

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 epinephrine 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 4 of 4.

This report contains results for the scenarios with no pre-existing condition requirement and an event of epinephrine. 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 anaphylaxis; (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 and International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes included in this request.

<u>Request ID</u>	Modular Program Specifications for Query ID msy4_mpr13_v1
<u>Glossary</u>	List of Terms found in this Report and their Definitions
<u>Table 1</u>	Summary of Incident IV Iron Exposure and Epinephrine 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
<u>Figure 1</u>	Number of New Epinephrine 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
<u>Table 2</u>	Summary of Incident IV Iron Exposure and Epinephrine 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
<u>Table 3</u>	Summary of Incident IV Iron Exposure and Epinephrine 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
<u>Table 4</u>	Summary of Incident IV Iron Exposure and Epinephrine 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
<u>Appendix A</u>	List of Diagnosis and Procedure Codes Included in this Request
<u>Appendix B</u>	Modular Program Specifications for Query ID msy4_mpr13_v1
<u>Notes:</u>	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 during the
- Care Setting** - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings
- 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 enrolled”
- Episode Gap** - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the
- Exposure Extension Period** - number of days post treatment period in which the outcomes/events are counted for a treatment episode.
- Lookback Period (pre-existing condition)** - number of days wherein a member is required to have evidence of pre-existing condition
- 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 considered
- 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 query period.
- 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 Epinephrine 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 Epinephrine 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	140,388	148,155	148,155	147,839	75	94,936,790	86,324,913,114	1.48	1.06	1.06	1.00	50.73
Within one day of exposure	140,388	148,155	148,155	288,066	78	94,936,790	86,324,913,114	1.48	1.06	1.06	1.00	27.08
Within two days of exposure	140,388	148,155	148,155	419,933	80	94,936,790	86,324,913,114	1.48	1.06	1.06	1.00	19.05
Within seven days of exposure	140,388	148,155	148,155	989,028	86	94,936,790	86,324,913,114	1.48	1.06	1.06	1.00	8.70
Within 14 days of exposure	140,388	148,155	148,155	1,539,695	92	94,936,790	86,324,913,114	1.48	1.06	1.06	1.00	5.98
<i>Event occurs in Outpatient Care Setting</i>												
On day of exposure	140,388	148,155	148,155	147,835	92	94,936,790	86,324,913,114	1.48	1.06	1.06	1.00	62.23
Within one day of exposure	140,388	148,155	148,155	288,045	98	94,936,790	86,324,913,114	1.48	1.06	1.06	1.00	34.02
Within two days of exposure	140,388	148,155	148,155	419,892	100	94,936,790	86,324,913,114	1.48	1.06	1.06	1.00	23.82
Within seven days of exposure	140,388	148,155	148,155	988,903	111	94,936,790	86,324,913,114	1.48	1.06	1.06	1.00	11.22
Within 14 days of exposure	140,388	148,155	148,155	1,539,476	123	94,936,790	86,324,913,114	1.48	1.06	1.06	1.00	7.99

Figure 1. Number of New Epinephrine 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

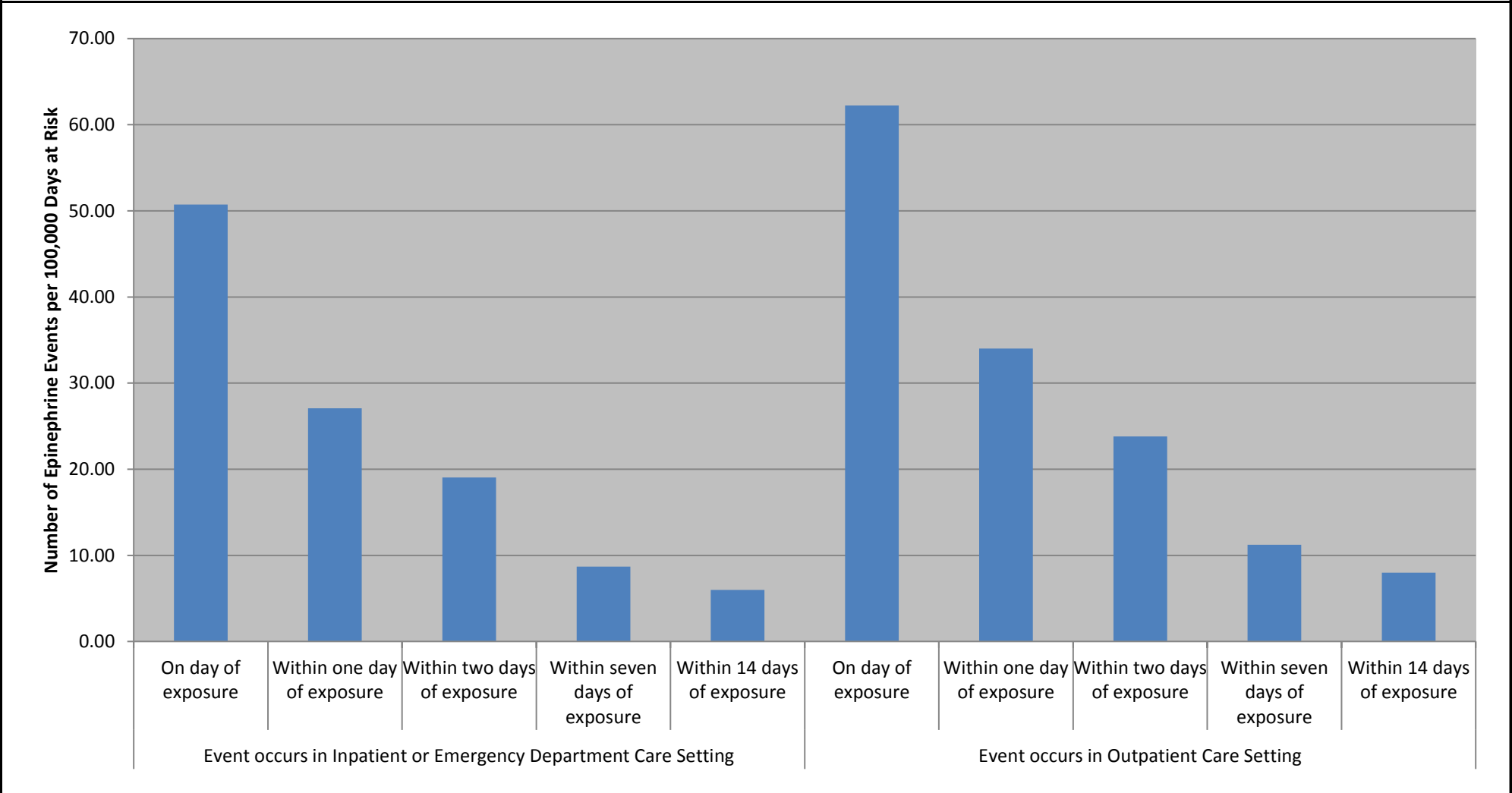


Table 2. Summary of Incident IV Iron Exposure and Epinephrine Events in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2012, by Outcome Care Setting, Length of Time to Outcome and Age Group -- No Pre-Existing Condition Requirement

	New Users	Dispensings	Total Days Supplied	Days at Risk	New Epinephrine 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	5	28,882,022	24,942,408,062	0.08	1.07	1.07	1.00	202.02
22-44 years	31,748	33,994	33,994	33,895	9	37,934,388	27,235,049,400	0.84	1.07	1.07	1.00	26.55
45-64 years	53,315	56,157	56,157	56,047	34	27,513,774	25,287,841,561	1.94	1.05	1.05	1.00	60.66
65+ years	53,014	55,521	55,521	55,422	27	8,363,750	8,859,614,091	6.34	1.05	1.05	1.00	48.72
<i>Within one day of exposure</i>												
00-21 years	2,311	2,483	2,483	4,781	5	28,882,022	24,942,408,062	0.08	1.07	1.07	1.00	104.58
22-44 years	31,748	33,994	33,994	65,598	10	37,934,388	27,235,049,400	0.84	1.07	1.07	1.00	15.24
45-64 years	53,315	56,157	56,157	109,299	35	27,513,774	25,287,841,561	1.94	1.05	1.05	1.00	32.02
65+ years	53,014	55,521	55,521	108,388	28	8,363,750	8,859,614,091	6.34	1.05	1.05	1.00	25.83
<i>Within two days of exposure</i>												
00-21 years	2,311	2,483	2,483	6,945	5	28,882,022	24,942,408,062	0.08	1.07	1.07	1.00	71.99
22-44 years	31,748	33,994	33,994	95,632	10	37,934,388	27,235,049,400	0.84	1.07	1.07	1.00	10.46
45-64 years	53,315	56,157	56,157	159,192	37	27,513,774	25,287,841,561	1.94	1.05	1.05	1.00	23.24
65+ years	53,014	55,521	55,521	158,164	28	8,363,750	8,859,614,091	6.34	1.05	1.05	1.00	17.70
<i>Within seven days of exposure</i>												
00-21 years	2,311	2,483	2,483	16,298	5	28,882,022	24,942,408,062	0.08	1.07	1.07	1.00	30.68
22-44 years	31,748	33,994	33,994	224,236	10	37,934,388	27,235,049,400	0.84	1.07	1.07	1.00	4.46
45-64 years	53,315	56,157	56,157	374,618	40	27,513,774	25,287,841,561	1.94	1.05	1.05	1.00	10.68
65+ years	53,014	55,521	55,521	373,876	31	8,363,750	8,859,614,091	6.34	1.05	1.05	1.00	8.29
<i>Within 14 days of exposure</i>												
00-21 years	2,311	2,483	2,483	25,770	5	28,882,022	24,942,408,062	0.08	1.07	1.07	1.00	19.40
22-44 years	31,748	33,994	33,994	345,860	10	37,934,388	27,235,049,400	0.84	1.07	1.07	1.00	2.89
45-64 years	53,315	56,157	56,157	584,884	41	27,513,774	25,287,841,561	1.94	1.05	1.05	1.00	7.01
65+ years	53,014	55,521	55,521	583,181	36	8,363,750	8,859,614,091	6.34	1.05	1.05	1.00	6.17

Table 2. Summary of Incident IV Iron Exposure and Epinephrine 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	Dispensings	Total Days Supplied	Days at Risk	New Epinephrine 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>												
<i>On day of exposure</i>												
00-21 years	2,311	2,483	2,483	2,475	11	28,882,022	24,942,408,062	0.08	1.07	1.07	1.00	444.44
22-44 years	31,748	33,994	33,994	33,890	31	37,934,388	27,235,049,400	0.84	1.07	1.07	1.00	91.47
45-64 years	53,315	56,157	56,157	56,047	30	27,513,774	25,287,841,561	1.94	1.05	1.05	1.00	53.53
65+ years	53,014	55,521	55,521	55,423	20	8,363,750	8,859,614,091	6.34	1.05	1.05	1.00	36.09
<i>Within one day of exposure</i>												
00-21 years	2,311	2,483	2,483	4,775	11	28,882,022	24,942,408,062	0.08	1.07	1.07	1.00	230.37
22-44 years	31,748	33,994	33,994	65,571	31	37,934,388	27,235,049,400	0.84	1.07	1.07	1.00	47.28
45-64 years	53,315	56,157	56,157	109,303	33	27,513,774	25,287,841,561	1.94	1.05	1.05	1.00	30.19
65+ years	53,014	55,521	55,521	108,396	23	8,363,750	8,859,614,091	6.34	1.05	1.05	1.00	21.22
<i>Within two days of exposure</i>												
00-21 years	2,311	2,483	2,483	6,934	11	28,882,022	24,942,408,062	0.08	1.07	1.07	1.00	158.64
22-44 years	31,748	33,994	33,994	95,583	32	37,934,388	27,235,049,400	0.84	1.07	1.07	1.00	33.48
45-64 years	53,315	56,157	56,157	159,199	33	27,513,774	25,287,841,561	1.94	1.05	1.05	1.00	20.73
65+ years	53,014	55,521	55,521	158,176	24	8,363,750	8,859,614,091	6.34	1.05	1.05	1.00	15.17
<i>Within seven days of exposure</i>												
00-21 years	2,311	2,483	2,483	16,267	11	28,882,022	24,942,408,062	0.08	1.07	1.07	1.00	67.62
22-44 years	31,748	33,994	33,994	224,086	32	37,934,388	27,235,049,400	0.84	1.07	1.07	1.00	14.28
45-64 years	53,315	56,157	56,157	374,658	38	27,513,774	25,287,841,561	1.94	1.05	1.05	1.00	10.14
65+ years	53,014	55,521	55,521	373,892	30	8,363,750	8,859,614,091	6.34	1.05	1.05	1.00	8.02
<i>Within 14 days of exposure</i>												
00-21 years	2,311	2,483	2,483	25,712	11	28,882,022	24,942,408,062	0.08	1.07	1.07	1.00	42.78
22-44 years	31,748	33,994	33,994	345,612	33	37,934,388	27,235,049,400	0.84	1.07	1.07	1.00	9.55
45-64 years	53,315	56,157	56,157	584,954	42	27,513,774	25,287,841,561	1.94	1.05	1.05	1.00	7.18
65+ years	53,014	55,521	55,521	583,198	37	8,363,750	8,859,614,091	6.34	1.05	1.05	1.00	6.34

Table 3. Summary of Incident IV Iron Exposure and Epinephrine 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 Epinephrine 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												
Female	92,232	97,976	97,976	97,763	36	48,405,265	44,569,227,784	1.91	1.06	1.06	1.00	36.82
Male	48,045	50,059	50,059	49,956	39	46,422,450	41,642,923,099	1.03	1.04	1.04	1.00	78.07
Unknown	111	120	120	120	0	109,075	112,762,231	1.02	1.08	1.08	1.00	0.00
Within one day of exposure												
Female	92,232	97,976	97,976	189,897	37	48,405,265	44,569,227,784	1.91	1.06	1.06	1.00	19.48
Male	48,045	50,059	50,059	97,938	41	46,422,450	41,642,923,099	1.03	1.04	1.04	1.00	41.86
Unknown	111	120	120	231	0	109,075	112,762,231	1.02	1.08	1.08	1.00	0.00
Within two days of exposure												
Female	92,232	97,976	97,976	277,258	39	48,405,265	44,569,227,784	1.91	1.06	1.06	1.00	14.07
Male	48,045	50,059	50,059	142,342	41	46,422,450	41,642,923,099	1.03	1.04	1.04	1.00	28.80
Unknown	111	120	120	333	0	109,075	112,762,231	1.02	1.08	1.08	1.00	0.00
Within seven days of exposure												
Female	92,232	97,976	97,976	653,906	42	48,405,265	44,569,227,784	1.91	1.06	1.06	1.00	6.42
Male	48,045	50,059	50,059	334,362	44	46,422,450	41,642,923,099	1.03	1.04	1.04	1.00	13.16
Unknown	111	120	120	760	0	109,075	112,762,231	1.02	1.08	1.08	1.00	0.00
Within 14 days of exposure												
Female	92,232	97,976	97,976	1,011,001	47	48,405,265	44,569,227,784	1.91	1.06	1.06	1.00	4.65
Male	48,045	50,059	50,059	527,538	45	46,422,450	41,642,923,099	1.03	1.04	1.04	1.00	8.53
Unknown	111	120	120	1,156	0	109,075	112,762,231	1.02	1.08	1.08	1.00	0.00
<i>Event occurs in Outpatient Care Setting</i>												
On day of exposure												
Female	92,232	97,976	97,976	97,759	72	48,405,265	44,569,227,784	1.91	1.06	1.06	1.00	73.65
Male	48,045	50,059	50,059	49,956	19	46,422,450	41,642,923,099	1.03	1.04	1.04	1.00	38.03
Unknown	111	120	120	120	1	109,075	112,762,231	1.02	1.08	1.08	1.00	833.33
Within one day of exposure												
Female	92,232	97,976	97,976	189,857	75	48,405,265	44,569,227,784	1.91	1.06	1.06	1.00	39.50
Male	48,045	50,059	50,059	97,958	22	46,422,450	41,642,923,099	1.03	1.04	1.04	1.00	22.46
Unknown	111	120	120	230	1	109,075	112,762,231	1.02	1.08	1.08	1.00	434.78
Within two days of exposure												
Female	92,232	97,976	97,976	277,181	76	48,405,265	44,569,227,784	1.91	1.06	1.06	1.00	27.42
Male	48,045	50,059	50,059	142,380	23	46,422,450	41,642,923,099	1.03	1.04	1.04	1.00	16.15
Unknown	111	120	120	331	1	109,075	112,762,231	1.02	1.08	1.08	1.00	302.11

Table 3. Summary of Incident IV Iron Exposure and Epinephrine 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 Epinephrine 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	92,232	97,976	97,976	653,663	82	48,405,265	44,569,227,784	1.91	1.06	1.06	1.00	12.54
Male	48,045	50,059	50,059	334,487	28	46,422,450	41,642,923,099	1.03	1.04	1.04	1.00	8.37
Unknown	111	120	120	753	1	109,075	112,762,231	1.02	1.08	1.08	1.00	132.80
Within 14 days of exposure												
Female	92,232	97,976	97,976	1,010,557	90	48,405,265	44,569,227,784	1.91	1.06	1.06	1.00	8.91
Male	48,045	50,059	50,059	527,777	32	46,422,450	41,642,923,099	1.03	1.04	1.04	1.00	6.06
Unknown	111	120	120	1,142	1	109,075	112,762,231	1.02	1.08	1.08	1.00	87.57

Table 4. Summary of Incident IV Iron Exposure and Epinephrine 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 Epinephrine 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>												
2000	484	502	502	502	0	7,429,879	1,261,163,697	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	1,279	0	8,013,982	2,495,247,583	0.16	1.03	1.03	1.00	0.00
2002	1,329	1,383	1,383	1,376	0	8,078,059	2,513,798,947	0.16	1.04	1.04	1.00	0.00
2003	1,897	1,957	1,957	1,945	0	8,027,688	2,499,758,737	0.24	1.03	1.03	1.00	0.00
2004	7,080	7,323	7,323	7,288	2	19,352,107	4,289,447,653	0.37	1.03	1.03	1.00	27.44
2005	9,296	9,807	9,807	9,764	4	21,327,339	6,154,729,780	0.44	1.05	1.05	1.00	40.97
2006	8,784	9,261	9,261	9,250	5	22,753,027	6,435,268,022	0.39	1.05	1.05	1.00	54.05
2007	9,738	10,314	10,314	10,303	5	25,509,516	6,867,234,302	0.38	1.06	1.06	1.00	48.53
2008	18,145	19,309	19,309	19,286	8	46,733,690	10,628,047,234	0.39	1.06	1.06	1.00	41.48
2009	27,057	28,776	28,776	28,718	14	47,693,852	13,678,802,495	0.57	1.06	1.06	1.00	48.75
2010	27,199	28,658	28,658	28,597	21	46,118,546	13,289,702,101	0.59	1.05	1.05	1.00	73.43
2011	22,938	24,116	24,116	24,070	15	44,560,376	12,803,384,123	0.51	1.05	1.05	1.00	62.32
2012	5,198	5,465	5,465	5,461	1	24,728,543	3,408,328,440	0.21	1.05	1.05	1.00	18.31
<i>Within one day of exposure</i>												
2000	484	502	502	986	0	7,429,879	1,261,163,697	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	2,521	0	8,013,982	2,495,247,583	0.16	1.03	1.03	1.00	0.00
2002	1,329	1,383	1,383	2,705	0	8,078,059	2,513,798,947	0.16	1.04	1.04	1.00	0.00
2003	1,897	1,957	1,957	3,841	0	8,027,688	2,499,758,737	0.24	1.03	1.03	1.00	0.00
2004	7,080	7,323	7,323	14,364	2	19,352,107	4,289,447,653	0.37	1.03	1.03	1.00	13.92
2005	9,296	9,807	9,807	19,049	5	21,327,339	6,154,729,780	0.44	1.05	1.05	1.00	26.25
2006	8,784	9,261	9,261	18,022	6	22,753,027	6,435,268,022	0.39	1.05	1.05	1.00	33.29
2007	9,738	10,314	10,314	20,028	5	25,509,516	6,867,234,302	0.38	1.06	1.06	1.00	24.97
2008	18,145	19,309	19,309	37,412	8	46,733,690	10,628,047,234	0.39	1.06	1.06	1.00	21.38
2009	27,057	28,776	28,776	55,741	14	47,693,852	13,678,802,495	0.57	1.06	1.06	1.00	25.12
2010	27,199	28,658	28,658	55,763	22	46,118,546	13,289,702,101	0.59	1.05	1.05	1.00	39.45
2011	22,938	24,116	24,116	46,982	15	44,560,376	12,803,384,123	0.51	1.05	1.05	1.00	31.93
2012	5,198	5,465	5,465	10,652	1	24,728,543	3,408,328,440	0.21	1.05	1.05	1.00	9.39

Table 4. Summary of Incident IV Iron Exposure and Epinephrine 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 Epinephrine 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	7,429,879	1,261,163,697	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	3,719	0	8,013,982	2,495,247,583	0.16	1.03	1.03	1.00	0.00
2002	1,329	1,383	1,383	4,001	0	8,078,059	2,513,798,947	0.16	1.04	1.04	1.00	0.00
2003	1,897	1,957	1,957	5,705	0	8,027,688	2,499,758,737	0.24	1.03	1.03	1.00	0.00
2004	7,080	7,323	7,323	21,256	2	19,352,107	4,289,447,653	0.37	1.03	1.03	1.00	9.41
2005	9,296	9,807	9,807	27,890	5	21,327,339	6,154,729,780	0.44	1.05	1.05	1.00	17.93
2006	8,784	9,261	9,261	26,318	6	22,753,027	6,435,268,022	0.39	1.05	1.05	1.00	22.80
2007	9,738	10,314	10,314	29,072	5	25,509,516	6,867,234,302	0.38	1.06	1.06	1.00	17.20
2008	18,145	19,309	19,309	54,299	9	46,733,690	10,628,047,234	0.39	1.06	1.06	1.00	16.57
2009	27,057	28,776	28,776	80,897	15	47,693,852	13,678,802,495	0.57	1.06	1.06	1.00	18.54
2010	27,199	28,658	28,658	81,195	22	46,118,546	13,289,702,101	0.59	1.05	1.05	1.00	27.10
2011	22,938	24,116	24,116	68,626	15	44,560,376	12,803,384,123	0.51	1.05	1.05	1.00	21.86
2012	5,198	5,465	5,465	15,499	1	24,728,543	3,408,328,440	0.21	1.05	1.05	1.00	6.45
Within seven days of exposure												
2000	484	502	502	3,653	1	7,429,879	1,261,163,697	0.07	1.04	1.04	1.00	27.37
2001	1,243	1,284	1,284	9,382	0	8,013,982	2,495,247,583	0.16	1.03	1.03	1.00	0.00
2002	1,329	1,383	1,383	10,096	0	8,078,059	2,513,798,947	0.16	1.04	1.04	1.00	0.00
2003	1,897	1,957	1,957	14,521	0	8,027,688	2,499,758,737	0.24	1.03	1.03	1.00	0.00
2004	7,080	7,323	7,323	53,565	2	19,352,107	4,289,447,653	0.37	1.03	1.03	1.00	3.73
2005	9,296	9,807	9,807	67,725	5	21,327,339	6,154,729,780	0.44	1.05	1.05	1.00	7.38
2006	8,784	9,261	9,261	63,000	7	22,753,027	6,435,268,022	0.39	1.05	1.05	1.00	11.11
2007	9,738	10,314	10,314	68,025	5	25,509,516	6,867,234,302	0.38	1.06	1.06	1.00	7.35
2008	18,145	19,309	19,309	126,243	9	46,733,690	10,628,047,234	0.39	1.06	1.06	1.00	7.13
2009	27,057	28,776	28,776	188,110	17	47,693,852	13,678,802,495	0.57	1.06	1.06	1.00	9.04
2010	27,199	28,658	28,658	188,686	24	46,118,546	13,289,702,101	0.59	1.05	1.05	1.00	12.72
2011	22,938	24,116	24,116	160,290	15	44,560,376	12,803,384,123	0.51	1.05	1.05	1.00	9.36
2012	5,198	5,465	5,465	35,732	1	24,728,543	3,408,328,440	0.21	1.05	1.05	1.00	2.80

Table 4. Summary of Incident IV Iron Exposure and Epinephrine 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 Epinephrine 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	6,294	1	7,429,879	1,261,163,697	0.07	1.04	1.04	1.00	15.89
2001	1,243	1,284	1,284	16,575	0	8,013,982	2,495,247,583	0.16	1.03	1.03	1.00	0.00
2002	1,329	1,383	1,383	17,611	0	8,078,059	2,513,798,947	0.16	1.04	1.04	1.00	0.00
2003	1,897	1,957	1,957	25,373	1	8,027,688	2,499,758,737	0.24	1.03	1.03	1.00	3.94
2004	7,080	7,323	7,323	92,357	3	19,352,107	4,289,447,653	0.37	1.03	1.03	1.00	3.25
2005	9,296	9,807	9,807	111,172	5	21,327,339	6,154,729,780	0.44	1.05	1.05	1.00	4.50
2006	8,784	9,261	9,261	99,899	7	22,753,027	6,435,268,022	0.39	1.05	1.05	1.00	7.01
2007	9,738	10,314	10,314	105,589	5	25,509,516	6,867,234,302	0.38	1.06	1.06	1.00	4.74
2008	18,145	19,309	19,309	193,900	9	46,733,690	10,628,047,234	0.39	1.06	1.06	1.00	4.64
2009	27,057	28,776	28,776	290,500	17	47,693,852	13,678,802,495	0.57	1.06	1.06	1.00	5.85
2010	27,199	28,658	28,658	285,243	25	46,118,546	13,289,702,101	0.59	1.05	1.05	1.00	8.76
2011	22,938	24,116	24,116	241,672	17	44,560,376	12,803,384,123	0.51	1.05	1.05	1.00	7.03
2012	5,198	5,465	5,465	53,510	2	24,728,543	3,408,328,440	0.21	1.05	1.05	1.00	3.74
<i>Event occurs in Outpatient Care Setting</i>												
<i>On day of exposure</i>												
2000	484	502	502	502	0	7,429,879	1,261,163,697	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	1,279	1	8,013,982	2,495,247,583	0.16	1.03	1.03	1.00	78.19
2002	1,329	1,383	1,383	1,376	0	8,078,059	2,513,798,947	0.16	1.04	1.04	1.00	0.00
2003	1,897	1,957	1,957	1,945	0	8,027,688	2,499,758,737	0.24	1.03	1.03	1.00	0.00
2004	7,080	7,323	7,323	7,288	8	19,352,107	4,289,447,653	0.37	1.03	1.03	1.00	109.77
2005	9,296	9,807	9,807	9,764	12	21,327,339	6,154,729,780	0.44	1.05	1.05	1.00	122.90
2006	8,784	9,261	9,261	9,250	12	22,753,027	6,435,268,022	0.39	1.05	1.05	1.00	129.73
2007	9,738	10,314	10,314	10,303	4	25,509,516	6,867,234,302	0.38	1.06	1.06	1.00	38.82
2008	18,145	19,309	19,309	19,282	6	46,733,690	10,628,047,234	0.39	1.06	1.06	1.00	31.12
2009	27,057	28,776	28,776	28,718	14	47,693,852	13,678,802,495	0.57	1.06	1.06	1.00	48.75
2010	27,199	28,658	28,658	28,597	14	46,118,546	13,289,702,101	0.59	1.05	1.05	1.00	48.96
2011	22,938	24,116	24,116	24,071	18	44,560,376	12,803,384,123	0.51	1.05	1.05	1.00	74.78
2012	5,198	5,465	5,465	5,460	3	24,728,543	3,408,328,440	0.21	1.05	1.05	1.00	54.95

Table 4. Summary of Incident IV Iron Exposure and Epinephrine 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 Epinephrine 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	7,429,879	1,261,163,697	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	2,520	1	8,013,982	2,495,247,583	0.16	1.03	1.03	1.00	39.68
2002	1,329	1,383	1,383	2,705	0	8,078,059	2,513,798,947	0.16	1.04	1.04	1.00	0.00
2003	1,897	1,957	1,957	3,841	0	8,027,688	2,499,758,737	0.24	1.03	1.03	1.00	0.00
2004	7,080	7,323	7,323	14,358	8	19,352,107	4,289,447,653	0.37	1.03	1.03	1.00	55.72
2005	9,296	9,807	9,807	19,041	12	21,327,339	6,154,729,780	0.44	1.05	1.05	1.00	63.02
2006	8,784	9,261	9,261	18,015	13	22,753,027	6,435,268,022	0.39	1.05	1.05	1.00	72.16
2007	9,738	10,314	10,314	20,029	4	25,509,516	6,867,234,302	0.38	1.06	1.06	1.00	19.97
2008	18,145	19,309	19,309	37,410	6	46,733,690	10,628,047,234	0.39	1.06	1.06	1.00	16.04
2009	27,057	28,776	28,776	55,741	15	47,693,852	13,678,802,495	0.57	1.06	1.06	1.00	26.91
2010	27,199	28,658	28,658	55,770	15	46,118,546	13,289,702,101	0.59	1.05	1.05	1.00	26.90
2011	22,938	24,116	24,116	46,980	21	44,560,376	12,803,384,123	0.51	1.05	1.05	1.00	44.70
2012	5,198	5,465	5,465	10,649	3	24,728,543	3,408,328,440	0.21	1.05	1.05	1.00	28.17
Within two days of exposure												
2000	484	502	502	1,456	0	7,429,879	1,261,163,697	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	3,717	1	8,013,982	2,495,247,583	0.16	1.03	1.03	1.00	26.90
2002	1,329	1,383	1,383	4,001	0	8,078,059	2,513,798,947	0.16	1.04	1.04	1.00	0.00
2003	1,897	1,957	1,957	5,705	0	8,027,688	2,499,758,737	0.24	1.03	1.03	1.00	0.00
2004	7,080	7,323	7,323	21,244	8	19,352,107	4,289,447,653	0.37	1.03	1.03	1.00	37.66
2005	9,296	9,807	9,807	27,874	12	21,327,339	6,154,729,780	0.44	1.05	1.05	1.00	43.05
2006	8,784	9,261	9,261	26,304	13	22,753,027	6,435,268,022	0.39	1.05	1.05	1.00	49.42
2007	9,738	10,314	10,314	29,074	4	25,509,516	6,867,234,302	0.38	1.06	1.06	1.00	13.76
2008	18,145	19,309	19,309	54,299	6	46,733,690	10,628,047,234	0.39	1.06	1.06	1.00	11.05
2009	27,057	28,776	28,776	80,896	16	47,693,852	13,678,802,495	0.57	1.06	1.06	1.00	19.78
2010	27,199	28,658	28,658	81,209	16	46,118,546	13,289,702,101	0.59	1.05	1.05	1.00	19.70
2011	22,938	24,116	24,116	68,619	21	44,560,376	12,803,384,123	0.51	1.05	1.05	1.00	30.60
2012	5,198	5,465	5,465	15,494	3	24,728,543	3,408,328,440	0.21	1.05	1.05	1.00	19.36

Table 4. Summary of Incident IV Iron Exposure and Epinephrine 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 Epinephrine 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	7,429,879	1,261,163,697	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	9,375	1	8,013,982	2,495,247,583	0.16	1.03	1.03	1.00	10.67
2002	1,329	1,383	1,383	10,096	0	8,078,059	2,513,798,947	0.16	1.04	1.04	1.00	0.00
2003	1,897	1,957	1,957	14,521	0	8,027,688	2,499,758,737	0.24	1.03	1.03	1.00	0.00
2004	7,080	7,323	7,323	53,524	8	19,352,107	4,289,447,653	0.37	1.03	1.03	1.00	14.95
2005	9,296	9,807	9,807	67,675	12	21,327,339	6,154,729,780	0.44	1.05	1.05	1.00	17.73
2006	8,784	9,261	9,261	62,957	14	22,753,027	6,435,268,022	0.39	1.05	1.05	1.00	22.24
2007	9,738	10,314	10,314	68,030	4	25,509,516	6,867,234,302	0.38	1.06	1.06	1.00	5.88
2008	18,145	19,309	19,309	126,263	6	46,733,690	10,628,047,234	0.39	1.06	1.06	1.00	4.75
2009	27,057	28,776	28,776	188,101	20	47,693,852	13,678,802,495	0.57	1.06	1.06	1.00	10.63
2010	27,199	28,658	28,658	188,732	18	46,118,546	13,289,702,101	0.59	1.05	1.05	1.00	9.54
2011	22,938	24,116	24,116	160,251	25	44,560,376	12,803,384,123	0.51	1.05	1.05	1.00	15.60
2012	5,198	5,465	5,465	35,722	3	24,728,543	3,408,328,440	0.21	1.05	1.05	1.00	8.40
Within two days of exposure												
2000	484	502	502	6,304	0	7,429,879	1,261,163,697	0.07	1.04	1.04	1.00	0.00
2001	1,243	1,284	1,284	16,561	1	8,013,982	2,495,247,583	0.16	1.03	1.03	1.00	6.04
2002	1,329	1,383	1,383	17,611	0	8,078,059	2,513,798,947	0.16	1.04	1.04	1.00	0.00
2003	1,897	1,957	1,957	25,373	0	8,027,688	2,499,758,737	0.24	1.03	1.03	1.00	0.00
2004	7,080	7,323	7,323	92,287	9	19,352,107	4,289,447,653	0.37	1.03	1.03	1.00	9.75
2005	9,296	9,807	9,807	111,093	13	21,327,339	6,154,729,780	0.44	1.05	1.05	1.00	11.70
2006	8,784	9,261	9,261	99,811	14	22,753,027	6,435,268,022	0.39	1.05	1.05	1.00	14.03
2007	9,738	10,314	10,314	105,587	4	25,509,516	6,867,234,302	0.38	1.06	1.06	1.00	3.79
2008	18,145	19,309	19,309	193,940	9	46,733,690	10,628,047,234	0.39	1.06	1.06	1.00	4.64
2009	27,057	28,776	28,776	290,470	23	47,693,852	13,678,802,495	0.57	1.06	1.06	1.00	7.92
2010	27,199	28,658	28,658	285,338	19	46,118,546	13,289,702,101	0.59	1.05	1.05	1.00	6.66
2011	22,938	24,116	24,116	241,604	28	44,560,376	12,803,384,123	0.51	1.05	1.05	1.00	11.59
2012	5,198	5,465	5,465	53,497	3	24,728,543	3,408,328,440	0.21	1.05	1.05	1.00	5.61

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, 4th 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	E1634
E1510	G0312	G0322	A4657	A4709	A4726	A4766	A4913	E1560	E1635
E1590	G0313	G0323	A4670	A4712	A4728	A4770	A4918	E1570	E1636
E1592	G0314	G0324	A4671	A4714	A4730	A4771	A4928	E1575	E1637
E1594	G0315	G0325	A4672	A4719	A4736	A4773	A4929	E1580	E1638
E1630	G0316	G0326	A4673	A4720	A4737	A4774	C1881	E1600	E1639
E1632	G0317	G0327	A4674	A4721	A4740	A4802	E1500	E1610	E1699
G0308	G0318	S9335	A4680	A4722	A4750	A4860	E1520	E1615	J0635
G0309	G0319	S9339	A4706	A4723	A4755	A4870	E1530	E1620	J0636
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 epinephrine procedures 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	Exposure Episode Gap	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	Incident Care Setting	Washout (days)	Washout Type	Principal Dx	Blackout Period
1	All IV Iron	All IV Iron	183	Single	0	0	0	0	None	N/A	N/A	N/A	N/A	Epinephrine	Epinephrine	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	Epinephrine	Epinephrine	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	Epinephrine	Epinephrine	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	Epinephrine	Epinephrine	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	Epinephrine	Epinephrine	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	Epinephrine	Epinephrine	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	Epinephrine	Epinephrine	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	Epinephrine	Epinephrine	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	Epinephrine	Epinephrine	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	Epinephrine	Epinephrine	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