Disclaimer

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

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

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

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

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Request ID: cder_mpl1r_wp078_nsdp_v01

Request Description: The goal of this request was to examine utilization patterns of hydroxyurea among patients with sickle cell anemia (SCA) in the Sentinel Distributed Database (SDD). This is report 2 of 2. Report 1 contains estimates of the number patients with SCA, the number of SCA patients who were dispensed hydroxyurea, and the average number of hospitalizations and emergency department visits per person-year among those patients in the SDD.

Sentinel Routine Querying Module: Cohort Identification and Descriptive Analysis (CIDA) module, version 5.2.1

Data Source: Data from January 1, 2000 to September 30, 2015 from 17 Data Partners contributing to the SDD were included in this report. This request was distributed on February 28, 2018. See Appendix A for a list of dates of available data for each Data Partner.

Study Design: The request was designed to calculate summary statistics on days supplied per dispensing of hydroxyurea, on length of hydroxyurea treatment episodes, per patient and per episode, and on the number and duration of gaps between treatment episodes. Results were stratified by age group.

Exposure of Interest: The exposure of interest was hydroxyurea, which was defined using National Drug Codes (NDCs). Please see Appendix B for generic and brand drug names used in this request.

Cohort Eligibility Criteria: Patients included in the cohort were required to be continuously enrolled in plans with medical and drug coverage for at least 90 days prior to their dispensing date, during which gaps in coverage of up to 45 days were allowed. The following age groups were included in the cohort: 0-1, 2-5, 6-11, 12-17, 18-49, and 50+ years. Patients were included if they had a diagnosis of SCA anytime in their available history prior to their dispensing date. Please see Appendix C for a list of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes used to define SCA.

   Incidence Criteria: To assess incidence, patients were excluded if they had a dispensing of hydroxyurea in the 90 days preceding their first valid dispensing. All valid episodes during the query period were included, starting from the first incident dispensing; cohort re-entry was allowed.

Follow-Up Time: Exposure episode lengths were defined using outpatient pharmacy dispensing days supplied to create a sequence of continuous exposure. Exposure episodes were considered continuous if gaps in days supply were less than 30 days. Exposure episodes were included until the first occurrence of any of the following: 1) disenrollment; 2) death; or 3) the end of the query period.

Please see Appendix D for the specifications of parameters used in the analyses for this request.

Limitations: Algorithms used to define exposures and inclusion criteria are imperfect; thus, it is possible that there may be misclassification. Therefore, data should be interpreted with this limitation in mind.

Notes: Please contact the Sentinel Operations Center (info@sentinelsystem.org) for questions and to provide comments/suggestions for future enhancements to this document.

Amount Supplied - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing.

Blackout Period - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.

Care Setting - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA). For laboratory results, possible care settings include: Emergency Department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). The Care Setting, along with the Principal Diagnosis Indicator, forms the Care Setting/PDX parameter.

> **Ambulatory Visit (AV) -** includes visits at outpatient clinics, same-day surgeries, urgent care visits, and other same-day ambulatory hospital encounters, but excludes emergency department encounters.

> **Emergency Department (ED) -** includes ED encounters that become inpatient stays (in which case inpatient stays would be a separate encounter). Excludes urgent care visits.

> **Inpatient Hospital Stay (IP) -** includes all inpatient stays, same-day hospital discharges, hospital transfers, and acute hospital care where the discharge is after the admission date.

> **Non-Acute Institutional Stay (IS) -** includes hospice, skilled nursing facility (SNF), rehab center, nursing home, residential, overnight non-hospital dialysis and other non-hospital stays.

> **Other Ambulatory Visit (OA) -** includes other non overnight AV encounters such as hospice visits, home health visits, skilled nursing facility visits, other non-hospital visits, as well as telemedicine, telephone and email consultations.

Cohort Definition (drug/exposure) - indicates how the cohort will be defined: 01: Cohort includes only the first valid treatment episode during the query period; 02: Cohort includes all valid treatment episodes during the query period; 03: Cohort includes all valid treatment episodes during the query period until an event occurs.

Days Supplied - number of days supplied for all dispensings in qualifying treatment episodes.

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

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

Episodes - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.

Episode Gap - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.

Event Deduplication - specifies how events are counted by the MP algorithm: 0: Counts all occurrences of an HOI during an exposure episode; 1: de-duplicates occurrences of the same HOI code and code type on the same day; 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).

Exposure Episode Length - number of days after exposure initiation that is considered "exposed time."

Exposure Extension Period - number of days post treatment period in which the outcomes/events are counted for a treatment episode. Extensions days are added after any episode gaps have been bridged.

Lookback Period - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

Maximum Episode Duration - truncates exposure episodes after a requester-specified number of exposed days. Applied after any gaps are bridged and extension days added to the length of the exposure episode.

Member-Years - sum of all days of enrollment with medical and drug coverage in the query period preceded by an exposure washout period all divided by 365.25.

Minimum Days Supplied - specifies a minimum number of days in length of the days supplied for the episode to be considered.

Minimum Episode Duration - specifies a minimum number of days in length of the episode for it to be considered. Applied after any gaps are bridged and extension days added to the length of the exposure episode.

Monitoring Period - used to define time periods of interest for both sequential analysis and simple cohort characterization requests.

Principal Diagnosis (PDX) - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.

Query Period - period in which the modular program looks for exposures and outcomes of interest.

Treatment Episode Truncation Indicator - indicates whether the exposure episode will be truncated at the occurrence of a requester-specified code.

Washout Period (drug/exposure) - number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.

Washout Period (event/outcome) - number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.

Years at Risk - number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

*all terms may not be used in this report

Table 1a. Distribution of Days Supplied per Dispensing of Hydroxyurea in the Sentinel Distributed Database (SDD) between January 1, 2000 and September 30, 2015, by Age Group

	Age Group										
	0-1 years		2-5 years		6-11 years		12-17 years		18-49 years		50+ years	
Days Supplied	Number of Dispensings	Percent	Number of Dispensings	Percent	Number of Dispensings	Percent	Number of Dispensings	Percent	Number of Dispensings	Percent	Number of Dispensings	Percent
Total Dispensings	1,067	100	4,818	100	10,363	100	8,577	100	57,849	100	9,481	100
1-30 days	1,002	93.9	4,394	91.2	8,778	84.7	7,507	87.5	52,868	91.4	8,020	84.6
31-60 days	39	3.7	329	6.8	1,201	11.6	763	8.9	2,363	4.1	527	5.6
61-90 days	*****	*****	46	1	254	2.5	229	2.7	2,333	4	848	8.9
91+ days	*****	*****	49	1	130	1.3	78	0.9	285	0.5	86	0.9

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

Table 1b. Descriptive Statistics of Days Supplied per Dispensing of Hydroxyurea in the Sentinel Distributed Database (SDD) between January 1, 2000 and September 30, 2015, by Age Group

	Age Group					
	0-1 years	2-5 years	6-11 years	12-17 years	18-49 years	50+ years
Distribution	**Days**	**Days**	**Days**	**Days**	**Days**	**Days**
Min	0	0	0	0	0	0
1st	5	6	5	5	5	5
3rd	12	13	10	10	14	14
5th	16	14	15	15	18	17
10th	28	18	24	26	30	30
20th	30	30	28	30	30	30
25th	30	30	30	30	30	30
50th	30	30	30	30	30	30
Mean	31.4	30.7	33	32.4	32.3	36
Median	30	30	30	30	30	30
Mode	30	30	30	30	30	30
75th	30	30	30	30	30	30
80th	30	30	30	30	30	30
90th	30	30	56	40	30	63
95th	58	60	60	60	60	90
97th	60	60	75	90	90	90
99th	90	100	100	90	90	90
Max	121	500	251	220	180	180

Table 2a. Distribution of Total Exposure Episode Duration of Hydroxyurea per Episode in the Sentinel Distributed Database (SDD) between January 1, 2000 and September 30, 2015, by Age Group

	Age Group										
	0-1 years		2-5 years		6-11 years		12-17 years		18-49 years		50+ years	
Episode Duration	Number of Episodes	Percent	Number of Episodes	Percent	Number of Episodes	Percent	Number of Episodes	Percent	Number of Episodes	Percent	Number of Episodes	Percent
Total Episodes	157	100	821	100	2,048	100	2,545	100	25,587	100	2,813	100
1-30 days	*****	*****	29	3.5	49	2.4	61	2.4	1,280	5	194	6.9
31-60 days	*****	*****	*****	*****	48	2.3	70	2.8	1,100	4.3	133	4.7
61-89 days	*****	*****	*****	*****	33	1.6	49	1.9	451	1.8	63	2.2
90-179 days	14	8.9	53	6.5	123	6	208	8.2	3,814	14.9	332	11.8
180-364 days	13	8.3	94	11.4	197	9.6	405	15.9	6,449	25.2	688	24.5
365+ days	113	72	617	75.2	1,598	78	1,752	68.8	12,493	48.8	1,403	49.9

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

Table 2b. Descriptive Statistics of Total Exposure Episode Duration of Hydroxyurea per Episode in the Sentinel Distributed Database (SDD) between January 1, 2000 and September 30, 2015, by Age Group

	Age Group					
	0-1 years	**2-5 years**	**6-11 years**	**12-17 years**	**18-49 years**	**50+ years**
Distribution	**Days**	**Days**	**Days**	**Days**	**Days**	**Days**
Min	14	1	1	1	1	1
1st	16	20	16	21	29	15
3rd	21	30	39	32	30	30
5th	30	60	60	60	33	30
10th	63	111	129	106	75	60
20th	167	245	294	211	140	124
25th	216	311.5	369	264	175	172
50th	626	617	866	668	363	367
Mean	809.7	884.7	1130.3	919.4	497.4	516.4
Median	626	617	866	668	363	367
Mode	1284	457	1113	60	30	30
75th	1284	1311	1642	1264	670	757
80th	1628	1424	1931	1561	762	839
90th	1772	1830	2659	2164	1057	1166
95th	2026	2664	3194	2729	1341	1458
97th	2071	3061	3329	3271	1625	1600
99th	2927	3701	3721	3901	2441	1954
Max	2927	4232	4493	4083	4789	4917

Table 3a. Distribution of Total Exposure Episode Duration of Hydroxyurea per Patient in the Sentinel Distributed Database (SDD) between January 1, 2000 and September 30, 2015, by Age Group

	Age Group											
	0-1 years		2-5 years		6-11 years		12-17 years		18-49 years		50+ years	
Episode Duration	Number of Patients	Percent	Number of Patients	Percent	Number of Patients	Percent	Number of Patients	Percent	Number of Patients	Percent	Number of Patients	Percent
Total Patients	60	100	260	100	512	100	564	100	6,844	100	1,042	100
1-30 days	*****	*****	29	11.2	49	9.6	61	10.8	1,273	18.6	194	18.6
31-60 days	*****	*****	*****	*****	32	6.3	44	7.8	628	9.2	87	8.3
61-89 days	*****	*****	*****	*****	19	3.7	29	5.1	282	4.1	52	5
90-179 days	*****	*****	34	13.1	70	13.7	82	14.5	1,370	20	164	15.7
180-364 days	*****	*****	41	15.8	73	14.3	112	19.9	1,416	20.7	213	20.4
365+ days	32	53.3	136	52.3	269	52.5	236	41.8	1,875	27.4	332	31.9

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

Table 3b. Descriptive Statistics of Total Exposure Episode Duration of Hydroxyurea per Patient in the Sentinel Distributed Database (SDD) between January 1, 2000 and September 30, 2015, by Age Group

| | Age Group | | | | | |
| | 0-1 years | 2-5 years | 6-11 years | 12-17 years | 18-49 years | 50+ years |
Distribution	Days	Days	Days	Days	Days	Days
Min	14	1	1	1	1	1
1st	14	15	7	7	10	6
3rd	16	23	20	20	27	21
5th	21	30	30	30	30	30
10th	30	56	56	44	30	30
20th	66.5	113	119	90	60	60
25th	139	157	156.5	120	65	88
50th	422	420	462	328	204	253.5
Mean	628.1	662.6	794.9	615.8	370.5	423.6
Median	422	420	462	328	204	253.5
Mode	30	30	30	30	30	30
75th	789	836	1144.5	877	505	599
80th	1028	1012	1416	991	617	719
90th	1772	1693	2160	1626	944	1065
95th	2026	2301	2659	2164	1277	1428
97th	2071	2664	2949	2545	1507	1561
99th	2927	3480	3548	3436	1878	1962
Max	2927	4232	4493	4083	4789	4917

Table 4a. Frequency of Gaps[1] between Treatment Episodes of Hydroxyurea in the Sentinel Distributed Database (SDD) between January 1, 2000 and September 30, 2015, by Age Group

Gap Number	Age Group											
	0-1 years		2-5 years		6-11 years		12-17 years		18-49 years		50+ years	
	Number[2]	%	Number	%	Number	%	Number	%	Number	%	Number	%
Total Episodes	157	100.0	821	100.0	2,048	100.0	2,545	100.0	25,587	100.0	2,813	100.0
1	33	21.0	139	16.9	316	15.4	398	15.6	4,698	18.4	565	20.1
2	18	11.5	88	10.7	227	11.1	303	11.9	3,520	13.8	372	13.2
3	14	8.9	67	8.2	173	8.4	235	9.2	2,695	10.5	271	9.6
4	*****	*****	53	6.5	138	6.7	191	7.5	2,059	8.0	183	6.5
5	*****	*****	45	5.5	111	5.4	154	6.1	1,562	6.1	124	4.4
6	*****	*****	41	5.0	90	4.4	119	4.7	1,160	4.5	77	2.7
7	*****	*****	32	3.9	77	3.8	104	4.1	847	3.3	56	2.0
8	*****	*****	25	3.0	67	3.3	89	3.5	612	2.4	37	1.3
9	*****	*****	23	2.8	52	2.5	76	3.0	460	1.8	28	1.0
10	*****	*****	17	2.1	48	2.3	62	2.4	323	1.3	18	0.6
11	0	0.0	13	1.6	43	2.1	55	2.2	224	0.9	14	0.5
12	0	0.0	*****	*****	39	1.9	46	1.8	153	0.6	*****	*****
13	0	0.0	*****	*****	33	1.6	40	1.6	107	0.4	*****	*****
14	0	0.0	*****	*****	26	1.3	30	1.2	78	0.3	*****	*****
15	0	0.0	*****	*****	19	0.9	22	0.9	62	0.2	*****	*****
16	0	0.0	*****	*****	18	0.9	15	0.6	47	0.2	*****	*****
17	0	0.0	0	0.0	15	0.7	13	0.5	37	0.1	0	0.0
18	0	0.0	0	0.0	12	0.6	*****	*****	27	0.1	0	0.0
19	0	0.0	0	0.0	*****	*****	*****	*****	18	0.1	0	0.0
20	0	0.0	0	0.0	*****	*****	*****	*****	13	0.1	0	0.0
21	0	0.0	0	0.0	*****	*****	*****	*****	11	0.0	0	0.0
22	0	0.0	0	0.0	*****	*****	*****	*****	*****	*****	0	0.0
23	0	0.0	0	0.0	*****	*****	*****	*****	*****	*****	0	0.0
24	0	0.0	0	0.0	*****	*****	*****	*****	*****	*****	0	0.0
25	0	0.0	0	0.0	0	0.0	0	0.0	*****	*****	0	0.0
26	0	0.0	0	0.0	0	0.0	0	0.0	*****	*****	0	0.0
27	0	0.0	0	0.0	0	0.0	0	0.0	*****	*****	0	0.0
28	0	0.0	0	0.0	0	0.0	0	0.0	*****	*****	0	0.0
29	0	0.0	0	0.0	0	0.0	0	0.0	*****	*****	0	0.0
30	0	0.0	0	0.0	0	0.0	0	0.0	*****	*****	0	0.0
31	0	0.0	0	0.0	0	0.0	0	0.0	*****	*****	0	0.0
32	0	0.0	0	0.0	0	0.0	0	0.0	*****	*****	0	0.0
33	0	0.0	0	0.0	0	0.0	0	0.0	*****	*****	0	0.0
Gap from last episode until censoring	60	38.2	260	31.7	512	25.0	564	22.2	6,844	26.7	1,042	37.0

[1]Gap refers to any period of time between two exposure episodes that is longer than the allowable duration of 30 days. Episodes with gaps in days supplied under 30 days are bridged together, and a gap is not considered to have occurred.

[2]"Number" represents the number of episodes with the specified number of gaps (e.g., when gap number = 2,"Number" is the number of episodes that had 2 treatment gaps)
*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.*

Table 4b. Descriptive Statistics of the Duration (in Days) of Gaps[1] between Treatment Episodes of Hydroxyurea in the Sentinel Distributed Database (SDD) between January 1, 2000 and September 30, 2015, by Age Group

| | Age Group | | | | | | | | | | | | | | | | | |
| | 0-1 years | | | 2-5 years | | | 6-11 years | | | 12-17 years | | | 18-49 years | | | 50+ years | | |
Gap Number	Median	Mean	Standard Deviation	Median	Mean	Standard Deviation	Median	Mean	Standard Deviation	Median	Mean	Standard Deviation	Median	Mean	Standard Deviation	Median	Mean	Standard Deviation
Total Episodes	43	126.5	282.8	47	146.9	387.0	55	136.6	317.4	69	167.3	334.4	84	191.6	313.5	60	151.2	264.4
1	81	166.0	199.8	65	239.1	516.4	62	175.9	351.2	78	174.1	269.2	99	208.0	305.4	71	139.9	195.5
2	58	123.9	173.5	60	118.1	208.8	56	126.4	242.8	68	135.6	196.2	93	178.0	236.8	72	124.0	153.9
3	46	111.5	152.0	74	112.6	132.7	59	100.7	196.9	69	132.2	190.1	82	152.5	200.8	62	98.2	111.2
4	57	133.6	206.9	50	117.5	200.4	61	85.8	84.3	73	119.4	192.0	82	146.2	195.2	61	103.9	125.0
5	79	127.8	109.5	56	102.8	114.4	55	96.8	95.1	81	169.6	300.1	79	130.6	159.7	60	98.0	115.0
6	37	57.0	37.6	58	97.8	106.0	60	90.5	94.6	65	131.2	189.3	79	128.9	155.3	62	91.4	84.9
7	62	103.8	111.7	61	66.8	34.7	64	99.3	96.0	70	122.9	141.8	76	119.6	165.8	70	97.7	87.2
8	42	48.8	17.8	45	77.4	106.0	78	104.7	86.1	73	140.0	236.6	70	104.0	108.9	69	121.8	171.9
9	*****	*****	*****	44	57.7	28.2	54	81.9	71.8	89	124.0	113.4	74	104.4	104.5	68	97.7	76.1
10	*****	*****	*****	42	52.6	20.9	70	109.1	107.0	71	111.7	115.8	69	99.5	98.9	54	65.2	29.8
11				48	171.1	387.8	61	100.7	100.3	82	161.9	236.3	65	122.8	176.7	56	75.9	49.0
12				43	55.6	37.6	74	109.3	97.9	101	174.8	241.7	72	116.0	191.1	43	54.6	23.5
13				46	55.5	25.6	84	121.5	91.8	79	110.7	93.5	64	143.3	204.8	40	59.7	41.3
14				39	40.8	10.8	80	125.0	138.9	66	132.8	136.9	57	97.1	108.2	60	64.2	36.7
15				79	78.5	21.9	126	126.5	69.5	77	158.1	228.7	61	89.7	89.3	47	61.0	37.9
16				*****	*****	*****	74	115.0	92.2	61	80.8	74.7	59	110.9	149.0	85	79.7	38.3
17							56	107.7	119.6	52	118.8	167.9	72	105.2	88.1			
18							59	89.4	57.8	50	82.5	67.6	72	112.3	126.5			
19							60	108.1	77.5	65	92.7	66.9	64	75.9	69.2			
20							48	138.6	238.0	43	55.2	26.5	73	139.6	218.7			
21							75	99.0	59.0	72	68.0	25.9	48	67.0	54.2			
22							73	72.2	25.7	199	198.5	225.6	73	94.5	72.4			
23							106	175.5	199.9	*****	*****	*****	101	165.6	127.0			
24							189	189.0	154.1	*****	*****	*****	49	56.8	18.4			
25													66	68.0	39.4			
26													72	115.0	106.2			
27													45	44.5	2.1			
28													*****	*****	*****			
29													*****	*****	*****			
30													*****	*****	*****			
31													*****	*****	*****			
32													*****	*****	*****			
33													*****	*****	*****			
Gap from last episode until censoring	0	123.2	406.8	0	173.5	531.6	0	188.2	517.1	25	255.2	576.2	81	277.1	464.0	31	209.9	379.3

[1]Gap refers to any period of time between two exposure episodes that is longer than the allowable duration of 30 days. Episodes with gaps in days supplied under 30 days are bridged together, and a gap is not considered to have occurred.

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

cder_mpl1r_wp078

DP ID	Start Date	End Date
DP01	1/1/2000	10/31/2014
DP02	6/1/2007	9/30/2015
DP03	1/1/2000	9/30/2015
DP04	1/1/2008	9/30/2015
DP05	1/1/2006	9/30/2015
DP06	1/1/2000	9/30/2015
DP07	1/1/2008	9/30/2015
DP08	1/1/2010	9/30/2015
DP09	1/1/2000	9/30/2015
DP10	1/1/2000	5/31/2015
DP11	1/1/2000	9/30/2015
DP12	1/1/2000	9/30/2015
DP13	1/1/2005	9/30/2015
DP14	1/1/2004	9/30/2015
DP15	1/1/2000	9/30/2015
DP16	1/1/2000	9/30/2015
DP17	1/1/2012	9/30/2015

Appendix B. List of Generic and Brand Drug Names Used to Define Exposures in this Request

Generic Name	Brand Name
HYDROXYUREA	Droxia
HYDROXYUREA	Hydrea
HYDROXYUREA	hydroxyurea
HYDROXYUREA	hydroxyurea (bulk)
HYDROXYUREA	Mylocel

Appendix C. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Diagnosis Codes Used to Define Inclusion Criteria in this Request

Code	Description	Code Type
282.6	Sickle-cell disease	ICD-9-CM
282.60	Sickle-cell disease, unspecified	ICD-9-CM
282.61	Hb-SS disease without crisis	ICD-9-CM
282.62	Hb-SS disease with crisis	ICD-9-CM
282.63	Sickle-cell/Hb-C disease without crisis	ICD-9-CM
282.64	Sickle-cell/Hb-C disease with crisis	ICD-9-CM
282.68	Other sickle-cell disease without crisis	ICD-9-CM
282.69	Other sickle-cell disease with crisis	ICD-9-CM

Appendix D. Specifications for Parameters for this Request

This request used the Cohort Identification and Descriptive Analysis (CIDA) module, version 5.2.1, to examine the use of hydroxyurea among patients with sickle cell anemia in the Sentinel Distributed Database (SDD).

Query Period: January 1, 2000 to September 30, 2015
Enrollment Requirement: 90 days
Enrollment Gap: 45 days
Coverage Requirement: Medical and Drug
Age Groups: 0-1, 2-5, 6-11, 12-17, 18-49, 50+ years
Results Stratified by: Age

	Exposure						Exposure		Pre-existing Conditions			
Scenario	Exposure	Incidence Criteria	Washout (Days)	Episode Gap (Days)	Intent to Treat (Days)	Cohort Definition	Censor due to Query End	Censor due to Evidence of Death	Condition	Inclusion or Exclusion	Caresetting	Lookback
1	Hydroxyurea	Hydroxyurea	90	30	N/A	Include all valid episodes during the query period	Yes	Yes	Sickle Cell Anemia	Include	Any	Any time prior to index date

International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes are provided by Optum360.
National Drug Codes (NDCs) checked against First Data Bank's "National Drug Data File (NDDF®) Plus".