

Disclaimer

The following report(s) provides findings from an FDA-initiated query using its Mini-Sentinel pilot. While Mini-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 Mini-Sentinel, and seeking to better understand the capabilities of the Mini-Sentinel pilot.

Data obtained through Mini-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 the Mini-Sentinel pilot in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Mini-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 msy4_mpr13

Request Description Mini-Sentinel's IV Iron Workgroup requested execution of Modular Program #3 (MP3) to investigate exposure to IV Iron procedures and anaphylaxis events for all patients. This involved one run of MP3. The time window for the request is January 1, 2000 – December 31, 2012. The package was distributed to Data Partners on January 17, 2013. This is Report 3 of 4.

This report contains results for the scenarios with no pre-existing condition requirement and an event of anaphylaxis. There are three other reports that were generated for this request that contain results for the scenarios with (1) no pre-existing condition requirement and an event of epinephrine; (2) a pre-existing condition of dialysis and an event of anaphylaxis; and (3) a pre-existing condition of dialysis and an event of epinephrine.

Results provide counts of new IV iron patients, dispensings, total days supplied, eligible members, and member-days for all patients (i.e., no specific pre-existing condition criteria applied). A patient was considered new if he/she was not exposed to any IV iron in the prior 183 days. Differing exposure extension periods were examined; these represented the time window in which the program sought an event. Incidence criteria for the event of interest included a 30-day lookback period only and incidence with respect to the diagnosis itself. The query period was from January 1, 2000 to December 31, 2012. See Appendix A for a list of specific Healthcare Common Procedure Coding System (HCPCS) procedure codes, Current Procedural Terminology, Fourth Edition (CPT-4) procedure codes, and International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes included in this request.

Request ID msy4_mpr13_v1

Glossary List of Terms found in this Report and their Definitions

Table 1 Summary of Incident IV Iron Exposure and Anaphylaxis Events in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2012, by Outcome Care Setting and Length of Time to Outcome -- No Pre-Existing Condition Requirement

Figure 1 Number of New Anaphylaxis Events per 100,000 Days at Risk between October 19, 2010 and December 31, 2011 by Care Setting of Event and Length of Time to Event- No Pre-Existing Condition Requirement

Table 2 Summary of Incident IV Iron Exposure and Anaphylaxis Events in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2012, by Outcome Care Setting, Length of Time to Outcome and Age Group -- No Pre-Existing Condition Requirement

Table 3 Summary of Incident IV Iron Exposure and Anaphylaxis Events in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2012, by Outcome Care Setting, Length of Time to Outcome and Sex -- No Pre-Existing Condition Requirement

Table 4 Summary of Incident IV Iron Exposure and Anaphylaxis Events in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2012, by Outcome Care Setting, Length of Time to Outcome and Year -- No Pre-Existing Condition Requirement

Appendix A List of Diagnosis and Procedure Codes Included in this Request

Appendix B Modular Program Specifications for Query ID msy4_mpr13_v1

Notes: Please contact the Sentinel Operations Center Query Fulfillment Team (qf@sentinelssystem.org) for questions and to provide comments/suggestions for future enhancements to this document.

Glossary of Terms in Modular Program 3*

- Blackout Period** - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs
- Care Setting** - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible
- Days at Risk** - number of days supplied plus any episode gaps and exposure extension periods.
- 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
- Episode Gap** - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be
- Exposure Extension Period** - number of days post treatment period in which the outcomes/events are counted for a
- Lookback Period (pre-existing condition)** - number of days wherein a member is required to have evidence of pre-existing
- Member-Days** - sum of all days of enrollment with medical and drug coverage** in the query period preceded by an exposure washout period.
- Minimum Days Supplied** - specifies a minimum number of days in length of the days supplied for the episode to be
- Minimum Episode Duration** - specifies a minimum number of days in length of the episode for it to be considered
- New Episodes** - new treatment episodes; length of episode is determined by days supplied in one dispensing (or consecutive dispensings bridged by the episode gap).
- New Users** - number of members with incident exposure during the query period. Member must have no evidence of exposure (s) of interest (defined by incidence criteria) in the prior washout period. A user may only be counted once in a
- Principal Diagnosis** - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. YES will only consider diagnoses flagged as Principal
- Query Period** - period in which the modular program looks for exposures and outcomes of interest.
- Total Days Supplied** - number of days supplied for all dispensings in qualifying treatment episodes.
- 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.
- Washout Type (drug/exposure)- *Minimum washout type*** will consider the first treatment episode in the query period as long as it is the first treatment episode in the user's entire available history. *Single* and *Multiple washout types* will use the washout period to establish incidence, however *Single* will only consider the first treatment episode whereas *Multiple* will consider all qualifying incident treatment episodes.
- Washout Type (event/outcome)- *Minimum washout type*** considers the first event in a valid episode as long as it is the first event in the user's entire available history. *Multiple washout type* uses the washout period to establish incidence and considers all qualifying incident treatment episodes. The program will only consider one event per episode, but the *Multiple washout type* will consider more than one event per user if a user has more than one incident episode.

*all terms may not be used in this report

**incident treatment episodes must be incident to both the exposure and the event

Table 1. Summary of Incident IV Iron Exposure and Anaphylaxis Events in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2012, by Outcome Care Setting and Length of Time to Outcome -- No Pre-Existing Condition Requirement

	New Users	Dispensings	Total Days Supplied	Days at Risk	New Anaphylaxis Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing	New Events/ 100k Days at Risk
<i>Event occurs in Inpatient or Emergency Department Care Setting</i>												
On day of exposure	140,459	148,241	148,241	147,926	22	94,936,996	86,331,279,365	1.48	1.06	1.06	1.00	14.87
Within one day of exposure	140,459	148,241	148,241	288,277	24	94,936,996	86,331,279,365	1.48	1.06	1.06	1.00	8.33
Within two days of exposure	140,459	148,241	148,241	420,266	24	94,936,996	86,331,279,365	1.48	1.06	1.06	1.00	5.71
Within seven days of exposure	140,459	148,241	148,241	989,947	24	94,936,996	86,331,279,365	1.48	1.06	1.06	1.00	2.42
Within 14 days of exposure	140,459	148,241	148,241	1,541,314	25	94,936,996	86,331,279,365	1.48	1.06	1.06	1.00	1.62
<i>Event occurs in Outpatient Care Setting</i>												
On day of exposure	140,459	148,241	148,241	147,926	20	94,936,996	86,331,279,365	1.48	1.06	1.06	1.00	13.52
Within one day of exposure	140,459	148,241	148,241	288,279	21	94,936,996	86,331,279,365	1.48	1.06	1.06	1.00	7.28
Within two days of exposure	140,459	148,241	148,241	420,271	22	94,936,996	86,331,279,365	1.48	1.06	1.06	1.00	5.23
Within seven days of exposure	140,459	148,241	148,241	989,956	27	94,936,996	86,331,279,365	1.48	1.06	1.06	1.00	2.73
Within 14 days of exposure	140,459	148,241	148,241	1,541,322	27	94,936,996	86,331,279,365	1.48	1.06	1.06	1.00	1.75

Figure 1. Number of New Anaphylaxis Events per 100,000 Days at Risk between October 19, 2010 and December 31, 2011 by Care Setting of Event and Length of Time to Event- No Pre-Existing Condition Requirement

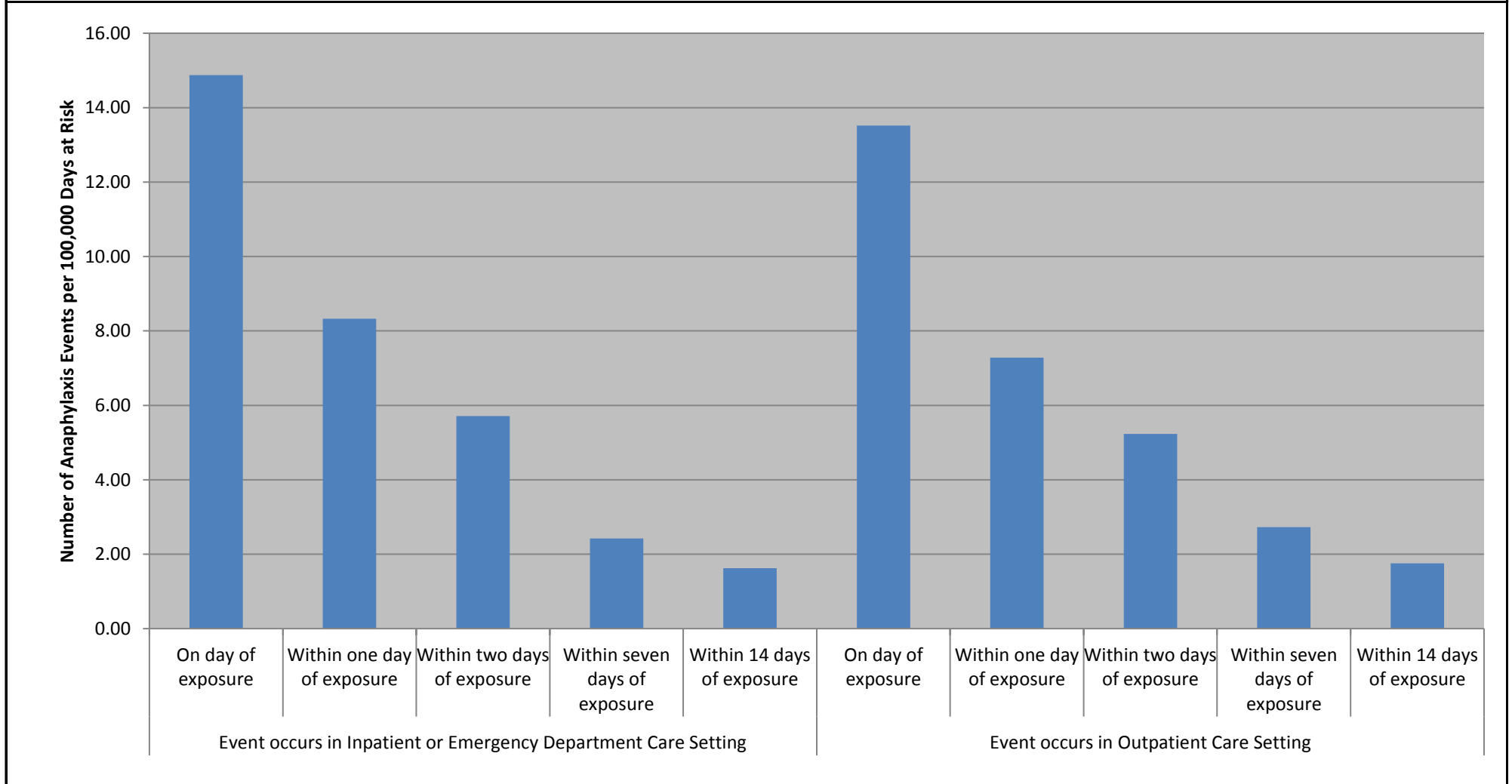


Table 2. Summary of Incident IV Iron Exposure and Anaphylaxis Events in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2012, by Outcome Care Setting, Length of Time to Outcome and Age Group -- No Pre-Existing Condition Requirement

	New Users	Total Days Dispensings Supplied	Days at Risk	New Anaphylaxis Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing	New Events/ 100k Days at Risk	
<i>Event occurs in Inpatient or Emergency Department Care Setting</i>												
<i>On day of exposure</i>												
00-21 years	2,311	2,483	2,483	2,475	1	28,882,059	24,942,657,149	0.08	1.07	1.07	1.00	40.40
22-44 years	31,757	34,003	34,003	33,904	11	37,934,453	27,235,937,526	0.84	1.07	1.07	1.00	32.44
45-64 years	53,345	56,198	56,198	56,088	6	27,513,860	25,290,358,691	1.94	1.05	1.05	1.00	10.70
65+ years	53,046	55,557	55,557	55,459	4	8,363,806	8,862,325,999	6.34	1.05	1.05	1.00	7.21
<i>Within one day of exposure</i>												
00-21 years	2,311	2,483	2,483	4,785	1	28,882,059	24,942,657,149	0.08	1.07	1.07	1.00	20.90
22-44 years	31,757	34,003	34,003	65,614	13	37,934,453	27,235,937,526	0.84	1.07	1.07	1.00	19.81
45-64 years	53,345	56,198	56,198	109,398	6	27,513,860	25,290,358,691	1.94	1.05	1.05	1.00	5.48
65+ years	53,046	55,557	55,557	108,480	4	8,363,806	8,862,325,999	6.34	1.05	1.05	1.00	3.69
<i>Within two days of exposure</i>												
00-21 years	2,311	2,483	2,483	6,953	1	28,882,059	24,942,657,149	0.08	1.07	1.07	1.00	14.38
22-44 years	31,757	34,003	34,003	95,653	13	37,934,453	27,235,937,526	0.84	1.07	1.07	1.00	13.59
45-64 years	53,345	56,198	56,198	159,349	6	27,513,860	25,290,358,691	1.94	1.05	1.05	1.00	3.77
65+ years	53,046	55,557	55,557	158,311	4	8,363,806	8,862,325,999	6.34	1.05	1.05	1.00	2.53
<i>Within seven days of exposure</i>												
00-21 years	2,311	2,483	2,483	16,322	1	28,882,059	24,942,657,149	0.08	1.07	1.07	1.00	6.13
22-44 years	31,757	34,003	34,003	224,277	13	37,934,453	27,235,937,526	0.84	1.07	1.07	1.00	5.80
45-64 years	53,345	56,198	56,198	375,048	6	27,513,860	25,290,358,691	1.94	1.05	1.05	1.00	1.60
65+ years	53,046	55,557	55,557	374,300	4	8,363,806	8,862,325,999	6.34	1.05	1.05	1.00	1.07
<i>Within 14 days of exposure</i>												
00-21 years	2,311	2,483	2,483	25,816	1	28,882,059	24,942,657,149	0.08	1.07	1.07	1.00	3.87
22-44 years	31,757	34,003	34,003	345,915	13	37,934,453	27,235,937,526	0.84	1.07	1.07	1.00	3.76
45-64 years	53,345	56,198	56,198	585,633	7	27,513,860	25,290,358,691	1.94	1.05	1.05	1.00	1.20
65+ years	53,046	55,557	55,557	583,950	4	8,363,806	8,862,325,999	6.34	1.05	1.05	1.00	0.68

Table 2. Summary of Incident IV Iron Exposure and Anaphylaxis Events in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2012, by Outcome Care Setting, Length of Time to Outcome and Age Group -- No Pre-Existing Condition Requirement

	New Users	Total Days Dispensings Supplied	Days at Risk	New Anaphylaxis Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing	New Events/ 100k Days at Risk	
<i>Event occurs in Outpatient Care Setting</i>												
On day of exposure												
00-21 years	2,311	2,483	2,483	2,475	3	28,882,059	24,942,657,149	0.08	1.07	1.07	1.00	121.21
22-44 years	31,757	34,003	34,003	33,904	9	37,934,453	27,235,937,526	0.84	1.07	1.07	1.00	26.55
45-64 years	53,345	56,198	56,198	56,088	4	27,513,860	25,290,358,691	1.94	1.05	1.05	1.00	7.13
65+ years	53,046	55,557	55,557	55,459	4	8,363,806	8,862,325,999	6.34	1.05	1.05	1.00	7.21
Within one day of exposure												
00-21 years	2,311	2,483	2,483	4,783	3	28,882,059	24,942,657,149	0.08	1.07	1.07	1.00	62.72
22-44 years	31,757	34,003	34,003	65,616	9	37,934,453	27,235,937,526	0.84	1.07	1.07	1.00	13.72
45-64 years	53,345	56,198	56,198	109,400	4	27,513,860	25,290,358,691	1.94	1.05	1.05	1.00	3.66
65+ years	53,046	55,557	55,557	108,480	5	8,363,806	8,862,325,999	6.34	1.05	1.05	1.00	4.61
Within two days of exposure												
00-21 years	2,311	2,483	2,483	6,949	3	28,882,059	24,942,657,149	0.08	1.07	1.07	1.00	43.17
22-44 years	31,757	34,003	34,003	95,659	9	37,934,453	27,235,937,526	0.84	1.07	1.07	1.00	9.41
45-64 years	53,345	56,198	56,198	159,353	5	27,513,860	25,290,358,691	1.94	1.05	1.05	1.00	3.14
65+ years	53,046	55,557	55,557	158,310	5	8,363,806	8,862,325,999	6.34	1.05	1.05	1.00	3.16
Within seven days of exposure												
00-21 years	2,311	2,483	2,483	16,308	3	28,882,059	24,942,657,149	0.08	1.07	1.07	1.00	18.40
22-44 years	31,757	34,003	34,003	224,293	13	37,934,453	27,235,937,526	0.84	1.07	1.07	1.00	5.80
45-64 years	53,345	56,198	56,198	375,061	6	27,513,860	25,290,358,691	1.94	1.05	1.05	1.00	1.60
65+ years	53,046	55,557	55,557	374,294	5	8,363,806	8,862,325,999	6.34	1.05	1.05	1.00	1.34
Within 14 days of exposure												
00-21 years	2,311	2,483	2,483	25,788	3	28,882,059	24,942,657,149	0.08	1.07	1.07	1.00	11.63
22-44 years	31,757	34,003	34,003	345,940	13	37,934,453	27,235,937,526	0.84	1.07	1.07	1.00	3.76
45-64 years	53,345	56,198	56,198	585,657	6	27,513,860	25,290,358,691	1.94	1.05	1.05	1.00	1.02
65+ years	53,046	55,557	55,557	583,937	5	8,363,806	8,862,325,999	6.34	1.05	1.05	1.00	0.86

Table 3. Summary of Incident IV Iron Exposure and Anaphylaxis Events in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2012, by Outcome Care Setting, Length of Time to Outcome and Sex -- No Pre-Existing Condition Requirement

	New Users	Total Days Dispensings Supplied	Days at Risk	New Anaphylaxis Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing	New Events/ 100k Days at Risk	
Event occurs in Inpatient or Emergency Department Care Setting												
On day of exposure												
Female	92,271	98,022	98,022	97,810	20	48,405,350	44,572,448,928	1.91	1.06	1.06	1.00	20.45
Male	48,077	50,099	50,099	49,996	2	46,422,571	41,646,060,971	1.04	1.04	1.04	1.00	4.00
Unknown	111	120	120	120	0	109,075	112,769,466	1.02	1.08	1.08	1.00	0.00
Within one day of exposure												
Female	92,271	98,022	98,022	189,999	21	48,405,350	44,572,448,928	1.91	1.06	1.06	1.00	11.05
Male	48,077	50,099	50,099	98,047	3	46,422,571	41,646,060,971	1.04	1.04	1.04	1.00	3.06
Unknown	111	120	120	231	0	109,075	112,769,466	1.02	1.08	1.08	1.00	0.00
Within two days of exposure												
Female	92,271	98,022	98,022	277,415	21	48,405,350	44,572,448,928	1.91	1.06	1.06	1.00	7.57
Male	48,077	50,099	50,099	142,518	3	46,422,571	41,646,060,971	1.04	1.04	1.04	1.00	2.10
Unknown	111	120	120	333	0	109,075	112,769,466	1.02	1.08	1.08	1.00	0.00
Within seven days of exposure												
Female	92,271	98,022	98,022	654,323	21	48,405,350	44,572,448,928	1.91	1.06	1.06	1.00	3.21
Male	48,077	50,099	50,099	334,864	3	46,422,571	41,646,060,971	1.04	1.04	1.04	1.00	0.90
Unknown	111	120	120	760	0	109,075	112,769,466	1.02	1.08	1.08	1.00	0.00
Within 14 days of exposure												
Female	92,271	98,022	98,022	1,011,707	22	48,405,350	44,572,448,928	1.91	1.06	1.06	1.00	2.17
Male	48,077	50,099	50,099	528,451	3	46,422,571	41,646,060,971	1.04	1.04	1.04	1.00	0.57
Unknown	111	120	120	1,156	0	109,075	112,769,466	1.02	1.08	1.08	1.00	0.00
Event occurs in Outpatient Care Setting												
On day of exposure												
Female	92,271	98,022	98,022	97,810	15	48,405,350	44,572,448,928	1.91	1.06	1.06	1.00	15.34
Male	48,077	50,099	50,099	49,996	5	46,422,571	41,646,060,971	1.04	1.04	1.04	1.00	10.00
Unknown	111	120	120	120	0	109,075	112,769,466	1.02	1.08	1.08	1.00	0.00
Within one day of exposure												
Female	92,271	98,022	98,022	190,004	16	48,405,350	44,572,448,928	1.91	1.06	1.06	1.00	8.42
Male	48,077	50,099	50,099	98,044	5	46,422,571	41,646,060,971	1.04	1.04	1.04	1.00	5.10
Unknown	111	120	120	231	0	109,075	112,769,466	1.02	1.08	1.08	1.00	0.00
Within two days of exposure												
Female	92,271	98,022	98,022	277,425	16	48,405,350	44,572,448,928	1.91	1.06	1.06	1.00	5.77
Male	48,077	50,099	50,099	142,513	6	46,422,571	41,646,060,971	1.04	1.04	1.04	1.00	4.21
Unknown	111	120	120	333	0	109,075	112,769,466	1.02	1.08	1.08	1.00	0.00

Table 3. Summary of Incident IV Iron Exposure and Anaphylaxis Events in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2012, by Outcome Care Setting, Length of Time to Outcome and Sex -- No Pre-Existing Condition Requirement

	New Users	Dispensings	Total Days Supplied	Days at Risk	New Anaphylaxis Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing	New Events/ 100k Days at Risk
Within seven days of exposure												
Female	92,271	98,022	98,022	654,348	21	48,405,350	44,572,448,928	1.91	1.06	1.06	1.00	3.21
Male	48,077	50,099	50,099	334,848	6	46,422,571	41,646,060,971	1.04	1.04	1.04	1.00	1.79
Unknown	111	120	120	760	0	109,075	112,769,466	1.02	1.08	1.08	1.00	0.00
Within 14 days of exposure												
Female	92,271	98,022	98,022	1,011,745	21	48,405,350	44,572,448,928	1.91	1.06	1.06	1.00	2.08
Male	48,077	50,099	50,099	528,421	6	46,422,571	41,646,060,971	1.04	1.04	1.04	1.00	1.14
Unknown	111	120	120	1,156	0	109,075	112,769,466	1.02	1.08	1.08	1.00	0.00

Table 4. Summary of Incident IV Iron Exposure and Anaphylaxis Events in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2012, by Outcome Care Setting, Length of Time to Outcome and Year -- No Pre-Existing Condition Requirement

	New Users	Dispensings	Total Days Supplied	Days at Risk	New Anaphylaxis Events	Eligible Members	Member-Days	New Users/1K Eligible Members	Dispensings/User	Days Supplied/User	Days Supplied/Dispensing	New Events/100k Days at Risk
<i>Event occurs in Inpatient or Emergency Department Care Setting</i>												
On day of exposure												
2000	484	502	502	502	0	7,429,886	1,261,164,611	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	1,279	0	8,013,999	2,495,260,483	0.16	1.03	1.03	1.00	0.00
2002	1,329	1,383	1,383	1,376	0	8,078,064	2,513,817,340	0.16	1.04	1.04	1.00	0.00
2003	1,897	1,961	1,961	1,949	0	8,027,680	2,499,767,286	0.24	1.03	1.03	1.00	0.00
2004	7,081	7,322	7,322	7,287	0	19,352,195	4,289,659,989	0.37	1.03	1.03	1.00	0.00
2005	9,303	9,814	9,814	9,771	1	21,327,484	6,155,145,867	0.44	1.05	1.05	1.00	10.23
2006	8,786	9,265	9,265	9,254	1	22,753,232	6,435,751,709	0.39	1.05	1.05	1.00	10.81
2007	9,742	10,318	10,318	10,307	1	25,509,649	6,867,836,642	0.38	1.06	1.06	1.00	9.70
2008	18,158	19,322	19,322	19,299	3	46,734,248	10,628,894,776	0.39	1.06	1.06	1.00	15.54
2009	27,073	28,800	28,800	28,742	4	47,694,195	13,679,936,227	0.57	1.06	1.06	1.00	13.92
2010	27,221	28,683	28,683	28,622	8	46,118,786	13,290,985,875	0.59	1.05	1.05	1.00	27.95
2011	22,942	24,120	24,120	24,075	3	44,560,507	12,804,512,611	0.51	1.05	1.05	1.00	12.46
2012	5,200	5,467	5,467	5,463	1	24,728,518	3,408,545,949	0.21	1.05	1.05	1.00	18.30
Within one day of exposure												
2000	484	502	502	986	0	7,429,886	1,261,164,611	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	2,521	0	8,013,999	2,495,260,483	0.16	1.03	1.03	1.00	0.00
2002	1,329	1,383	1,383	2,705	0	8,078,064	2,513,817,340	0.16	1.04	1.04	1.00	0.00
2003	1,897	1,961	1,961	3,845	0	8,027,680	2,499,767,286	0.24	1.03	1.03	1.00	0.00
2004	7,081	7,322	7,322	14,366	0	19,352,195	4,289,659,989	0.37	1.03	1.03	1.00	0.00
2005	9,303	9,814	9,814	19,066	1	21,327,484	6,155,145,867	0.44	1.05	1.05	1.00	5.24
2006	8,786	9,265	9,265	18,032	2	22,753,232	6,435,751,709	0.39	1.05	1.05	1.00	11.09
2007	9,742	10,318	10,318	20,040	1	25,509,649	6,867,836,642	0.38	1.06	1.06	1.00	4.99
2008	18,158	19,322	19,322	37,443	3	46,734,248	10,628,894,776	0.39	1.06	1.06	1.00	8.01
2009	27,073	28,800	28,800	55,791	5	47,694,195	13,679,936,227	0.57	1.06	1.06	1.00	8.96
2010	27,221	28,683	28,683	55,823	8	46,118,786	13,290,985,875	0.59	1.05	1.05	1.00	14.33
2011	22,942	24,120	24,120	47,003	3	44,560,507	12,804,512,611	0.51	1.05	1.05	1.00	6.38
2012	5,200	5,467	5,467	10,656	1	24,728,518	3,408,545,949	0.21	1.05	1.05	1.00	9.38

Table 4. Summary of Incident IV Iron Exposure and Anaphylaxis Events in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2012, by Outcome Care Setting, Length of Time to Outcome and Year -- No Pre-Existing Condition Requirement

	New Users	Dispensings	Total Days Supplied	Days at Risk	New Anaphylaxis Events	Eligible Members	Member-Days	New Users/1K Eligible Members	Dispensings/User	Days Supplied/User	Days Supplied/Dispensing	New Events/100k Days at Risk
Within two days of exposure												
2000	484	502	502	1,456	0	7,429,886	1,261,164,611	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	3,719	0	8,013,999	2,495,260,483	0.16	1.03	1.03	1.00	0.00
2002	1,329	1,383	1,383	4,001	0	8,078,064	2,513,817,340	0.16	1.04	1.04	1.00	0.00
2003	1,897	1,961	1,961	5,709	0	8,027,680	2,499,767,286	0.24	1.03	1.03	1.00	0.00
2004	7,081	7,322	7,322	21,261	0	19,352,195	4,289,659,989	0.37	1.03	1.03	1.00	0.00
2005	9,303	9,814	9,814	27,916	1	21,327,484	6,155,145,867	0.44	1.05	1.05	1.00	3.58
2006	8,786	9,265	9,265	26,335	2	22,753,232	6,435,751,709	0.39	1.05	1.05	1.00	7.59
2007	9,742	10,318	10,318	29,091	1	25,509,649	6,867,836,642	0.38	1.06	1.06	1.00	3.44
2008	18,158	19,322	19,322	54,348	3	46,734,248	10,628,894,776	0.39	1.06	1.06	1.00	5.52
2009	27,073	28,800	28,800	80,972	5	47,694,195	13,679,936,227	0.57	1.06	1.06	1.00	6.17
2010	27,221	28,683	28,683	81,290	8	46,118,786	13,290,985,875	0.59	1.05	1.05	1.00	9.84
2011	22,942	24,120	24,120	68,663	3	44,560,507	12,804,512,611	0.51	1.05	1.05	1.00	4.37
2012	5,200	5,467	5,467	15,505	1	24,728,518	3,408,545,949	0.21	1.05	1.05	1.00	6.45
Within seven days of exposure												
2000	484	502	502	3,656	0	7,429,886	1,261,164,611	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	9,382	0	8,013,999	2,495,260,483	0.16	1.03	1.03	1.00	0.00
2002	1,329	1,383	1,383	10,096	0	8,078,064	2,513,817,340	0.16	1.04	1.04	1.00	0.00
2003	1,897	1,961	1,961	14,520	0	8,027,680	2,499,767,286	0.24	1.03	1.03	1.00	0.00
2004	7,081	7,322	7,322	53,589	0	19,352,195	4,289,659,989	0.37	1.03	1.03	1.00	0.00
2005	9,303	9,814	9,814	67,788	1	21,327,484	6,155,145,867	0.44	1.05	1.05	1.00	1.48
2006	8,786	9,265	9,265	63,049	2	22,753,232	6,435,751,709	0.39	1.05	1.05	1.00	3.17
2007	9,742	10,318	10,318	68,077	1	25,509,649	6,867,836,642	0.38	1.06	1.06	1.00	1.47
2008	18,158	19,322	19,322	126,383	3	46,734,248	10,628,894,776	0.39	1.06	1.06	1.00	2.37
2009	27,073	28,800	28,800	188,307	5	47,694,195	13,679,936,227	0.57	1.06	1.06	1.00	2.66
2010	27,221	28,683	28,683	188,940	8	46,118,786	13,290,985,875	0.59	1.05	1.05	1.00	4.23
2011	22,942	24,120	24,120	160,409	3	44,560,507	12,804,512,611	0.51	1.05	1.05	1.00	1.87
2012	5,200	5,467	5,467	35,751	1	24,728,518	3,408,545,949	0.21	1.05	1.05	1.00	2.80

Table 4. Summary of Incident IV Iron Exposure and Anaphylaxis Events in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2012, by Outcome Care Setting, Length of Time to Outcome and Year -- No Pre-Existing Condition Requirement

	New Users	Dispensings	Total Days Supplied	Days at Risk	New Anaphylaxis Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing	New Events/ 100k Days at Risk
<i>Within two days of exposure</i>												
2000	484	502	502	6,304	0	7,429,886	1,261,164,611	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	16,575	0	8,013,999	2,495,260,483	0.16	1.03	1.03	1.00	0.00
2002	1,329	1,383	1,383	17,611	0	8,078,064	2,513,817,340	0.16	1.04	1.04	1.00	0.00
2003	1,897	1,961	1,961	25,365	0	8,027,680	2,499,767,286	0.24	1.03	1.03	1.00	0.00
2004	7,081	7,322	7,322	92,409	0	19,352,195	4,289,659,989	0.37	1.03	1.03	1.00	0.00
2005	9,303	9,814	9,814	111,283	1	21,327,484	6,155,145,867	0.44	1.05	1.05	1.00	0.90
2006	8,786	9,265	9,265	99,997	2	22,753,232	6,435,751,709	0.39	1.05	1.05	1.00	2.00
2007	9,742	10,318	10,318	105,676	1	25,509,649	6,867,836,642	0.38	1.06	1.06	1.00	0.95
2008	18,158	19,322	19,322	194,148	3	46,734,248	10,628,894,776	0.39	1.06	1.06	1.00	1.55
2009	27,073	28,800	28,800	290,819	6	47,694,195	13,679,936,227	0.57	1.06	1.06	1.00	2.06
2010	27,221	28,683	28,683	285,660	8	46,118,786	13,290,985,875	0.59	1.05	1.05	1.00	2.80
2011	22,942	24,120	24,120	241,913	3	44,560,507	12,804,512,611	0.51	1.05	1.05	1.00	1.24
2012	5,200	5,467	5,467	53,554	1	24,728,518	3,408,545,949	0.21	1.05	1.05	1.00	1.87
<i>Event occurs in Outpatient Care Setting</i>												
<i>On day of exposure</i>												
2000	484	502	502	502	0	7,429,886	1,261,164,611	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	1,279	0	8,013,999	2,495,260,483	0.16	1.03	1.03	1.00	0.00
2002	1,329	1,383	1,383	1,376	1	8,078,064	2,513,817,340	0.16	1.04	1.04	1.00	72.67
2003	1,897	1,961	1,961	1,949	0	8,027,680	2,499,767,286	0.24	1.03	1.03	1.00	0.00
2004	7,081	7,322	7,322	7,287	3	19,352,195	4,289,659,989	0.37	1.03	1.03	1.00	41.17
2005	9,303	9,814	9,814	9,771	1	21,327,484	6,155,145,867	0.44	1.05	1.05	1.00	10.23
2006	8,786	9,265	9,265	9,254	2	22,753,232	6,435,751,709	0.39	1.05	1.05	1.00	21.61
2007	9,742	10,318	10,318	10,307	1	25,509,649	6,867,836,642	0.38	1.06	1.06	1.00	9.70
2008	18,158	19,322	19,322	19,299	3	46,734,248	10,628,894,776	0.39	1.06	1.06	1.00	15.54
2009	27,073	28,800	28,800	28,742	3	47,694,195	13,679,936,227	0.57	1.06	1.06	1.00	10.44
2010	27,221	28,683	28,683	28,622	4	46,118,786	13,290,985,875	0.59	1.05	1.05	1.00	13.98
2011	22,942	24,120	24,120	24,075	2	44,560,507	12,804,512,611	0.51	1.05	1.05	1.00	8.31
2012	5,200	5,467	5,467	5,463	0	24,728,518	3,408,545,949	0.21	1.05	1.05	1.00	0.00

Table 4. Summary of Incident IV Iron Exposure and Anaphylaxis Events in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2012, by Outcome Care Setting, Length of Time to Outcome and Year -- No Pre-Existing Condition Requirement

	New Users	Dispensings	Total Days Supplied	Days at Risk	New Anaphylaxis Events	Eligible Members	Member-Days	New Users/1K Eligible Members	Dispensings/User	Days Supplied/User	Days Supplied/Dispensing	New Events/100k Days at Risk
Within one day of exposure												
2000	484	502	502	986	0	7,429,886	1,261,164,611	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	2,521	0	8,013,999	2,495,260,483	0.16	1.03	1.03	1.00	0.00
2002	1,329	1,383	1,383	2,704	1	8,078,064	2,513,817,340	0.16	1.04	1.04	1.00	36.98
2003	1,897	1,961	1,961	3,845	0	8,027,680	2,499,767,286	0.24	1.03	1.03	1.00	0.00
2004	7,081	7,322	7,322	14,363	3	19,352,195	4,289,659,989	0.37	1.03	1.03	1.00	20.89
2005	9,303	9,814	9,814	19,066	1	21,327,484	6,155,145,867	0.44	1.05	1.05	1.00	5.24
2006	8,786	9,265	9,265	18,031	2	22,753,232	6,435,751,709	0.39	1.05	1.05	1.00	11.09
2007	9,742	10,318	10,318	20,040	1	25,509,649	6,867,836,642	0.38	1.06	1.06	1.00	4.99
2008	18,158	19,322	19,322	37,443	3	46,734,248	10,628,894,776	0.39	1.06	1.06	1.00	8.01
2009	27,073	28,800	28,800	55,792	3	47,694,195	13,679,936,227	0.57	1.06	1.06	1.00	5.38
2010	27,221	28,683	28,683	55,827	5	46,118,786	13,290,985,875	0.59	1.05	1.05	1.00	8.96
2011	22,942	24,120	24,120	47,004	2	44,560,507	12,804,512,611	0.51	1.05	1.05	1.00	4.25
2012	5,200	5,467	5,467	10,657	0	24,728,518	3,408,545,949	0.21	1.05	1.05	1.00	0.00
Within two days of exposure												
2000	484	502	502	1,456	0	7,429,886	1,261,164,611	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	3,719	0	8,013,999	2,495,260,483	0.16	1.03	1.03	1.00	0.00
2002	1,329	1,383	1,383	3,999	1	8,078,064	2,513,817,340	0.16	1.04	1.04	1.00	25.01
2003	1,897	1,961	1,961	5,709	0	8,027,680	2,499,767,286	0.24	1.03	1.03	1.00	0.00
2004	7,081	7,322	7,322	21,255	3	19,352,195	4,289,659,989	0.37	1.03	1.03	1.00	14.11
2005	9,303	9,814	9,814	27,916	1	21,327,484	6,155,145,867	0.44	1.05	1.05	1.00	3.58
2006	8,786	9,265	9,265	26,334	2	22,753,232	6,435,751,709	0.39	1.05	1.05	1.00	7.59
2007	9,742	10,318	10,318	29,091	1	25,509,649	6,867,836,642	0.38	1.06	1.06	1.00	3.44
2008	18,158	19,322	19,322	54,348	3	46,734,248	10,628,894,776	0.39	1.06	1.06	1.00	5.52
2009	27,073	28,800	28,800	80,975	4	47,694,195	13,679,936,227	0.57	1.06	1.06	1.00	4.94
2010	27,221	28,683	28,683	81,297	5	46,118,786	13,290,985,875	0.59	1.05	1.05	1.00	6.15
2011	22,942	24,120	24,120	68,665	2	44,560,507	12,804,512,611	0.51	1.05	1.05	1.00	2.91
2012	5,200	5,467	5,467	15,507	0	24,728,518	3,408,545,949	0.21	1.05	1.05	1.00	0.00

Table 4. Summary of Incident IV Iron Exposure and Anaphylaxis Events in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2012, by Outcome Care Setting, Length of Time to Outcome and Year -- No Pre-Existing Condition Requirement

	New Users	Dispensings	Total Days Supplied	Days at Risk	New Anaphylaxis Events	Eligible Members	Member-Days	New Users/1K Eligible Members	Dispensings/User	Days Supplied/User	Days Supplied/Dispensing	New Events/100k Days at Risk
Within seven days of exposure												
2000	484	502	502	3,656	0	7,429,886	1,261,164,611	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	9,382	0	8,013,999	2,495,260,483	0.16	1.03	1.03	1.00	0.00
2002	1,329	1,383	1,383	10,085	2	8,078,064	2,513,817,340	0.16	1.04	1.04	1.00	19.83
2003	1,897	1,961	1,961	14,520	0	8,027,680	2,499,767,286	0.24	1.03	1.03	1.00	0.00
2004	7,081	7,322	7,322	53,568	3	19,352,195	4,289,659,989	0.37	1.03	1.03	1.00	5.60
2005	9,303	9,814	9,814	67,788	1	21,327,484	6,155,145,867	0.44	1.05	1.05	1.00	1.48
2006	8,786	9,265	9,265	63,048	2	22,753,232	6,435,751,709	0.39	1.05	1.05	1.00	3.17
2007	9,742	10,318	10,318	68,077	1	25,509,649	6,867,836,642	0.38	1.06	1.06	1.00	1.47
2008	18,158	19,322	19,322	126,383	3	46,734,248	10,628,894,776	0.39	1.06	1.06	1.00	2.37
2009	27,073	28,800	28,800	188,319	4	47,694,195	13,679,936,227	0.57	1.06	1.06	1.00	2.12
2010	27,221	28,683	28,683	188,956	9	46,118,786	13,290,985,875	0.59	1.05	1.05	1.00	4.76
2011	22,942	24,120	24,120	160,416	2	44,560,507	12,804,512,611	0.51	1.05	1.05	1.00	1.25
2012	5,200	5,467	5,467	35,758	0	24,728,518	3,408,545,949	0.21	1.05	1.05	1.00	0.00
Within two days of exposure												
2000	484	502	502	6,304	0	7,429,886	1,261,164,611	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	16,575	0	8,013,999	2,495,260,483	0.16	1.03	1.03	1.00	0.00
2002	1,329	1,383	1,383	17,586	2	8,078,064	2,513,817,340	0.16	1.04	1.04	1.00	11.37
2003	1,897	1,961	1,961	25,365	0	8,027,680	2,499,767,286	0.24	1.03	1.03	1.00	0.00
2004	7,081	7,322	7,322	92,367	3	19,352,195	4,289,659,989	0.37	1.03	1.03	1.00	3.25
2005	9,303	9,814	9,814	111,283	1	21,327,484	6,155,145,867	0.44	1.05	1.05	1.00	0.90
2006	8,786	9,265	9,265	99,990	2	22,753,232	6,435,751,709	0.39	1.05	1.05	1.00	2.00
2007	9,742	10,318	10,318	105,677	1	25,509,649	6,867,836,642	0.38	1.06	1.06	1.00	0.95
2008	18,158	19,322	19,322	194,148	3	46,734,248	10,628,894,776	0.39	1.06	1.06	1.00	1.55
2009	27,073	28,800	28,800	290,849	4	47,694,195	13,679,936,227	0.57	1.06	1.06	1.00	1.38
2010	27,221	28,683	28,683	285,683	9	46,118,786	13,290,985,875	0.59	1.05	1.05	1.00	3.15
2011	22,942	24,120	24,120	241,927	2	44,560,507	12,804,512,611	0.51	1.05	1.05	1.00	0.83
2012	5,200	5,467	5,467	53,568	0	24,728,518	3,408,545,949	0.21	1.05	1.05	1.00	0.00

Appendix A. List of Diagnosis and Procedure Codes included in this Request

IV Iron Healthcare Common Procedure Coding System (HCPCS) Procedure Codes

J1750	J1752	J1770	J2915	S0098	J1755	Q0138
J1751	J1760	J1780	J2916	W0231	J1756	Q0139

Anaphylaxis International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Diagnosis Code

995.0

Epinephrine HCPCS Codes

J0170	J0171
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Dialysis Codes

ICD-9-CM Diagnosis Codes

996.56	996.73	V45.1
996.68	458.21	V56

ICD-9-CM Procedure Codes

39.95
54.98

Current Procedural Terminology Fourth Edition (CPT-4) Procedure Codes

90918	90921	90924	90937	90993	93990	36800	36825	36832
90919	90922	90925	90945	90997	99512	36810	36830	36833
90920	90923	90935	90947	90999	36145	36815	36831	

HCPCS Procedures

A4690	G0311	G0321	A4656	A4708	A4725	A4765	A4911	E1550
E1510	G0312	G0322	A4657	A4709	A4726	A4766	A4913	E1560
E1590	G0313	G0323	A4670	A4712	A4728	A4770	A4918	E1570
E1592	G0314	G0324	A4671	A4714	A4730	A4771	A4928	E1575
E1594	G0315	G0325	A4672	A4719	A4736	A4773	A4929	E1580
E1630	G0316	G0326	A4673	A4720	A4737	A4774	C1881	E1600
E1632	G0317	G0327	A4674	A4721	A4740	A4802	E1500	E1610
G0308	G0318	S9335	A4680	A4722	A4750	A4860	E1520	E1615
G0309	G0319	S9339	A4706	A4723	A4755	A4870	E1530	E1620
G0310	G0320	A4653	A4707	A4724	A4760	A4890	E1540	E1625

Appendix B: Modular Program Specifications for Query ID msy4_mpr13_v1

Modular Program #3 was used to investigate diagnosis of Anaphylaxis and exposure to IV iron procedures for all patients (i.e., no specific pre-existing condition criteria applied). The query period was from January 1, 2000 to December 31, 2012. The enrollment gap was set at 45 days, and age groups will be split as follows: 00-21, 22-44, 45-64, and 65+ years. In total, 10 different scenarios were examined in this report. See below for a description of each of these scenarios. See the next tab for a glossary of selected terms, and see Appendix A for a list of codes included in the exposure of interest, the event of interest, and the pre-existing conditions of interest.

Scenario	Drug/Exposure									Pre-Existing Condition				Event/Outcome							
	Incident exposure	Incident w/ respect to:	Washout (days)	Washout Type	Episode Gap	Exposure Extension Period	Min. Episode Duration	Minimum Days Supplied	Pre-Existing Condition	Lookback Type	Lookback Period	Care Setting	Principal Dx	Event/ Outcome	Incident w/ respect to:	Care Setting	Care Setting	Washout (days)	Washout Type	Principal Dx	Blackout Period
1	All IV Iron	All IV Iron	183	Singls	0	0	0	0	None	N/A	N/A	N/A	N/A	Anaphylaxis	Anaphylaxis	IP, ED	ALL	30	Multiple	NO	0
2	All IV Iron	All IV Iron	183	Single	0	1	0	0	None	N/A	N/A	N/A	N/A	Anaphylaxis	Anaphylaxis	IP, ED	ALL	30	Multiple	NO	0
3	All IV Iron	All IV Iron	183	Single	0	2	0	0	None	N/A	N/A	N/A	N/A	Anaphylaxis	Anaphylaxis	IP, ED	ALL	30	Multiple	NO	0
4	All IV Iron	All IV Iron	183	Single	0	7	0	0	None	N/A	N/A	N/A	N/A	Anaphylaxis	Anaphylaxis	IP, ED	ALL	30	Multiple	NO	0
5	All IV Iron	All IV Iron	183	Single	0	14	0	0	None	N/A	N/A	N/A	N/A	Anaphylaxis	Anaphylaxis	IP, ED	ALL	30	Multiple	NO	0
6	All IV Iron	All IV Iron	183	Single	0	0	0	0	None	N/A	N/A	N/A	N/A	Anaphylaxis	Anaphylaxis	AV	ALL	30	Multiple	NO	0
7	All IV Iron	All IV Iron	183	Single	0	1	0	0	None	N/A	N/A	N/A	N/A	Anaphylaxis	Anaphylaxis	AV	ALL	30	Multiple	NO	0
8	All IV Iron	All IV Iron	183	Single	0	2	0	0	None	N/A	N/A	N/A	N/A	Anaphylaxis	Anaphylaxis	AV	ALL	30	Multiple	NO	0
9	All IV Iron	All IV Iron	183	Single	0	7	0	0	None	N/A	N/A	N/A	N/A	Anaphylaxis	Anaphylaxis	AV	ALL	30	Multiple	NO	0
10	All IV Iron	All IV Iron	183	Single	0	14	0	0	None	N/A	N/A	N/A	N/A	Anaphylaxis	Anaphylaxis	AV	ALL	30	Multiple	NO	0

National Drug Codes (NDC) codes checked against First Data Bank's "National Drug Data File (NDDF®) Plus"

International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes checked against "Ingenix 2012 ICD-9-CM Data File" provided by OptumInsight

Healthcare Common Procedure Coding System (HCPCS) codes checked against "Optum 2012 HCPCS Level II Data File" provided by OptumInsight

Current Procedural Terminology, Fourth Edition (CPT-4) codes checked against "Optum 2012 Current Procedure Codes & Relative Values Data File" provided by OptumInsight