Modular Program Report

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	
Request Description	The FDA requested execution of Modular Program #6 (MP6), version 6.0, to investigate prevalent use of several drug products and subsequent new diagnoses of hemolysis events (see Appendix B for hemolysis codes) among patients with a pre-existing condition of idiopathic thrombocytopenic purpura (ITP - see Appendix A for inclusion/exclusion codes) within 3, 14, and 21 days of index drug dispensing. The query was run against the Mini-Sentinel Distributed Database (MSDD) for the time period of January 1, 2006 through December 31, 2012. This request was distributed on October 23, 2013 to 18 Mini-Sentinel Data Partners. Results provide counts of prevalent users, lookup periods, total lookup period duration (days), number of users with a new event, eligible members, and member-years.
Request ID	msy5_mpr04_v1, Report 1 of 1
Specifications	Program parameter inputs and scenarios
Glossary	List of terms found in this report and their definitions
Table 1	Table of Summary of Prevalent Drug Use and Incident Hemolysis Events in the MSDD between January 1, 2006 and December 31, 2012, by Drug Product and Risk Window
Table 2	Table of Summary of Prevalent Drug Use and Incident Hemolysis Events in the MSDD between January 1, 2006 and December 31, 2012, by Drug Product, Risk Window, and Age Group
Table 3	Table of Summary of Prevalent Drug Use and Incident Hemolysis Events in the MSDD between January 1, 2006 and December 31, 2012, by Drug Product, Risk Window, and Sex
Table 4	Table of Summary of Prevalent Drug Use and Incident Hemolysis Events in the MSDD between January 1, 2006 and December 31, 2012, by Drug Product, Risk Window, and Year
Appendix A	List of Inclusion ITP Diagnoses and Exclusion Immunoglobulin/Anti-D Use Codes
Appendix B	List of Hemolysis Event Codes
Notes:	Please contact the Mini-Sentinel Operations Center (MSOC_Requests@harvardpilgrim.org) for questions and to provide comments/suggestions for future enhancements to this document.

Modular Program Specifications MSY5_MPR04_V1

Modular Program #6 (MP6), version 6.0, was used to investigate use of several products (see Appendix A) and subsequent diagnosis of hemolysis (see Appendix B) among patients with a pre-existing diagnosis of idiopathic thrombocytopenic purpura (ITP). Users with prior or concomitant use of intravenous immunoglobulin (IVIg) or Anti-D were excluded from the analysis (Anti-D exposure scenario users were excluded just for prior or concomitant use of IVIg). The query period was from January 1, 2006 to December 31, 2012, and the enrollment gap was set at 45 days. Age groups were split as follows: 0-17, 18-44, 45-64, and 65+ years. The program considered exposure, inclusion/exclusion criteria, and outcome events in the outpatient, emergency department, and inpatient care setting only. In total, 12 unique scenarios were examined in this request with differing exposures of interest, lookup period duration, and exclusion criteria. See below for a description of each of these scenarios.

Coverage Requirement	Drug and Medical Coverage
Query Period	January 1, 2006 to December 31, 2012
Enrollment Gap	45 Days
Enrollment Days	90
Age Stratifications	0-17, 18 - 44, 45-64, 65+
Minimum Lookup Period Duration	0 Days

	Exposure Criteria (Event file in MP6)						Exclusion/Inclusion Criteria						Outcome (Post-event treatment file in MP6)					
Scenario	**Incident exposure**	**Incident w/ respect to:**	**Incidence Type**	**Washout Period (days)**	**Lookup Period Duration**	**Exposure Care Setting**	**Condition**	**Exclude/ Include**	**Lookback Period Start**	**Lookback Period End**	**Care Setting**	**Principal Dx**	**Event/ Outcome**	**Incident w/ respect to:**	**Incidence Type**	**Washout Period (days)**	**Care Setting**	**Principal Dx**
1	Anti-D	Anti-D	Multiple	0	3	IP, ED, OA, AV	IVIg	Exclude	-30	2	IP, ED, OA, AV	Any	Hemolysis	Hemolysis	Multiple	90	IP, ED, OA, AV	Any
							ITP	Include	-30	2	IP, ED, OA, AV	Any						
2	Anti-D	Anti-D	Multiple	0	14	IP, ED, OA, AV	IVIg	Exclude	-30	13	IP, ED, OA, AV	Any	Hemolysis	Hemolysis	Multiple	90	IP, ED, OA, AV	Any
							ITP	Include	-30	13	IP, ED, OA, AV	Any						
3	Anti-D	Anti-D	Multiple	0	21	IP, ED, OA, AV	IVIg	Exclude	-30	20	IP, ED, OA, AV	Any	Hemolysis	Hemolysis	Multiple	90	IP, ED, OA, AV	Any
							ITP	Include	-30	20	IP, ED, OA, AV	Any						
4	Dexamethasone	Dexamethasone	Multiple	0	3	IP, ED, OA, AV	IVIg or Anti-D	Exclude	-30	2	IP, ED, OA, AV	Any	Hemolysis	Hemolysis	Multiple	90	IP, ED, OA, AV	Any
							ITP	Include	-30	2	IP, ED, OA, AV	Any						
5	Dexamethasone	Dexamethasone	Multiple	0	14	IP, ED, OA, AV	IVIg or Anti-D	Exclude	-30	13	IP, ED, OA, AV	Any	Hemolysis	Hemolysis	Multiple	90	IP, ED, OA, AV	Any
							ITP	Include	-30	13	IP, ED, OA, AV	Any						
6	Dexamethasone	Dexamethasone	Multiple	0	21	IP, ED, OA, AV	IVIg or Anti-D	Exclude	-30	20	IP, ED, OA, AV	Any	Hemolysis	Hemolysis	Multiple	90	IP, ED, OA, AV	Any
							ITP	Include	-30	20	IP, ED, OA, AV	Any						
7	Prednisone	Prednisone	Multiple	0	3	IP, ED, OA, AV	IVIg or Anti-D	Exclude	-30	2	IP, ED, OA, AV	Any	Hemolysis	Hemolysis	Multiple	90	IP, ED, OA, AV	Any
							ITP	Include	-30	2	IP, ED, OA, AV	Any						

8	Prednisone	Prednisone	Multiple	0	14	IP, ED, OA, AV	IVIg or Anti-D	Exclude	-30	13	IP, ED, OA, AV	Any	Hemolysis	Hemolysis	Multiple	90	IP, ED, OA, AV	Any
							ITP	Include	-30	13	IP, ED, OA, AV	Any						
9	Prednisone	Prednisone	Multiple	0	21	IP, ED, OA, AV	IVIg or Anti-D	Exclude	-30	20	IP, ED, OA, AV	Any	Hemolysis	Hemolysis	Multiple	90	IP, ED, OA, AV	Any
							ITP	Include	-30	20	IP, ED, OA, AV	Any						
10	Romiplostim	Romiplostim	Multiple	0	3	IP, ED, OA, AV	IVIg or Anti-D	Exclude	-30	2	IP, ED, OA, AV	Any	Hemolysis	Hemolysis	Multiple	90	IP, ED, OA, AV	Any
							ITP	Include	-30	2	IP, ED, OA, AV	Any						
11	Romiplostim	Romiplostim	Multiple	0	14	IP, ED, OA, AV	IVIg or Anti-D	Exclude	-30	13	IP, ED, OA, AV	Any	Hemolysis	Hemolysis	Multiple	90	IP, ED, OA, AV	Any
							ITP	Include	-30	13	IP, ED, OA, AV	Any						
12	Romiplostim	Romiplostim	Multiple	0	21	IP, ED, OA, AV	IVIg or Anti-D	Exclude	-30	20	IP, ED, OA, AV	Any	Hemolysis	Hemolysis	Multiple	90	IP, ED, OA, AV	Any
							ITP	Include	-30	20	IP, ED, OA, AV	Any						

Glossary of Terms in Modular Program 6*

Care Setting - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA).

Eligible Members - Number of members eligible for an incident exposure/lookup period (defined by the exposure and event washout periods) with drug and medical coverage during the query period.

Enrollment Gap - number of days allowed between two consecutive enrollment periods without breaking a "continuously enrolled" sequence.

Incidence Type (drug/exposure)- *Minimum Incidence type* will consider the first exposure/lookup period in the query period as long as it is the first exposure/lookup period in the user's entire available history. *Single* and *Multiple Incidence types* will use the washout period to establish incidence; however, *Single* will only consider the first exposure/lookup period whereas *Multiple* will consider all qualifying exposures/lookup periods.

Incidence Type (event/outcome)- *Minimum Incidence 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 Incidence type* uses the washout period to establish incidence and considers all qualifying incident exposures/lookup periods.

Inclusion/Exclusion Indicator - indicates whether condition(s) of interest are used for inclusion or exclusion criteria. A value of 1 instructs the program that members must have the condition of interest (inclusion criteria); a value of 0 instructs the program that members must not have the condition of interest (exclusion criteria).

Lookback Period Start and End - range of days relative to index that the program looks for inclusion/exclusion conditions of interest. For example, if the Inclusion/Exclusion Indicator =1, Lookback Period Start = -183 and Lookback Period End = 0, the cohort will only include members with the condition of interest present in the 183 days prior to and including the index date (the index date is day 0).

Lookup Period - fixed period of time following an incident exposure that the MP6 program searches for events of interest.

Member-Days - sum of all days a member is eligible for an incident exposure/lookup period (i.e., days that the member meets all inclusion criteria such a incidence, pre-existing condition, and enrollment requirements).

Minimum Lookup Period Duration - minimum number of enrollment days required after an incident exposure/lookup period start. For example, if the minimum duration =10, a member must have 10 or more days of continuous enrollment in drug and medical benefit coverage following the exposure/lookup period start in order for the lookup period to be included in output metrics.

New Users - number of members with incident exposure/lookup period during the query 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 evaluates exposures of interest.

Time-to-Event (tte)- number of days between the start of an event lookup period (index date) and the first treatment episode/procedure/diagnosis claim.

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 exposure/lookup period.

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 exposure/lookup period.

*all terms may not be used in this report

Table 1. Summary of Prevalent Drug Use and Incident Hemolysis Events in the MSDD between January 1, 2006 and December 31, 2012, by Drug Product and Risk Window

	Users	Lookup Periods	Lookup Period Duration	Users with a New Event	Eligible Members	Member-Years	Users/ 1000 Eligible Members	% Users with a New Event
Anti-D								
3 day risk window	1,620	3,735	11,205	5	699,494	140,435	2.32	0.31
14 day risk window	1,668	3,617	50,638	22	701,553	172,329	2.38	1.32
21 day risk window	1,735	3,513	73,773	23	702,973	191,591	2.47	1.33
Dexamethasone								
3 day risk window	40,352	91,037	273,111	73	698,614	140,192	57.76	0.18
14 day risk window	47,378	89,837	1,257,718	182	700,144	169,034	67.67	0.38
21 day risk window	49,851	88,600	1,860,600	256	700,049	186,502	71.21	0.51
Prednisone								
3 day risk window	22,702	34,853	104,559	54	698,052	139,405	32.52	0.24
14 day risk window	25,709	39,124	547,736	168	700,288	170,468	36.71	0.65
21 day risk window	27,054	40,531	851,151	210	701,759	189,142	38.55	0.78
Romiplostim								
3 day risk window	901	19,937	59,811	6	699,445	141,644	1.29	0.67
14 day risk window	882	10,984	153,776	7	701,471	173,019	1.26	0.79
21 day risk window	866	7,906	166,026	6	702,868	192,184	1.23	0.69

Table 2. Summary of Prevalent Drug Use and Incident Hemolysis Events in the MSDD between January 1, 2006 and December 31, 2012, by Drug Product, Risk Window, and Age Group

	Users	Lookup Periods	Lookup Period Duration	Users with a New Event	Eligible Members	Member-Years	Users/ 1000 Eligible Members	% Users with a New Event
Anti-D								
3 day risk window								
0-17 years	264	497	1,491	1	39,924	7,690	6.61	0.38
18-44 years	717	1,424	4,272	1	149,029	26,438	4.81	0.14
45-64 years	395	1,271	3,813	1	247,962	48,968	1.59	0.25
65+ years	267	543	1,629	2	273,625	57,339	0.98	0.75
14 day risk window								
0-17 years	249	473	6,622	2	40,046	9,084	6.22	0.80
18-44 years	789	1,445	20,230	4	149,551	32,202	5.28	0.51
45-64 years	387	1,174	16,436	8	248,814	60,141	1.56	2.07
65+ years	266	525	7,350	8	274,715	70,902	0.97	3.01
21 day risk window								
0-17 years	246	451	9,471	2	40,123	9,968	6.13	0.81
18-44 years	870	1,449	30,429	3	149,871	35,697	5.80	0.34
45-64 years	382	1,113	23,373	10	249,388	66,899	1.53	2.62
65+ years	261	500	10,500	8	275,448	79,027	0.95	3.07
Dexamethasone								
3 day risk window								
0-17 years	1,647	2,696	8,088	2	39,890	7,700	41.29	0.12
18-44 years	5,541	10,620	31,860	7	148,945	26,729	37.20	0.13
45-64 years	18,280	41,960	125,880	37	247,553	48,703	73.84	0.20
65+ years	15,086	35,761	107,283	27	273,247	57,059	55.21	0.18
14 day risk window								
0-17 years	1,817	2,843	39,802	6	40,015	9,014	45.41	0.33
18-44 years	6,223	10,388	145,432	30	149,395	32,120	41.65	0.48
45-64 years	21,421	41,537	581,518	88	248,079	58,479	86.35	0.41
65+ years	18,148	35,069	490,966	58	274,178	69,421	66.19	0.32

Table 2. Summary of Prevalent Drug Use and Incident Hemolysis Events in the MSDD between January 1, 2006 and December 31, 2012, by Drug Product, Risk Window, and Age Group

	Users	Lookup Periods	Lookup Period Duration	Users with a New Event	Eligible Members	Member-Years	Users/ 1000 Eligible Members	% Users with a New Event
Dexamethasone (Continued)								
21 day risk window								
0-17 years	1,859	2,812	59,052	8	40,082	9,848	46.38	0.43
18-44 years	6,511	10,216	214,536	34	149,570	35,401	43.53	0.52
45-64 years	22,481	40,534	851,214	118	247,815	64,401	90.72	0.52
65+ years	19,244	35,038	735,798	96	274,346	76,851	70.14	0.50
Prednisone								
3 day risk window								
0-17 years	1,148	1,727	5,181	4	39,889	7,710	28.78	0.35
18-44 years	3,758	5,664	16,992	12	148,911	26,560	25.24	0.32
45-64 years	7,936	12,041	36,123	22	247,466	48,580	32.07	0.28
65+ years	9,987	15,421	46,263	16	272,782	56,556	36.61	0.16
14 day risk window								
0-17 years	1,275	1,896	26,544	14	40,009	9,052	31.87	1.10
18-44 years	4,081	6,015	84,210	37	149,431	32,204	27.31	0.91
45-64 years	9,013	13,601	190,414	66	248,405	59,468	36.28	0.73
65+ years	11,478	17,612	246,568	51	273,966	69,745	41.90	0.44
21 day risk window								
0-17 years	1,307	1,904	39,984	16	40,081	9,908	32.61	1.22
18-44 years	4,216	6,108	128,268	42	149,748	35,626	28.15	1.00
45-64 years	9,483	14,109	296,289	79	249,013	66,013	38.08	0.83
65+ years	12,202	18,410	386,610	73	274,725	77,595	44.42	0.60

Table 2. Summary of Prevalent Drug Use and Incident Hemolysis Events in the MSDD between January 1, 2006 and December 31, 2012, by Drug Product, Risk Window, and Age Group

	Users	Lookup Periods	Lookup Period Duration	Users with a New Event	Eligible Members	Member-Years	Users/ 1000 Eligible Members	% Users with a New Event
Romiplostim								
3 day risk window								
0-17 years	18	325	975	0	39,914	7,799	0.45	0.00
18-44 years	179	3,374	10,122	0	149,003	26,890	1.20	0.00
45-64 years	370	8,711	26,133	4	247,952	49,369	1.49	1.08
65+ years	350	7,527	22,581	2	273,619	57,586	1.28	0.57
14 day risk window								
0-17 years	17	178	2,492	0	40,030	9,162	0.42	0.00
18-44 years	174	1,811	25,354	0	149,510	32,542	1.16	0.00
45-64 years	365	4,771	66,794	5	248,792	60,335	1.47	1.37
65+ years	342	4,224	59,136	2	274,706	70,980	1.24	0.58
21 day risk window								
0-17 years	17	133	2,793	0	40,106	10,042	0.42	0.00
18-44 years	167	1,282	26,922	0	149,813	36,017	1.11	0.00
45-64 years	359	3,443	72,303	3	249,362	67,039	1.44	0.84
65+ years	339	3,048	64,008	3	275,434	79,086	1.23	0.88

Table 3. Summary of Prevalent Drug Use and Incident Hemolysis Events in the MSDD between January 1, 2006 and December 31, 2012, by Drug Product, Risk Window, and Sex

	Users	Lookup Periods	Lookup Period Duration	Users with a New Event	Eligible Members	Member-Years	Users/ 1000 Eligible Members	% Users with a New Event
Anti-D								
3 day risk window								
Female	1,058	2,335	7,005	1	333,184	67,003	3.18	0.09
Male	562	1,400	4,200	4	366,287	73,429	1.53	0.71
Unknown	0	0	0	0	23	3	0.00	---
14 day risk window								
Female	1,123	2,313	32,382	7	334,180	81,820	3.36	0.62
Male	545	1,304	18,256	15	367,350	90,505	1.48	2.75
Unknown	0	0	0	0	23	4	0.00	---
21 day risk window								
Female	1,203	2,307	48,447	8	334,828	90,760	3.59	0.67
Male	532	1,206	25,326	15	368,122	100,826	1.45	2.82
Unknown	0	0	0	0	23	5	0.00	---
Dexamethasone								
3 day risk window								
Female	20,213	45,032	135,096	38	332,775	67,122	60.74	0.19
Male	20,138	46,004	138,012	35	365,816	73,067	55.05	0.17
Unknown	1	1	3	0	23	3	43.48	0.00
14 day risk window								
Female	23,820	44,959	629,426	99	333,517	80,354	71.42	0.42
Male	23,557	44,877	628,278	83	366,604	88,676	64.26	0.35
Unknown	1	1	14	0	23	4	43.48	0.00
21 day risk window								
Female	25,054	44,502	934,542	137	333,350	88,375	75.16	0.55
Male	24,796	44,097	926,037	119	366,676	98,122	67.62	0.48
Unknown	1	1	21	0	23	5	43.48	0.00

Table 3. Summary of Prevalent Drug Use and Incident Hemolysis Events in the MSDD between January 1, 2006 and December 31, 2012, by Drug Product, Risk Window, and Sex

	Users	Lookup Periods	Lookup Period Duration	Users with a New Event	Eligible Members	Member-Years	Users/ 1000 Eligible Members	% Users with a New Event
Prednisone								
3 day risk window								
Female	10,558	16,524	49,572	27	332,576	66,771	31.75	0.26
Male	12,143	18,328	54,984	27	365,453	72,632	33.23	0.22
Unknown	1	1	3	0	23	3	43.48	0.00
14 day risk window								
Female	11,934	18,449	258,286	85	333,623	81,178	35.77	0.71
Male	13,774	20,674	289,436	83	366,642	89,287	37.57	0.60
Unknown	1	1	14	0	23	4	43.48	0.00
21 day risk window								
Female	12,520	18,990	398,790	108	334,297	89,848	37.45	0.86
Male	14,532	21,539	452,319	102	367,439	99,289	39.55	0.70
Unknown	2	2	42	0	23	5	86.96	0.00
Romiplostim								
3 day risk window								
Female	437	11,108	33,324	2	333,149	67,800	1.31	0.46
Male	464	8,829	26,487	4	366,273	73,841	1.27	0.86
Unknown	0	0	0	0	23	3	0.00	---
14 day risk window								
Female	427	5,973	83,622	3	334,118	82,312	1.28	0.70
Male	455	5,011	70,154	4	367,330	90,704	1.24	0.88
Unknown	0	0	0	0	23	4	0.00	---
21 day risk window								
Female	420	4,267	89,607	2	334,754	91,204	1.25	0.48
Male	446	3,639	76,419	4	368,091	100,976	1.21	0.90
Unknown	0	0	0	0	23	5	0.00	---

Table 4. Summary of Prevalent Drug Use and Incident Hemolysis Events in the MSDD between January 1, 2006 and December 31, 2012, by Drug Product, Risk Window, and Year

	Users	Lookup Periods	Lookup Period Duration	Users with a New Event	Eligible Members	Member-Years	Users/ 1000 Eligible Members	% Users with a New Event
Anti-D								
3 day risk window								
2006	225	406	1,218	2	50,050	6,543	4.50	0.89
2007	245	447	1,341	2	75,714	9,952	3.24	0.82
2008	421	847	2,541	1	130,691	18,103	3.22	0.24
2009	450	946	2,838	0	164,232	23,710	2.74	0.00
2010	284	513	1,539	0	185,765	27,007	1.53	0.00
2011	203	322	966	0	189,103	27,259	1.07	0.00
2012	169	254	762	0	194,674	27,863	0.87	0.00
14 day risk window								
2006	226	399	5,586	3	51,297	8,081	4.41	1.33
2007	251	434	6,076	4	77,387	12,245	3.24	1.59
2008	418	799	11,186	9	133,492	22,210	3.13	2.15
2009	460	904	12,656	3	167,921	29,062	2.74	0.65
2010	294	500	7,000	2	189,515	33,119	1.55	0.68
2011	215	315	4,410	1	192,917	33,531	1.11	0.47
2012	187	266	3,724	0	197,186	34,081	0.95	0.00
21 day risk window								
2006	225	379	7,959	2	52,073	9,019	4.32	0.89
2007	257	424	8,904	5	78,440	13,643	3.28	1.95
2008	418	750	15,750	8	135,252	24,694	3.09	1.91
2009	471	870	18,270	4	170,165	32,318	2.77	0.85
2010	310	490	10,290	3	191,691	36,809	1.62	0.97
2011	237	324	6,804	1	195,139	37,317	1.21	0.42
2012	201	276	5,796	0	198,909	37,789	1.01	0.00

Table 4. Summary of Prevalent Drug Use and Incident Hemolysis Events in the MSDD between January 1, 2006 and December 31, 2012, by Drug Product, Risk Window, and Year

	Users	Lookup Periods	Lookup Period Duration	Users with a New Event	Eligible Members	Member-Years	Users/ 1000 Eligible Members	% Users with a New Event
Dexamethasone								
3 day risk window								
2006	2,033	4,100	12,300	3	49,974	6,518	40.68	0.15
2007	3,149	6,449	19,347	9	75,611	9,955	41.65	0.29
2008	6,360	13,093	39,279	8	130,467	18,072	48.75	0.13
2009	8,236	17,325	51,975	13	164,021	23,667	50.21	0.16
2010	8,693	17,668	53,004	17	185,498	26,978	46.86	0.20
2011	8,087	16,176	48,528	10	188,877	27,238	42.82	0.12
2012	8,287	16,226	48,678	13	194,428	27,764	42.62	0.16
14 day risk window								
2006	2,420	4,103	57,442	14	51,171	7,917	47.29	0.58
2007	3,805	6,415	89,810	18	77,198	12,019	49.29	0.47
2008	7,559	12,880	180,320	30	133,090	21,738	56.80	0.40
2009	9,656	16,986	237,804	34	167,500	28,441	57.65	0.35
2010	10,170	17,437	244,118	30	189,025	32,491	53.80	0.29
2011	9,416	15,928	222,992	29	192,468	32,967	48.92	0.31
2012	9,645	16,088	225,232	27	196,777	33,461	49.01	0.28
21 day risk window								
2006	2,571	4,048	85,008	19	51,780	8,775	49.65	0.74
2007	3,993	6,300	132,300	24	78,053	13,284	51.16	0.60
2008	7,923	12,648	265,608	44	134,453	23,968	58.93	0.56
2009	10,211	16,788	352,548	46	169,191	31,349	60.35	0.45
2010	10,702	17,208	361,368	43	190,778	35,833	56.10	0.40
2011	9,990	15,845	332,745	46	194,324	36,434	51.41	0.46
2012	10,132	15,763	331,023	35	198,109	36,858	51.14	0.35

Table 4. Summary of Prevalent Drug Use and Incident Hemolysis Events in the MSDD between January 1, 2006 and December 31, 2012, by Drug Product, Risk Window, and Year

	Users	Lookup Periods	Lookup Period Duration	Users with a New Event	Eligible Members	Member-Years	Users/ 1000 Eligible Members	% Users with a New Event
Prednisone								
3 day risk window								
2006	1,407	1,906	5,718	4	49,939	6,472	28.17	0.28
2007	1,810	2,459	7,377	7	75,589	9,923	23.95	0.39
2008	2,793	3,785	11,355	11	130,497	18,068	21.40	0.39
2009	3,386	4,793	14,379	3	164,020	23,660	20.64	0.09
2010	4,645	6,446	19,338	10	185,235	26,835	25.08	0.22
2011	6,037	8,308	24,924	13	188,363	26,900	32.05	0.22
2012	5,331	7,156	21,468	6	194,065	27,548	27.47	0.11
14 day risk window								
2006	1,593	2,111	29,554	14	51,188	7,973	31.12	0.88
2007	2,059	2,743	38,402	17	77,274	12,156	26.65	0.83
2008	3,173	4,155	58,170	32	133,316	22,081	23.80	1.01
2009	3,892	5,418	75,852	16	167,703	28,898	23.21	0.41
2010	5,279	7,253	101,542	33	189,011	32,787	27.93	0.63
2011	6,842	9,397	131,558	29	192,215	32,969	35.60	0.42
2012	5,992	8,047	112,658	28	196,622	33,604	30.47	0.47
21 day risk window								
2006	1,657	2,143	45,003	16	51,951	8,883	31.90	0.97
2007	2,182	2,805	58,905	22	78,310	13,507	27.86	1.01
2008	3,334	4,277	89,817	40	135,051	24,503	24.69	1.20
2009	4,083	5,556	116,676	21	169,922	32,068	24.03	0.51
2010	5,588	7,567	158,907	38	191,208	36,368	29.22	0.68
2011	7,207	9,795	205,695	39	194,424	36,618	37.07	0.54
2012	6,301	8,388	176,148	37	198,353	37,195	31.77	0.59

Table 4. Summary of Prevalent Drug Use and Incident Hemolysis Events in the MSDD between January 1, 2006 and December 31, 2012, by Drug Product, Risk Window, and Year

	Users	Lookup Periods	Lookup Period Duration	Users with a New Event	Eligible Members	Member-Years	Users/ 1000 Eligible Members	% Users with a New Event
Romiplostim								
3 day risk window								
2006	0	0	0	0	50,046	6,588	0.00	---
2007	0	0	0	0	75,712	10,065	0.00	---
2008	1	1	3	0	130,675	18,284	0.01	0.00
2009	60	527	1,581	1	164,230	23,947	0.37	1.67
2010	333	5,239	15,717	1	185,770	27,255	1.79	0.30
2011	430	6,814	20,442	4	189,121	27,488	2.27	0.93
2012	470	7,356	22,068	0	194,665	28,018	2.41	0.00
14 day risk window								
2006	0	0	0	0	51,287	8,118	0.00	---
2007	0	0	0	0	77,382	12,340	0.00	---
2008	1	1	14	0	133,465	22,361	0.01	0.00
2009	60	291	4,074	1	167,910	29,263	0.36	1.67
2010	325	2,835	39,690	2	189,485	33,240	1.72	0.62
2011	420	3,720	52,080	4	192,887	33,606	2.18	0.95
2012	463	4,137	57,918	0	197,152	34,090	2.35	0.00
21 day risk window								
2006	0	0	0	0	52,055	9,054	0.00	---
2007	0	0	0	0	78,430	13,728	0.00	---
2008	1	1	21	0	135,226	24,839	0.01	0.00
2009	58	213	4,473	1	170,146	32,504	0.34	1.72
2010	318	2,022	42,462	2	191,649	36,913	1.66	0.63
2011	416	2,683	56,343	3	195,071	37,373	2.13	0.72
2012	455	2,987	62,727	0	198,850	37,773	2.29	0.00

Appendix A. Inclusion ITP Diagnoses and Exclusion Immunoglobulin/Anti-D Use

ITP Inclusion Diagnoses	Code	Code Type
Qualitative platelet defects	287.1	ICD-9 Diagnosis
Primary thrombocytopenia	287.3	ICD-9 Diagnosis
ITP	287.31	ICD-9 Diagnosis
Congenital and hereditary thrombocytopenic purpura	287.33	ICD-9 Diagnosis
Congenital and hereditary thrombocytopenic purpura	287.39	ICD-9 Diagnosis
Secondary thrombocytopenia	287.4	ICD-9 Diagnosis
Thrombocytopenia (unspecified)	287.5	ICD-9 Diagnosis

Exclusion Immunoglobulin Use	Code	Code Type
IVIg (Intravenous Immunoglobulin)		
Gammaplex	J1557, C9270	HCPCS
Privigen	J1459, Q4097	HCPCS
Gamunex	J1561, Q4092	HCPCS
Octagam	J1568, Q4087	HCPCS
Gammagard Liquid	J1569, Q4088	HCPCS
Flebogamma	J1572, Q4091	HCPCS
Lyophilized product IV	J1566, Q9941, Q9942	HCPCS
Non-lyophilized intramuscular route	90281, J1460, J1470, J1480, J1490, J1500, J1510, J1520, J1530, J1540, J1550, J1560, P9014	CPT and HCPCS
Non-lyophilized unspecified route	90399, 99.14	CPT and ICD-9 Procedure
Other IVIg, brand not specified	J1563, J1564, J1567, J1599, Q9943, Q9944, S9545, 90283	HCPCS
Anti-D		
Rh-immunoglobulin (rhogam) ordered	G8809	HCPCS
Injection, rho d immune globulin, human, full dose, 300 micrograms (1500 i.u.)	J2790	HCPCS
Injection, rho(d) immune globulin (human), (rhophylac), intramuscular or intravenous, 100 iu	J2791	HCPCS
Injection, rho d immune globulin, intravenous, human, solvent detergent, 100 iu	J2792	HCPCS
Injection, rho(d) immune globulin (human), (rhophylac), intramuscular or intravenous, 100 iu	Q4089	HCPCS
Rhogam	00562-7805	NDC
MicRhogam	00562-7806	NDC
HyperRho	13533-0631	NDC
HyperRho	13533-0661	NDC
Rhophylac	44206-0300	NDC
WinRho	53270-3000	NDC
WinRho	53270-3100	NDC

Anti-D (Continued)		
WinRho	53270-3120	NDC
WinRho	53270-3300	NDC
WinRho	00944-2950	NDC
WinRho	00944-0267	NDC
WinRho	00944-2967	NDC
WinRho	60492-0023	NDC
WinRho	60492-0024	NDC
WinRho	60492-0021	NDC

Appendix B. Hemolysis Events

Description	Code	Code Type
Acquired hemolytic anemias	283*	ICD-9
ABO incompatibility reaction	999.6	ICD-9
Rh incompatibility reaction	999.7	ICD-9
Hemolytic transfusion reaction, incompatibility unspecified	999.83	ICD-9
Acute hemolytic transfusion reaction, incompatibility unspecified	999.84	ICD-9
Delayed hemolytic transfusion reaction, incompatibility unspecified	999.85	ICD-9