounded up to the nearest 10 before percentages are calculated, so the sum each of the values in one category may not total to 100%.

**Fact** - (Medical Fact) A unit of utilization that represents a medical observation on a patient (e.g., diagnosis, procedure, clinical observation).

**Filter** - A method of limiting terms included in queries to a specific subset of data. Filters include age at time of event, data source (electronic health record or natural language processing); brand name, route, and strength for medication terms; occurrence (first or most recent) for lab terms; and priority for diagnosis and procedure terms.

**Group** - A series of codes and terms defined with Boolean logic that are used to create a query cohort. For each group, users have the ability to specified time periods of interest, and the number of instances that the group must occur for cohort entry.

**Subgroup** - Within a group, additional subgroups can be specified to define temporal relationships between the terms in the subgroup (e.g., terms in subgroup B must occur within 5 days after terms in subgroup A). Users can require that these temporal constraints be applied to the 1) first, 2) last, or 3) any instance of each subgroup.

**Health Care Organization (HCO)** - Organizations that contribute electronic healthcare record data to the TriNetX data networks. HCOs include academic institutions and community health provider systems and a single HCO may contain one or more individual sites or facilities.

**Index** - The first date when a patient meets all of the cohort-defining criteria. In Analytics modules, the index can be defined as the date when a patient meets all of the cohort criteria, or only one specific group's criteria.

**Module** - A subsection of the TriNetX platform that performs a distinct functionality. Cohorts are created using the Query Builder module. Descriptive modules include Healthcare Organizations, Explore Cohorts, Rate of Arrival, Summary Statistics, and Analyze Criteria. Advanced analytic modules include Analyze Outcomes, Compare Outcomes, Compare Cohorts, Treatment Pathways, and Incidence and Prevalence.

**Network** - An aggregation of HCOs contributing data to the platform. Multiple networks are available for querying on the platform; the different networks represent subsets of HCOs organized by date-shifting practices or availability of downloadable datasets.

**Outcome** - A medical fact (e.g., diagnosis, procedure, lab result) that occurred on or after the cohort-defining index event.

**Query** - In the TriNetX platform, a query is a distinct cohort with a unique set of terms and logic. Query cohorts are created using the Query Builder platform module.

**Risk** - In Advanced Analytics modules, risk refers to the percentage of patients in each cohort with the specified outcome of interest.

**Priority** - An indication whether the code was the condition that the provider spent the most time evaluating or treating during a visit. Possible values include primary, secondary, or unknown.

**Term** - The codes used to specify patient cohort criteria in a query. Code options include diagnoses, procedures, medications, labs, demographics, genomics, and visits. Terms can be linked together using and/or Boolean logic. TriNetX also creates terms that group together multiple medical codes into single clinical concepts.

**Cannot Have Term** - A category of terms within a query group that patients must not have evidence of to be included in the cohort.

**Must Have Term** - A category of terms within a query group that patients must have evidence of to be included in the cohort.

## Glossary of Terms for Analyses Using TriNetX Live™ Platform\*

**Time Constraint** - used to define time periods of interest for each group within a query. Time constraints can be defined relative to the date the query was run (e.g., any time before today), or defined based on specific dates (e.g., January 1, 2015 to September 30, 2020).

**Treatment Pathway** - In Advanced Analytics modules, the Treatment Pathways module returns the order in which patients received treatment and the prevalence of treatments, including combination of medications, following an index event.

**TriNetX Codes** - For commonly used laboratory terms, TriNetX aggregates Logical Observation Identifiers Names and Codes (LOINC) laboratory codes at a clinically significant level to new queryable TNX:LAB terms.

**Visit** - A type of term used to specify the type of medical encounter or facility where the encounter was recorded. Visit terms are derived by TriNetX from the source data. Visits are recorded separately from the codes or labs that occurred during the encounter; care settings are not attached to individual codes. Values for visit terms include: ambulatory, emergency, field, home health, inpatient encounter, inpatient acute, inpatient non-acute, laboratory, observation, pharmacy, pre-admission, short stay, virtual, and unknown.

\*all terms may not be used in this report

**Table 1. Most Frequent Diagnoses\* Among Patients with Atogepant Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024**

	Atogepant Users	
	N	%
Total Number of Patients	19,680	100.0
Migraine (G43)	12,700	64.5
Chronic migraine without aura (G43.7)	6,650	33.8
Pain, not elsewhere classified (G89)	3,290	16.7
Chronic pain, not elsewhere classified (G89.2)	2,840	14.4
Sleep disorders (G47)	3,230	16.4
Sleep apnea (G47.3)	1,810	9.2
Other headache syndromes (G44)	2,850	14.5
Other specified headache syndromes (G44.8)	850	4.3
<b>Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (R00-R99)</b>	<b>11,830</b>	<b>60.1</b>
Headache (R51)	4,160	21.1
Headache, unspecified (R51.9)	3,960	20.1
Abdominal and pelvic pain (R10)	2,870	14.6
Unspecified abdominal pain (R10.9)	1,400	7.1
Malaise and fatigue (R53)	2,700	13.7
Other malaise and fatigue (R53.8)	2,250	11.4
Abnormalities of breathing (R06)	2,150	10.9
Dyspnea (R06.0)	1,640	8.3
<b>Factors influencing health status and contact with health services (Z00-Z99)</b>	<b>10,630</b>	<b>54.0</b>
Encounter for screening for malignant neoplasms (Z12)	3,420	17.4
Encounter for screening for malignant neoplasm of breast (Z12.3)	2,500	12.7
Body mass index [BMI] (Z68)	3,210	16.3
Body mass index [BMI] 30-39, adult (Z68.3)	1,430	7.3
Long term (current) drug therapy (Z79)	3,200	16.3
Other long term (current) drug therapy (Z79.8)	2,910	14.8
Encounter for general examination without complaint, suspected or reported diagnosis (Z00)	3,160	16.1
Encounter for general adult medical examination (Z00.0)	3,070	15.6
<b>Diseases of the musculoskeletal system and connective tissue (M00-M99)</b>	<b>8,960</b>	<b>45.5</b>
Dorsalgia (M54)	5,010	25.5
Cervicalgia (M54.2)	2,510	12.8
Other and unspecified soft tissue disorders, not elsewhere classified (M79)	3,730	19.0
Pain in limb, hand, foot, fingers and toes (M79.6)	1,750	8.9
Other joint disorder, not elsewhere classified (M25)	3,300	16.8
Pain in joint (M25.5)	3,110	15.8
<b>Endocrine, nutritional and metabolic diseases (E00-E89)</b>	<b>7,530</b>	<b>38.3</b>
Disorders of lipoprotein metabolism and other lipidemias (E78)	3,290	16.7
Hyperlipidemia, unspecified (E78.5)	1,870	9.5
Overweight and obesity (E66)	2,730	13.9
Obesity due to excess calories (E66.0)	1,560	7.9
<b>Mental, Behavioral and Neurodevelopmental disorders (F01-F99)</b>	<b>7,210</b>	<b>36.6</b>
Other anxiety disorders (F41)	4,510	22.9
Anxiety disorder, unspecified (F41.9)	3,290	16.7
Depressive episode (F32)	2,750	14.0
Depression, unspecified (F32.A)	2,020	10.3
<b>Diseases of the digestive system (K00-K95)</b>	<b>5,540</b>	<b>28.2</b>
Gastro-esophageal reflux disease (K21)	3,140	16.0
Gastro-esophageal reflux disease without esophagitis (K21.9)	2,990	15.2
<b>Diseases of the circulatory system (I00-I99)</b>	<b>5,350</b>	<b>27.2</b>
Essential (primary) hypertension (I10)	3,420	17.4

\*Diagnoses were assessed using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnoses codes over the period of -365 to -1 days before index atogepant date.



**Table 2. Most Frequent Procedures\* Among Patients with Atogepant Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024**

	Atogepant Users	
	N	%
Total Number of Patients	19,680	100.0
<b>Evaluation and Management (CPT: 1013625)</b>	<b>12,560</b>	<b>63.8</b>
Established Patient (CPT: 1013638)	10,530	53.5
New Patient (CPT: 1013627)	5,700	29.0
Emergency Department Services (CPT: 1013711)	2,840	14.4
Preventative Medicine Services (CPT: 1013829)	2,500	12.7
Consultations (CPT: 1013686)	1,230	6.3
<b>Radiology Procedures (CPT: 1010251)</b>	<b>8,620</b>	<b>43.8</b>
Diagnostic Radiology (Diagnostic Imaging) Procedures of the Head and Neck (CPT: 1010253)	3,540	18.0
Diagnostic Ultrasound Procedures (CPT: 1010759)	2,480	12.6
Diagnostic Radiology (Diagnostic Imaging) Procedures of the Chest (CPT: 1010334)	2,380	12.1
Breast, Mammography (CPT: 1015090)	2,290	11.6
Diagnostic Radiology (Diagnostic Imaging) Procedures of the Spine and Pelvis (CPT: 1010367)	2,250	11.4
Diagnostic Radiology (Diagnostic Imaging) Procedures of the Abdomen (CPT: 1010520)	1,620	8.2
Diagnostic Radiology (Diagnostic Imaging) Procedures of the Lower Extremities (CPT: 1010477)	1,610	8.2
Diagnostic Radiology (Diagnostic Imaging) Procedures of the Upper Extremities (CPT: 1010437)	1,080	5.5
<b>Surgery (CPT: 1003143)</b>	<b>8,220</b>	<b>41.8</b>
Collection of venous blood by venipuncture (CPT: 36415)	4,790	24.3
Destruction by Neurolytic Agent (eg, Chemical, Thermal, Electrical or Radiofrequency) Procedures on the Somatic Nerves (CPT: 1009588)	2,090	10.6
Chemodestruction of muscle(s); muscle(s) innervated by facial, trigeminal, cervical spinal and accessory nerves, bilateral (eg, for chronic migraine) (CPT: 64615)	1,910	9.7
Surgical Procedures on the Musculoskeletal System (CPT: 1003679)	1,590	8.1
Surgical Procedures on the Digestive System (CPT: 1006964)	1,170	5.9
<b>Medicine Services and Procedures (CPT: 1012569)</b>	<b>8,170</b>	<b>41.5</b>
Electrocardiogram, routine ECG with at least 12 leads (CPT: 1013012)	2,820	14.3
Therapeutic, prophylactic, or diagnostic injection (specify substance or drug) (CPT: 1019333)	2,580	13.1
Vaccines, Toxoids (CPT: 1012602)	1,620	8.2
Immunization Administration for Vaccines/Toxoids (CPT: 1012589)	1,610	8.2
Neurology and Neuromuscular Procedures (CPT: 1013309)	1,250	6.4
Physical Medicine and Rehabilitation Therapeutic Procedures (CPT: 1013510)	1,150	5.8
Hydration (CPT: 1019105)	1,060	5.4
Physical Therapy Evaluations (CPT: 1029677)	1,030	5.2
<b>Pathology and Laboratory Procedures (CPT: 1011136)</b>	<b>6,990</b>	<b>35.5</b>
Blood count (CPT: 1011761)	4,010	20.4
Comprehensive metabolic panel This panel must include the following: Albumin (82040) Bilirubin, total (82247) Calcium, total (82310) Carbon dioxide (bicarbonate) (82374) Chloride (82435) Creatinine (82565) Glucose (82947) Phosphatase, alkaline (84075) Potassium (84132) Protein, total (84155) Sodium (84295) Transferase, alanine amino (ALT) (SGPT) (84460) Transferase, aspartate amino (AST) (SGOT) (84450) Urea nitrogen (BUN) (84520) (CPT: 80053)	3,430	17.4
Thyroid stimulating hormone (TSH) (CPT: 84443)	2,310	11.7
Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these... (CPT: 1011224)	2,160	11.0
Infectious Agent Antigen Detection (deprecated 2022) (CPT: 1018176)	1,980	10.1
Lipid panel This panel must include the following: Cholesterol, serum, total (82465) Lipoprotein, direct measurement, high density cholesterol (HDL cholesterol) (83718) Triglycerides (84478) (CPT: 80061)	1,900	9.7

**Table 2. Most Frequent Procedures\* Among Patients with Atogepant Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024**

	Atogepant Users	
	N	%
Immunology Procedures (CPT: 1011874)	1,800	9.1
Hemoglobin (CPT: 1011483)	1,740	8.8
Basic metabolic panel (Calcium, total) This panel must include the following: Calcium, total (82310) Carbon dioxide (bicarbonate) (82374) Chloride (82435) Creatinine (82565) Glucose (82947) Potassium (84132) Sodium (84295) Urea nitrogen (BUN) (84520) (CPT: 80048)	1,620	8.2
Surgical Pathology Procedures (CPT: 1012454)	1,540	7.8
Infectious agent detection by nucleic acid (DNA or RNA) (CPT: 1012255)	1,490	7.6
Vitamin D (CPT: 1020198)	1,230	6.3
Cyanocobalamin (Vitamin B-12) (CPT: 1014264)	1,070	5.4
<b>HCPCS J: Drugs Administered Other Than Oral Method, Chemotherapy Drugs (J)</b>	<b>4,500</b>	<b>22.9</b>
Injection, onabotulinumtoxin A, 1 unit (HCPCS: J0585)	1,420	7.2
Injection, ketorolac tromethamine, per 15 mg (HCPCS: J1885)	1,390	7.1
Injection, ondansetron hydrochloride, per 1 mg (HCPCS: J2405)	1,070	5.4

\* The procedures were assessed over the period of -365 to -1 days before index atogepant date using the following coding systems:

ICD-10-PCS: International Classification of Diseases, Tenth Revision, Procedure Coding System; CPT - Current Procedural Terminology, HCPCS: Healthcare Common Procedure Coding System; SNOMED: Systemized Nomenclature of Medicine – Clinical Terms

The 7-digit CPT codes in the list of procedure codes refer to the CPT subsets, which are developed for EHR systems and specific physician specialties for ease of data capture or data retrieval (hierarchical tree). The CPT subsets are parent terms, which encompass child terms beneath, which could be other 7-digit subset or 5-digit CPT codes.

**Table 3. Most Frequent Prescribed Medication Classes\* Among Patients with Atogepant Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024**

	Atogepant Users	
	N	%
Total Number of Patients	19,680	100.0
Antimigraine agents (CN105)	11,610	59.0
Anticonvulsants (CN400)	6,920	35.2
Antidepressants, other (CN609)	6,240	31.7
Opioid analgesics (CN101)	5,610	28.5
Non-opioid analgesics (CN103)	5,570	28.3
Local anesthetics, injection (CN204)	5,000	25.4
Benzodiazepine derivative sedatives/hypnotics (CN302)	4,370	22.2
CNS medications, other (CN900)	3,700	18.8
<b>Hormones/synthetics/modifiers (HS000)</b>	<b>10,320</b>	<b>52.4</b>
Glucocorticoids (HS051)	7,700	39.1
<b>Musculoskeletal medications (MS000)</b>	<b>10,020</b>	<b>50.9</b>
Nonsalicylate NSAIDs, antirheumatic (MS102)	6,770	34.4
Skeletal muscle relaxants (MS200)	4,430	22.5
<b>Ophthalmic agents (OP000)</b>	<b>9,950</b>	<b>50.6</b>
Ophthalmics, other (OP900)	7,500	38.1
Anti-inflammatories, topical ophthalmic (OP300)	5,790	29.4
Anesthetics, topical ophthalmic (OP700)	4,690	23.8
<b>Dermatological agents (DE000)</b>	<b>9,690</b>	<b>49.2</b>
Dermatologicals, topical other (DE900)	5,960	30.3
Anti-inflammatory, topical (DE200)	5,020	25.5
Local anesthetics, topical (DE700)	4,740	24.1
Anti-infective, topical (DE100)	3,710	18.9
<b>Cardiovascular medications (CV000)</b>	<b>9,540</b>	<b>48.5</b>
Antiarrhythmics (CV300)	4,690	23.8
Beta blockers/related (CV100)	3,900	19.8
<b>Gastrointestinal medications (GA000)</b>	<b>8,990</b>	<b>45.7</b>
Antiemetics (GA605)	6,150	31.3
Gastric medications, other (GA900)	4,090	20.8
<b>Nasal and throat agents, topical (NT000)</b>	<b>8,360</b>	<b>42.5</b>
Nasal and throat, topical, other (NT900)	5,770	29.3
Anesthetics, mucosal (NT300)	4,760	24.2
Anti-inflammatories, nasa (NT200)	3,630	18.4
<b>Respiratory tract medications (RE000)</b>	<b>8,080</b>	<b>41.1</b>
Respiratory agents, other (RE900)	5,240	26.6
Bronchodilators, sympathomimetic, inhalation (RE102)	3,670	18.6
<b>Antimicrobials (AM000)</b>	<b>7,000</b>	<b>35.6</b>
Penicillins and beta-lactam antimicrobials (AM114)	3,570	18.1
<b>Therapeutic nutrients/minerals/electrolytes (TN000)</b>	<b>6,410</b>	<b>32.6</b>
Sodium (TN440)	5,120	26.0
<b>Genitourinary medications (GU000)</b>	<b>6,270</b>	<b>31.9</b>
Genito-urinary agents, other (GU900)	4,740	24.1

\*The medication drug classes coded based on Veterans Affairs (VA) drug classification system were assessed over the period of -365 to -1 days before index atogepant date. The VA classification system classifies all medication products available in the United States. Please note that a specific generic ingredient can be listed in multiple classes, based on their route of administration.

**Table 4. Most Frequent Lab Terms\* Among Patients with Atogepant Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024**

	Atogepant Users		Mean ± SD	Min	Max
	N	%			
Total Number of Patients	19,680	100.0	N/A	N/A	N/A
<b>Lab Category: Metabolic Panel**:</b>					
Glucose (mg/dL) in Serum, Plasma or Blood (TNX: 9025)	8,920	45.3	102 ± 32.5	4	646
Sodium (mmol/L) in Serum, Plasma or Blood (TNX: 9029)	8,850	45.0	139 ± 2.51	124	149
Chloride (mmol/L) in Serum, Plasma or Blood (TNX: 9023)	8,850	45.0	104 ± 3.38	83	123
Calcium (mg/dL) in Serum, Plasma or Blood (TNX: 9022)	8,850	45.0	9.36 ± 0.526	1.22	11.5
Potassium (mmol/L) IN Serum, Plasma or Blood (TNX: 9028)	8,840	44.9	4.12 ± 0.416	1.6	6.4
Creatinine (mg/dL) in Serum, Plasma or Blood (TNX: 9024)	8,840	44.9	1.58 ± 10.3	0	193
Bicarbonate (mmol/L) in Serum, Plasma or Blood (TNX: 9021)	8,830	44.9	25.2 ± 3.09	11	39
Urea nitrogen (mg/dL) in Serum, Plasma or Blood (TNX: 9030)	8,670	44.1	13.4 ± 5.26	1.02	108
Magnesium (mg/dL) in Serum, Plasma or Blood (TNX: 9026)	1,990	10.1	1.98 ± 0.306	0.5	6.9
Phosphate (mg/dL) in Serum, Plasma or Blood (TNX: 9027)	1,000	5.1	3.46 ± 1.34	1	38
<b>Lab Category: Complete Blood Count**:</b>					
Hematocrit (%) of Blood (TNX: 9013)	8,460	43.0	39.9 ± 6.46	0	57.6
Hemoglobin (g/dL) in Blood (TNX: 9014)	8,450	42.9	13.3 ± 1.48	6.4	19
Platelets (10 <sup>3</sup> /uL) in Blood (TNX: 9020)	8,440	42.9	279 ± 75.5	30	1,181
Erythrocyte mean corpuscular volume (fL) (TNX: 9011)	8,430	42.8	89.8 ± 5.69	59.1	117
Erythrocytes (10 <sup>6</sup> /uL) in Blood (TNX: 9012)	8,420	42.8	4.47 ± 0.694	0.003	7.35
Erythrocyte mean corpuscular hemoglobin concentration (g/dL) (TNX: 9010)	8,250	41.9	32.6 ± 2.71	0.031	37.4
Erythrocyte distribution width (Ratio) (TNX: 9008)	8,010	40.7	13.4 ± 1.62	10	47.2
Erythrocyte mean corpuscular hemoglobin (pg) (TNX: 9009)	7,910	40.2	29.6 ± 2.28	16.1	42
Leukocytes (10 <sup>3</sup> /uL) in Blood (TNX: 9015)	7,830	39.8	8.64 ± 72.2	<0.0001	4,530
Monocytes/100 leukocytes in Blood (TNX: 9017)	7,240	36.8	7.51 ± 2.39	0	41.3
Basophils/100 leukocytes in Blood (TNX: 9006)	7,090	36.0	0.674 ± 1.13	0	63
Eosinophils/100 leukocytes in Blood (TNX: 9007)	7,070	35.9	2.29 ± 2.38	0	68
Lymphocytes/100 leukocytes in Blood (TNX: 9016)	6,970	35.4	29.1 ± 9.74	1	91.8
Neutrophils (10 <sup>3</sup> /uL) in Blood (TNX: 9018)	6,740	34.2	144 ± 781	0.002	8,198
Platelet mean volume (fL) in Blood (TNX: 9019)	6,240	31.7	9.98 ± 1.18	5.8	15
<b>Lab Category: Liver Function**:</b>					
Aspartate aminotransferase (U/L) in Serum or Plasma (TNX: 9047)	8,020	40.8	22.4 ± 22.2	2	1,514
Alanine aminotransferase (U/L) in Serum, Plasma or Blood (TNX: 9044)	7,980	40.5	22.7 ± 20.7	0	522
Alkaline phosphatase (U/L) in Serum, Plasma or Blood (TNX: 9046)	7,940	40.3	78.4 ± 30.5	16	1,005
Bilirubin.total (mg/dL) in Serum, Plasma or Blood (TNX: 9050)	7,680	39.0	0.457 ± 0.299	0	11.2
Bilirubin.direct (mg/dL) in Serum or Plasma (TNX: 9048)	890	4.5	0.144 ± 0.116	0	1.3
Bilirubin.indirect (mg/dL) in Serum or Plasma (TNX: 9049)	400	2.0	0.397 ± 0.266	0	2.2
Protein (g/dL) in Serum or Plasma (TNX: 9053)	7,540	38.3	7.07 ± 0.579	3.7	10.7
Albumin (g/dL) in Serum, Plasma or Blood (TNX: 9045)	7,350	37.3	4.2 ± 0.437	1.7	8.1
Lactate dehydrogenase (U/L) in Serum or Plasma (TNX: 9052)	300	1.5	200 ± 86.1	1.56	832
Gamma glutamyl transferase (U/L) in Serum or Plasma (TNX: 9051)	210	1.1	60.2 ± 125	5	1,298
<b>Lab Category: Lipid Panel**:</b>					
Triglyceride (mg/dL) in Serum, Plasma or Blood (TNX: 9004)	4,850	24.6	134 ± 87	17	1,425
Cholesterol in HDL (mg/dL) in Serum or Plasma (TNX: 9001)	4,840	24.6	55.9 ± 18.9	9	198
Cholesterol in LDL (mg/dL) in Serum or Plasma (TNX: 9002)	4,780	24.3	109 ± 36.9	3	432
Cholesterol (mg/dL) in Serum or Plasma (TNX: 9000)	4,610	23.4	189 ± 42.8	4	510
<b>Lab Category: Endocrinology**:</b>					

**Table 4. Most Frequent Lab Terms\* Among Patients with Atogepant Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024**

	Atogepant Users		Mean ± SD	Min	Max
	N	%			
Thyrotropin [m(IU)/L] in Serum, Plasma or Blood (TNX: 9040)	5,600	28.5	2.03 ± 3.27	0	110
Hemoglobin A1c/Hemoglobin.total in Blood (TNX: 9037)	3,710	18.9	5.81 ± 1.38	3	16.1
Thyroxine (T4) (ug/dL) in Serum, Plasma or Blood (TNX: 9041)	240	1.2	7.91 ± 2.85	0.77	25
<b>Lab Category: Other Chemistry**:</b>					
Cobalamin (Vitamin B12) (pg/mL) in Serum, Plasma or Blood (TNX: 9065)	2,370	12.0	584 ± 382	1	6,001
Erythrocyte sedimentation rate (mm/hr) (TNX: 9066)	1,770	9.0	16.5 ± 16.9	0	123
C reactive protein (mg/L) in Serum, Plasma or Blood (TNX: 9063)	1,470	7.5	9.05 ± 23.7	0	372
Folate (ng/mL) in Serum, Plasma or Blood (TNX: 9067)	910	4.6	12.6 ± 6.22	0	56.6
<b>Lab Category: Vitals**:</b>					
Body height (inches) (TNX: 9077)	13,100	66.6	65.1 ± 3.34	56	81
Body weight (pounds) (TNX: 9081)	11,810	60.0	182 ± 50.9	80	428
Blood pressure, diastolic (mm Hg) (TNX: 9086)	11,610	59.0	76.9 ± 10.7	20	177
Blood pressure, systolic (mm Hg) (TNX: 9085)	11,600	58.9	124 ± 16.3	60	227
Heart rate (beats/min) (TNX: 9074)	10,190	51.8	81.2 ± 14.7	1	187
BMI (kg/m <sup>2</sup> ) (TNX: 9083)	9,930	50.5	30.6 ± 49.7	0	4,893
Body temperature (°F) (TNX: 9076)	7,080	36.0	87.2 ± 23.1	34.7	104
Respiratory rate (breaths/min) (TNX: 9073)	5,830	29.6	17 ± 2.27	1	74
Oxygen saturation (%) (TNX: 9075)	2,360	12.0	95.4 ± 11.6	2	100
Body surface area (m <sup>2</sup> ) (TNX: 9087)	340	1.7	2.02 ± 0.571	1.18	6
BMI percentile (%) (TNX: 9084)	70	0.4	46 ± 25.9	1	99.3
Body height percentile (%) (TNX: 9078)	10	0.1	48.3 ± 40.5	0	98.4
Head circumference (centimeters) (TNX: 9079)	10	0.1	38.1 ± 25.3	20.2	56
Body weight percentile (%) (TNX: 9082)	10	0.1	79.9 ± 35	9.23	99.6

\* The lab terms presented were assessed over the period of -365 to -1 days before index atogepant date using TriNetX aggregate lab terms (TNX:LAB) that group clinically relevant Logical Observation Identifiers Names and Codes (LOINC) together for each test.

\*\* The lab tests within categories were curated by TriNetX internal team to harmonize related codes

N/A: Not applicable

**Appendix A. List of RxNorm Medication Terms Used to Define Exposure in this Request**

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<b>Code Type</b>	<b>Code</b>	<b>Description</b>
RxNorm	2571813	Atogepant

**Appendix B. Specifications Defining Query Builder Modules in this Request**

<b>Network:</b>	
USA Minimal Shift Network	
<b>Cohort 1: Atogepant</b>	
<b>Group 1:</b>	<b>Time Restrictions</b>
<b>Subgroup 1A</b>	
<i>Must Have:</i>	
Atogepant	December 18, 2020 - February 29, 2024

**Appendix C. Specifications Defining Analytic Modules in this Request**

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#	Module	Analysis Type	Cohort(s)	Window	Index Event(s)	Characteristics or Outcomes
1	Analyze Outcomes	Characteristics	Atogepant	[-365, -1]	Atogepant	Most frequent diagnoses
2	Analyze Outcomes	Characteristics	Atogepant	[-365, -1]	Atogepant	Most frequent procedures
3	Analyze Outcomes	Characteristics	Atogepant	[-365, -1]	Atogepant	Most frequent medications
4	Analyze Outcomes	Characteristics	Atogepant	[-365, -1]	Atogepant	Most frequent labs