

## 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

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

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## Overview for request: cder\_mpl1r\_wp195

**Request ID:** cder\_mpl1r\_wp195

**Request Description:** In this report, we evaluated utilization of hydroxyurea among individuals with sickle cell disease (SCD) in the Sentinel Distributed Database (SDD).

**Sentinel Routine Querying Module:** Cohort Identification and Descriptive Analysis (CIDA) tool, version 10.3.3.

**Data Source:** We distributed this request to 7 Sentinel Data Partners on July 27, 2021. The study period included data from January 1, 2000 through December 31, 2020. Please see Appendix A for a list of dates of available data for each Data Partner.

**Study Design:** We characterized hydroxyurea utilization among individuals with sickle cell disease (SCD). All qualifying dispensings for each member were included during the query period. Among this cohort, we assessed cumulative hydroxyurea episode duration, first hydroxyurea episode duration, all hydroxyurea episode durations, and gap length between episodes. Results were stratified by age group, race, year, and year group - age group. This is a Type 5 analysis as described in the Query Request Package (QRP) documentation.

**Exposure of Interest:** The exposure of interest, hydroxyurea, was defined using Healthcare Common Procedure Coding System (HCPCS) procedure codes, outpatient dispensing data and National Drug Codes (NDCs). Please refer to Appendix B for a list of generic and brand names of medical products and Appendix C for a list of HCPCS used to define the exposure.

**Cohort Eligibility Criteria:** We required members to be continuously enrolled in health plans with medical and drug coverage in the 183 days prior to their index date, during which gaps in coverage of up to 45 days were allowed. We defined the index date for each patient as the date of first hydroxyurea dispensing or administration. To ensure we only characterized patients with SCD, we required at least one diagnosis of SCD prior to each patient's index date. Patients with specific cancers which hydroxyurea may have been used to treat in the 183 days prior to the index date were excluded due to competing indications for hydroxyurea. Please see Appendix D for a list of International Classification of Diseases, Ninth and Tenth Revisions, Clinical Modification (ICD-9-CM and ICD-10-CM) diagnosis codes used to define inclusion and exclusion criteria in this request. We included patients of all ages and categorized into the following groups based on age at index date: 0-17 years, 18-49 years, and 50+ years. The first age group was further divided into groups of 0-5 years, 6-11 years, and 12-17 years; the final age group was further divided into groups of 50-59 years, and 60+ years. Using days supplied data from outpatient pharmacy dispensing, we created a sequence of continuous exposures known as exposure episodes. Exposure episodes were considered continuous if gaps between episodes based on days supplied were 30 days or shorter. Procedure codes for hydroxyurea were assigned a one-day supply. Consecutive dispensings of the same generic name that resulted in overlapping episodes were stockpiled up to 50% of the first dispensing's episode length based on its days supplied. All valid episodes during the query period were included, starting from the first dispensing. Exposure episodes were included until the earliest occurrence of any of the following: 1) disenrollment; 2) death; or 3) the end of the query period.

**Please see Appendices E, F, and G for the specifications of parameters used in this request.**

**Limitations:** Algorithms to define exposures, inclusion, and exclusion criteria are imperfect and may result in misclassification. Therefore, data should be interpreted with this limitation in mind.

**Notes:** Please contact the Sentinel Operations Center ([info@sentinelssystem.org](mailto:info@sentinelssystem.org)) for questions and to provide comments/suggestions for future enhancements to this document. For more information on Sentinel's routine querying modules, please refer to the documentation (<https://dev.sentinelssystem.org/projects/sentinel/repos/sentinel-routine-querying-tool-documentation/browse>).

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**Glossary of Terms for Analyses Using  
Cohort Identification and Descriptive Analysis (CIDA) Module\***

**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 (PDX), forms

**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.

**Charlson/Elixhauser Combined Comorbidity Score** - calculated based on comorbidities observed during a requester-defined window around the exposure episode start date (e.g., in the 183 days prior to index).

**Code Days** - the minimum number of times the diagnosis must be found during the evaluation period in order to fulfill the algorithm to identify the corresponding patient characteristic.

**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.

**Computed Start Marketing Date** - represents the first observed dispensing date among all valid users within a GROUP (scenario) within each Data Partner site.

**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"

**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 Modular Program (MP) algorithm: 0: Counts all occurrences of a health outcome of interest (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 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

**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.

**Switch Evaluation Step Value** - value used to differentiate evaluation step. Each switch pattern can support up to 2 evaluation steps (0 = switch pattern evaluation start; 1 = first evaluation; 2 = second evaluation).

**Switch Gap Inclusion Indicator** - indicator for whether gaps in treatment episodes that are included in a switch episode will be counted as part of the switch episode duration.

**Switch Pattern Cohort Inclusion Date** - indicates which date to use for inclusion into the switch pattern cohort of interest as well as optionally as the index date of the treatment episode initiating the switch pattern. Valid options are the product approval date, product marketing date, other requester defined date, or computed start marketing date.

**Switch Pattern Cohort Inclusion Strategy** - indicates how the switch pattern cohort inclusion date will be used: 01: used only as a switch cohort entry date. First treatment episode dispensing date is used as index for computing time to first switch; 02: used as switch cohort entry date and as initial switch step index date for computing time to first switch.

**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 Patients' Cumulative Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, Overall**

Exposure	Total Patients		Cumulative Hydroxyurea Exposure Episode Duration											
	Number	Percent	<3 Months		3 – <6 Months		6 – <12 Months		1 – <2 Years		2 – <5 Years		5+ Years	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Hydroxyurea	14,294	100.0	3,916	27.4	2,041	14.3	2,465	17.2	2,463	17.2	2,535	17.7	874	6.1

**Table 1b. Distribution of Patients' Cumulative Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, by Age Group**

Exposure	Total Patients		Cumulative Hydroxyurea Exposure Episode Duration											
	Number	Percent	<3 Months		3 – <6 Months		6 – <12 Months		1 – <2 Years		2 – <5 Years		5+ Years	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Hydroxyurea	<b>14,294</b>	<b>100.0</b>	<b>3,916</b>	<b>100.0</b>	<b>2,041</b>	<b>100.0</b>	<b>2,465</b>	<b>100.0</b>	<b>2,463</b>	<b>100.0</b>	<b>2,535</b>	<b>100.0</b>	<b>874</b>	<b>100.0</b>
0-17 Years	2,060	14.4	399	10.2	260	12.7	358	14.5	387	15.7	444	17.5	212	24.3
0-5 Years	417	2.9	81	2.1	45	2.2	68	2.8	88	3.6	88	3.5	47	5.4
6-11 Years	762	5.3	117	3.0	98	4.8	119	4.8	142	5.8	181	7.1	105	12.0
12-17 Years	881	6.2	201	5.1	117	5.7	171	6.9	157	6.4	175	6.9	60	6.9
18-49 Years	10,319	72.2	2,959	75.6	1,543	75.6	1,797	72.9	1,760	71.5	1,736	68.5	524	60.0
50+ Years	1,915	13.4	558	14.2	238	11.7	310	12.6	316	12.8	355	14.0	138	15.8
50-59 Years	1,225	8.6	335	8.6	158	7.7	193	7.8	204	8.3	229	9.0	106	12.1
60+ Years	690	4.8	223	5.7	80	3.9	117	4.7	112	4.5	126	5.0	32	3.7



**Table 1c. Distribution of Patients' Cumulative Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, by Race**

Exposure	Total Patients		Cumulative Hydroxyurea Exposure Episode Duration											
	Number	Percent	<3 Months		3 – <6 Months		6 – <12 Months		1 – <2 Years		2 – <5 Years		5+ Years	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Hydroxyurea	14,294	100.0	3916	100.0	2041	100.0	2465	100.0	2,463	100.0	2,535	100.0	874	100.0
Unknown	4,728	33.1	1,483	37.9	720	35.3	841	34.1	782	31.7	691	27.3	211	24.1
American Indian/Alaska Native	29	0.2	*****	*****	0	0.0	*****	*****	*****	*****	*****	*****	*****	*****
Asian	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
Black/African American	9,214	64.5	2,331	59.5	1,292	63.3	1,560	63.3	1,613	65.5	1,779	70.2	639	73.1
Native Hawaiian/Other Pacific Islander	*****	*****	*****	*****	0	0.0	0	0.0	*****	*****	*****	*****	*****	*****
White	292	2.0	86	2.2	*****	*****	*****	*****	54	2.2	50	2.0	*****	*****

\*\*\*\*\*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 1d. Distribution of Patients' Cumulative Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, by Year**

Exposure	Cumulative Hydroxyurea Exposure Episode Duration													
	Total Patients		<3 Months		3 – <6 Months		6 – <12 Months		1 – <2 Years		2 – <5 Years		5+ Years	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Hydroxyurea	<b>14,294</b>	<b>100.0</b>	<b>3,916</b>	<b>100.0</b>	<b>2,041</b>	<b>100.0</b>	<b>2,465</b>	<b>100.0</b>	<b>2,463</b>	<b>100.0</b>	<b>2,535</b>	<b>100.0</b>	<b>874</b>	<b>100.0</b>
2000	56	0.4	*****	*****	*****	*****	*****	*****	11	0.4	*****	*****	*****	*****
2001	73	0.5	*****	*****	*****	*****	*****	*****	*****	*****	16	0.6	22	2.5
2002	69	0.5	*****	*****	*****	*****	*****	*****	*****	*****	21	0.8	17	1.9
2003	76	0.5	14	0.4	*****	*****	*****	*****	11	0.4	12	0.5	20	2.3
2004	84	0.6	18	0.5	*****	*****	*****	*****	11	0.4	21	0.8	15	1.7
2005	59	0.4	13	0.3	11	0.5	*****	*****	*****	*****	*****	*****	*****	*****
2006	111	0.8	25	0.6	17	0.8	18	0.7	16	0.6	15	0.6	20	2.3
2007	156	1.1	37	0.9	15	0.7	26	1.1	21	0.9	31	1.2	26	3.0
2008	316	2.2	78	2.0	42	2.1	54	2.2	55	2.2	67	2.6	20	2.3
2009	398	2.8	105	2.7	63	3.1	66	2.7	55	2.2	66	2.6	43	4.9
2010	1,764	12.3	280	7.2	188	9.2	278	11.3	324	13.2	479	18.9	215	24.6
2011	1,640	11.5	332	8.5	177	8.7	270	11.0	317	12.9	354	14.0	190	21.7
2012	1,207	8.4	264	6.7	148	7.3	176	7.1	237	9.6	262	10.3	120	13.7
2013	1,188	8.3	281	7.2	154	7.5	207	8.4	210	8.5	258	10.2	78	8.9
2014	1,172	8.2	306	7.8	169	8.3	200	8.1	205	8.3	240	9.5	52	5.9
2015	1,219	8.5	335	8.6	162	7.9	214	8.7	224	9.1	270	10.7	14	1.6
2016	1,107	7.7	360	9.2	161	7.9	186	7.5	206	8.4	194	7.7	0	0.0
2017	1,052	7.4	338	8.6	176	8.6	193	7.8	195	7.9	150	5.9	0	0.0
2018	910	6.4	290	7.4	167	8.2	207	8.4	188	7.6	58	2.3	0	0.0
2019	947	6.6	366	9.3	180	8.8	251	10.2	150	6.1	0	0.0	0	0.0
2020	690	4.8	449	11.5	175	8.6	66	2.7	0	0.0	0	0.0	0	0.0

\*\*\*\*\*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 1e. Distribution of Patients' Cumulative Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, by Year Group and Age Group**

Exposure	Cumulative Hydroxyurea Exposure Episode Duration													
	Total Patients		<3 Months		3 – <6 Months		6 – <12 Months		1 – <2 Years		2 – <5 Years		5+ Years	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Hydroxyurea	<b>14,294</b>	<b>100.0</b>	<b>3916</b>	<b>100.0</b>	<b>2041</b>	<b>100.0</b>	<b>2465</b>	<b>100.0</b>	<b>2463</b>	<b>100.0</b>	<b>2535</b>	<b>100.0</b>	<b>874</b>	<b>100.0</b>
<b>2000 - 2005</b>	417	100.0	70	100.0	47	100.0	53	100.0	60	100.0	91	100.0	96	100.0
0-17 Years	135	32.4	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
0-5 Years	12	2.9	0	0.0	0	0.0	*****	*****	*****	*****	*****	*****	*****	*****
6-11 Years	51	12.2	*****	*****	0	0.0	*****	*****	*****	*****	*****	*****	*****	*****
12-17 Years	72	17.3	*****	*****	*****	*****	*****	*****	*****	*****	22	24.2	26	27.1
18-49 Years	271	65.0	*****	*****	*****	*****	41	77.4	42	70.0	49	53.8	34	35.4
50+ Years	11	2.6	*****	*****	0	0.0	*****	*****	*****	*****	*****	*****	*****	*****
50-59 Years	*****	*****	*****	*****	0	0.0	*****	*****	*****	*****	*****	*****	*****	*****
60+ Years	*****	*****	0	0.0	0	0.0	0	0.0	0	0.0	*****	*****	0	0.0
<b>2006 - 2010</b>	2,745	100.0	525	100.0	325	100.0	442	100.0	471	100.0	658	100.0	324	100.0
0-17 Years	486	17.7	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
0-5 Years	84	3.1	12	2.3	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
6-11 Years	181	6.6	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
12-17 Years	221	8.1	*****	*****	*****	*****	*****	*****	*****	*****	44	6.7	20	6.2
18-49 Years	1970	71.8	*****	*****	*****	*****	327	74.0	358	76.0	481	73.1	186	57.4
50+ Years	289	10.5	*****	*****	30	9.2	*****	*****	*****	*****	*****	*****	*****	*****
50-59 Years	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
60+ Years	*****	*****	27	5.1	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
<b>2011 - 2015</b>	6,426	100.0	1,518	100.0	810	100.0	1,067	100.0	1,193	100.0	1,384	100.0	454	100.0
0-17 Years	750	11.7	124	8.2	84	10.4	116	10.9	153	12.8	214	15.5	59	13.0
0-5 Years	175	2.7	26	1.7	*****	*****	23	2.2	*****	*****	47	3.4	17	3.7
6-11 Years	280	4.4	41	2.7	*****	*****	35	3.3	*****	*****	95	6.9	28	6.2
12-17 Years	295	4.6	57	3.8	33	4.1	58	5.4	61	5.1	72	5.2	14	3.1
18-49 Years	4812	74.9	1183	77.9	629	77.7	825	77.3	899	75.4	972	70.2	304	67.0
50+ Years	864	13.4	211	13.9	97	12.0	126	11.8	141	11.8	198	14.3	91	20.0
50-59 Years	574	8.9	141	9.3	*****	*****	*****	*****	*****	*****	122	8.8	*****	*****
60+ Years	290	4.5	70	4.6	*****	*****	*****	*****	*****	*****	76	5.5	*****	*****

**Table 1e. Distribution of Patients' Cumulative Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, by Year Group and Age Group**

Exposure	Total Patients		Cumulative Hydroxyurea Exposure Episode Duration											
	Number	Percent	<3 Months		3 – <6 Months		6 – <12 Months		1 – <2 Years		2 – <5 Years		5+ Years	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
<b>2016 - 2020</b>	4,706	100.0	1,803	100.0	859	100.0	903	100.0	739	100.0	402	100.0	0	0.0
0-17 Years	689	14.6	182	10.1	122	14.2	157	17.4	144	19.5	84	20.9	0	0.0
0-5 Years	146	3.1	43	2.4	18	2.1	33	3.7	36	4.9	16	4.0	0	0.0
6-11 Years	250	5.3	52	2.9	48	5.6	58	6.4	61	8.3	31	7.7	0	0.0
12-17 Years	293	6.2	87	4.8	56	6.5	66	7.3	47	6.4	37	9.2	0	0.0
18-49 Years	3266	69.4	1341	74.4	626	72.9	604	66.9	461	62.4	234	58.2	0	0.0
50+ Years	751	16.0	280	15.5	111	12.9	142	15.7	134	18.1	84	20.9	0	0.0
50-59 Years	427	9.1	154	8.5	69	8.0	73	8.1	80	10.8	51	12.7	0	0.0
60+ Years	324	6.9	126	7.0	42	4.9	69	7.6	54	7.3	33	8.2	0	0.0

\*\*\*\*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 2a. Descriptive Statistics of Patients' Cumulative Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, Overall**

<b>Exposure</b>	<b>Total Patients</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
Hydroxyurea	14,294	525.21	671.37	1	90	262	696	6,290

**Table 2b. Descriptive Statistics of Patients' Cumulative Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Age Group**

<b>Exposure</b>	<b>Total Patients</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
Hydroxyurea	<b>14,294</b>	<b>525.21</b>	<b>671.37</b>	<b>1</b>	<b>90</b>	<b>262</b>	<b>696</b>	<b>6,290</b>
0-17 Years	2,060	699.10	836.61	1	132	374	942	5,688
0-5 Years	417	739.09	889.96	1	126	428	999	4,533
6-11 Years	762	813.33	907.12	1	166	457	1,124	5,688
12-17 Years	881	581.36	725.05	1	106	305	782	5,196
18-49 Years	10,319	485.43	621.18	1	89	240	638	6,290
50+ Years	1,915	552.47	700.71	1	88	275	753	6,267
50-59 Years	1,225	593.87	753.90	2	90	289	791	6,267
60+ Years	690	478.98	588.03	1	66	258	663	3,131

**Table 2c. Descriptive Statistics of Patients' Cumulative Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Race**

<b>Exposure</b>	<b>Total Patients</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
Hydroxyurea	<b>14,294</b>	<b>525.21</b>	<b>671.37</b>	<b>1</b>	<b>90</b>	<b>262</b>	<b>696</b>	<b>6,290</b>
Unknown	4,728	449.02	615.27	1	64	210	578	4,544
American Indian/Alaska Native	29	601.00	625.61	26	90	478	777	2,528
Asian	*****	598.65	692.71	14	90	277	1,050	2,934
Black/African American	9,214	562.81	692.24	1	90	288	769	6,290
Native Hawaiian/Other Pacific Islander	*****	865.60	719.30	30	532	673	1,162	1,931
White	292	552.44	767.44	3	88	288	699	5,196

\*\*\*\*\*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 2d. Descriptive Statistics of Patients' Cumulative Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Year**

<b>Exposure</b>	<b>Total Patients</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
Hydroxyurea	<b>14,294</b>	<b>525.21</b>	<b>671.37</b>	<b>1</b>	<b>90</b>	<b>262</b>	<b>696</b>	<b>6,290</b>
2000	56	939.25	1117.93	16	198	611	1,186	5,230
2001	73	1422.82	1503.97	21	210	812	2,280	6,290
2002	69	1231.65	1295.39	30	201	781	1,795	6,267
2003	76	1148.14	1399.91	20	146	524	2,058	5,688
2004	84	999.58	1168.88	10	141	490	1,316	4,365
2005	59	949.22	1234.68	10	92	424	1,375	4,418
2006	111	802.72	1045.12	5	110	315	937	4,533
2007	156	799.28	978.59	5	94	368	1,111	4,544
2008	316	559.05	657.60	1	91	305	789	4,116
2009	398	633.86	834.10	2	89	258	830	4,152
2010	1,764	796.27	829.12	4	170	477	1,159	3,931
2011	1,640	715.34	793.70	1	128	399	1,008	3,539
2012	1,207	655.23	717.38	1	120	383	897	3,109
2013	1,188	560.42	612.39	1	106	312	842	2,774
2014	1,172	496.29	543.25	2	90	281	729	2,501
2015	1,219	456.03	476.55	1	90	270	686	2,063
2016	1,107	368.83	387.83	1	60	209	562	1,762
2017	1,052	325.18	325.08	1	66	195	497	1,361
2018	910	261.54	239.75	1	63	180	393	989
2019	947	187.10	152.75	1	60	136	297	676
2020	690	84.55	67.98	1	30	62	120	360



**Table 2e. Descriptive Statistics of Patients' Cumulative Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Year Group and Age Group**

Exposure	Total Patients	Mean	Standard Deviation	Min	Q1	Median	Q3	Max
Hydroxyurea	<b>14,294</b>	<b>525.21</b>	<b>671.37</b>	<b>1</b>	<b>90</b>	<b>262</b>	<b>696</b>	<b>6,290</b>
<b>2000 - 2005</b>	417	1123.92	1,303.54	10	150	569	1,621	6,290
0-17 Years	135	1861.61	1,394.09	30	636	1521	2,899	5,688
0-5 Years	12	2510.00	1,548.82	217	729	3329	3,883	4,027
6-11 Years	51	2057.04	1,388.50	30	781	1906	3,127	5,688
12-17 Years	72	1615.13	1,333.62	30	547	1258	2,443	5,196
18-49 Years	271	745.96	1,051.86	10	105	329	847	6,290
50+ Years	11	1382.18	1,865.56	30	90	769	1,561	6,267
50-59 Years	*****	1443.5	*****	*****	*****	*****	*****	*****
60+ Years	*****	769.0	*****	*****	*****	*****	*****	*****
<b>2006 - 2010</b>	2,745	745.85	835.23	1	130	407	1,073	4,544
0-17 Years	486	917.28	990.88	2	163	467	1,354	4,533
0-5 Years	84	1225.94	1,183.55	15	239	971	1,933	4,533
6-11 Years	181	1139.59	1,073.77	3	253	733	2,122	3,770
12-17 Years	221	617.89	724.98	2	106	326	896	3,645
18-49 Years	1970	690.69	766.76	1	126	391	973	4,544
50+ Years	289	833.56	946.42	2	116	450	1,196	4,116
50-59 Years	*****	913.42	985.61	2	158	550	1,294	4,116
60+ Years	*****	605.71	786.64	12	63	270	911	3,095
<b>2011 - 2015</b>	6,426	586.27	658.32	1	104	332	838	3,539
0-17 Years	750	689.52	668.44	4	163	474	1,033	3,539
0-5 Years	175	720.78	720.50	6	171	488	1,063	3,539
6-11 Years	280	795.70	720.70	8	177	640	1,184	3,194
12-17 Years	295	570.20	559.05	4	146	361	840	2,577
18-49 Years	4812	554.75	636.91	1	94	307	775	3,509
50+ Years	864	672.18	745.08	2	96	362	984	3,370
50-59 Years	574	676.46	771.56	3	93	357	951	3,370
60+ Years	290	663.70	690.90	2	103	391	1,044	3,131

**Table 2e. Descriptive Statistics of Patients' Cumulative Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Year Group and Age Group**

<b>Exposure</b>	<b>Total Patients</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
<b>2016 - 2020</b>	4,706	260.07	291.13	1	60	150	355	1,762
0-17 Years	689	327.84	317.23	1	88	216	490	1,629
0-5 Years	146	335.37	322.78	1	70	248	500	1,616
6-11 Years	250	343.16	309.46	1	118	248	512	1,629
12-17 Years	293	311.01	321.25	1	74	188	452	1,374
18-49 Years	3266	237.88	276.04	1	59	130	311	1,762
50+ Years	751	294.43	316.45	1	60	173	412	1,658
50-59 Years	427	302.79	321.79	2	60	160	427	1,658
60+ Years	324	283.42	309.42	1	60	178	391	1,576

\*\*\*\*\*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 3a. Distribution of First Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, Overall**

Exposure	Total Episodes		First Hydroxyurea Exposure Episode Duration											
			1-30 Days		31-60 Days		61-90 Days		91-183 Days		184-365 Days		366+ Days	
			Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Hydroxyurea	14,294	100.0	6,923	48.4	1,095	7.7	1,911	13.4	1,800	12.6	1,268	8.9	1,297	9.1

**Table 3b. Distribution of First Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, by Age Group**

Exposure	Total Episodes		First Hydroxyurea Exposure Episode Duration											
			1-30 Days		31-60 Days		61-90 Days		91-183 Days		184-365 Days		366+ Days	
			Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Hydroxyurea	<b>14,294</b>	<b>100.0</b>	<b>6,923</b>	<b>100.0</b>	<b>1,095</b>	<b>100.0</b>	<b>1,911</b>	<b>100.0</b>	<b>1,800</b>	<b>100.0</b>	<b>1,268</b>	<b>100.0</b>	<b>1,297</b>	<b>100.0</b>
0-17 Years	2,060	14.4	627	9.1	164	15.0	234	12.2	365	20.3	294	23.2	376	29.0
0-5 Years	417	2.9	121	1.7	28	2.6	38	2.0	76	4.2	60	4.7	94	7.2
6-11 Years	762	5.3	199	2.9	64	5.8	82	4.3	148	8.2	115	9.1	154	11.9
12-17 Years	881	6.2	307	4.4	72	6.6	114	6.0	141	7.8	119	9.4	128	9.9
18-49 Years	10,319	72.2	5,618	81.1	789	72.1	1,372	71.8	1,155	64.2	728	57.4	657	50.7
50+ Years	1,915	13.4	678	9.8	142	13.0	305	16.0	280	15.6	246	19.4	264	20.4
50-59 Years	1,225	8.6	479	6.9	69	6.3	186	9.7	170	9.4	140	11.0	181	14.0
60+ Years	690	4.8	199	2.9	73	6.7	119	6.2	110	6.1	106	8.4	83	6.4

**Table 3c. Distribution of First Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, by Race**

Exposure	Total Episodes		First Hydroxyurea Exposure Episode Duration											
			1-30 Days		31-60 Days		61-90 Days		91-183 Days		184-365 Days		366+ Days	
			Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Hydroxyurea	14,294	100.0	6,923	100.0	1,095	100.0	1,911	100.0	1,800	100.0	1,268	100.0	1,297	100.0
Unknown	4,728	33.1	2,054	29.7	368	33.6	597	31.2	705	39.2	507	40.0	497	38.3
American Indian/Alaska Native	29	0.2	16	0.2	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
Asian	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
Black/African American	9,214	64.5	4,705	68.0	698	63.7	1,271	66.5	1,064	59.1	724	57.1	752	58.0
Native Hawaiian/Other Pacific Islander	*****	*****	*****	*****	0	0.0	*****	*****	0	0.0	0	0.0	*****	*****
White	292	2.0	134	1.9	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****

\*\*\*\*\*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 3d. Distribution of First Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, by Year**

Exposure	First Hydroxyurea Exposure Episode Duration													
	Total Episodes		1-30 Days		31-60 Days		61-90 Days		91-183 Days		184-365 Days		366+ Days	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Hydroxyurea	<b>14,294</b>	<b>100.0</b>	<b>6,923</b>	<b>100.0</b>	<b>1,095</b>	<b>100.0</b>	<b>1,911</b>	<b>100.0</b>	<b>1,800</b>	<b>100.0</b>	<b>1,268</b>	<b>100.0</b>	<b>1,297</b>	<b>100.0</b>
2000	56	0.4	29	0.4	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
2001	73	0.5	27	0.4	12	1.1	*****	*****	12	0.7	*****	*****	*****	*****
2002	69	0.5	24	0.3	*****	*****	*****	*****	14	0.8	*****	*****	*****	*****
2003	76	0.5	23	0.3	*****	*****	*****	*****	14	0.8	*****	*****	17	1.3
2004	84	0.6	28	0.4	13	1.2	*****	*****	*****	*****	13	1.0	11	0.8
2005	59	0.4	23	0.3	*****	*****	*****	*****	13	0.7	*****	*****	*****	*****
2006	111	0.8	43	0.6	*****	*****	14	0.7	13	0.7	*****	*****	18	1.4
2007	156	1.1	67	1.0	21	1.9	14	0.7	21	1.2	16	1.3	17	1.3
2008	316	2.2	147	2.1	26	2.4	52	2.7	41	2.3	26	2.1	24	1.9
2009	398	2.8	178	2.6	18	1.6	53	2.8	64	3.6	40	3.2	45	3.5
2010	1,764	12.3	946	13.7	122	11.1	266	13.9	184	10.2	117	9.2	129	9.9
2011	1,640	11.5	867	12.5	113	10.3	214	11.2	175	9.7	127	10.0	144	11.1
2012	1,207	8.4	617	8.9	90	8.2	139	7.3	131	7.3	106	8.4	124	9.6
2013	1,188	8.3	594	8.6	83	7.6	151	7.9	138	7.7	96	7.6	126	9.7
2014	1,172	8.2	584	8.4	68	6.2	151	7.9	153	8.5	93	7.3	123	9.5
2015	1,219	8.5	587	8.5	90	8.2	165	8.6	140	7.8	113	8.9	124	9.6
2016	1,107	7.7	523	7.6	87	7.9	142	7.4	141	7.8	104	8.2	110	8.5
2017	1,052	7.4	515	7.4	64	5.8	126	6.6	148	8.2	99	7.8	100	7.7
2018	910	6.4	390	5.6	88	8.0	122	6.4	131	7.3	90	7.1	89	6.9
2019	947	6.6	398	5.7	84	7.7	147	7.7	116	6.4	129	10.2	73	5.6
2020	690	4.8	313	4.5	78	7.1	113	5.9	132	7.3	54	4.3	0	0.0

\*\*\*\*\*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 3e. Distribution of First Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, by Year Group and Age Group**

Exposure	First Hydroxyurea Exposure Episode Duration													
	Total Episodes		1-30 Days		31-60 Days		61-90 Days		91-183 Days		184-365 Days		366+ Days	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
<b>Hydroxyurea</b>	<b>14,294</b>	<b>100.0</b>	<b>6,923</b>	<b>100.0</b>	<b>1,095</b>	<b>100.0</b>	<b>1,911</b>	<b>100.0</b>	<b>1,800</b>	<b>100.0</b>	<b>1,268</b>	<b>100.0</b>	<b>1,297</b>	<b>100.0</b>
<b>2000 - 2005</b>	417	100.0	154	100.0	53	100.0	42	100.0	72	100.0	45	100.0	51	100.0
0-17 Years	135	32.4	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
0-5 Years	12	2.9	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
6-11 Years	51	12.2	*****	*****	*****	*****	*****	*****	15	20.8	*****	*****	*****	*****
12-17 Years	72	17.3	*****	*****	*****	*****	*****	*****	*****	*****	13	28.9	18	35.3
18-49 Years	271	65.0	128	83.1	38	71.7	28	66.7	41	56.9	20	44.4	16	31.4
50+ Years	11	2.6	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
50-59 Years	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
60+ Years	*****	*****	0	0.0	0	0.0	0	0.0	*****	*****	0	0.0	0	0.0
<b>2006 - 2010</b>	2,745	100.0	1,381	100.0	197	100.0	399	100.0	323	100.0	212	100.0	233	100.0
0-17 Years	486	17.7	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
0-5 Years	84	3.1	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
6-11 Years	181	6.6	*****	*****	*****	*****	*****	*****	32	9.9	*****	*****	*****	*****
12-17 Years	221	8.1	*****	*****	*****	*****	*****	*****	*****	*****	19	9.0	32	13.7
18-49 Years	1,970	71.8	1,094	79.2	149	75.6	284	71.2	213	65.9	122	57.5	108	46.4
50+ Years	289	10.5	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
50-59 Years	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
60+ Years	*****	*****	29	2.1	*****	*****	19	4.8	*****	*****	*****	*****	*****	*****
<b>2011 - 2015</b>	6,426	100.0	3,249	100.0	444	100.0	820	100.0	737	100.0	535	100.0	641	100.0
0-17 Years	750	11.7	236	7.3	52	11.7	89	10.9	126	17.1	98	18.3	149	23.2
0-5 Years	175	2.7	58	1.8	*****	*****	*****	*****	34	4.6	18	3.4	39	6.1
6-11 Years	280	4.4	77	2.4	*****	*****	*****	*****	48	6.5	36	6.7	66	10.3
12-17 Years	295	4.6	101	3.1	25	5.6	37	4.5	44	6.0	44	8.2	44	6.9
18-49 Years	4,812	74.9	2,714	83.5	335	75.5	606	73.9	487	66.1	323	60.4	347	54.1
50+ Years	864	13.4	299	9.2	57	12.8	125	15.2	124	16.8	114	21.3	145	22.6
50-59 Years	574	8.9	231	7.1	*****	*****	79	9.6	76	10.3	*****	*****	*****	*****
60+ Years	290	4.5	68	2.1	*****	*****	46	5.6	48	6.5	*****	*****	*****	*****

**Table 3e. Distribution of First Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, by Year Group and Age Group**

Exposure	Total Episodes		First Hydroxyurea Exposure Episode Duration											
			1-30 Days		31-60 Days		61-90 Days		91-183 Days		184-365 Days		366+ Days	
			Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
<b>2016 - 2020</b>	4,706	100.0	2,139	100.0	401	100.0	650	100.0	668	100.0	476	100.0	372	100.0
0-17 Years	689	14.6	197	9.2	65	16.2	76	11.7	138	20.7	113	23.7	100	26.9
0-5 Years	146	3.1	34	1.6	13	3.2	14	2.2	28	4.2	26	5.5	31	8.3
6-11 Years	250	5.3	68	3.2	25	6.2	25	3.8	53	7.9	44	9.2	35	9.4
12-17 Years	293	6.2	95	4.4	27	6.7	37	5.7	57	8.5	43	9.0	34	9.1
18-49 Years	3,266	69.4	1,682	78.6	267	66.6	454	69.8	414	62.0	263	55.3	186	50.0
50+ Years	751	16.0	260	12.2	69	17.2	120	18.5	116	17.4	100	21.0	86	23.1
50-59 Years	427	9.1	158	7.4	30	7.5	66	10.2	67	10.0	52	10.9	54	14.5
60+ Years	324	6.9	102	4.8	39	9.7	54	8.3	49	7.3	48	10.1	32	8.6

\*\*\*\*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 4a. Descriptive Statistics of First Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, Overall**

<b>Exposure</b>	<b>Total Episodes</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
Hydroxyurea	14,294	141.34	274.26	1	30	41	124	3,558

**Table 4b. Descriptive Statistics of First Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Age Group**

Exposure	Total Episodes	Mean	Standard Deviation	Min	Q1	Median	Q3	Max
Hydroxyurea	<b>14,294</b>	<b>141.34</b>	<b>274.26</b>	<b>1</b>	<b>30</b>	<b>41</b>	<b>124</b>	<b>3,558</b>
0-17 Years	2,060	227.99	350.76	1	30	91	267	3,558
0-5 Years	417	294.29	468.29	1	30	115	340	3,558
6-11 Years	762	248.64	360.33	1	30	113	299	2,828
12-17 Years	881	178.75	258.93	1	30	80	208	2,399
18-49 Years	10,319	115.01	242.03	1	30	30	90	3,509
50+ Years	1,915	190.01	315.25	1	30	85	193	3,319
50-59 Years	1,225	198.34	347.14	2	30	78	189	3,319
60+ Years	690	175.23	248.31	1	30	90	195	1,992

**Table 4c. Descriptive Statistics of First Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Race**

<b>Exposure</b>	<b>Total Episodes</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
Hydroxyurea	<b>14,294</b>	<b>141.34</b>	<b>274.26</b>	<b>1</b>	<b>30</b>	<b>41</b>	<b>124</b>	<b>3,558</b>
Unknown	4,728	153.88	269.30	1	30	60	153	3,558
American Indian/Alaska Native	29	135.69	214.24	26	30	30	126	800
Asian	*****	309.62	608.51	14	30	49	244	2,849
Black/African American	9,214	133.53	274.96	1	30	30	107	3,509
Native Hawaiian/Other Pacific Islander	*****	262.00	297.46	30	30	81	532	637
White	292	168.34	278.45	3	30	51	179	2,083

\*\*\*\*\*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 4d. Descriptive Statistics of First Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Year**

<b>Exposure</b>	<b>Total Episodes</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
Hydroxyurea	<b>14,294</b>	<b>141.34</b>	<b>274.26</b>	<b>1</b>	<b>30</b>	<b>41</b>	<b>124</b>	<b>3,558</b>
2000	56	147.59	329.12	15	30	30	93	1,759
2001	73	131.36	231.24	5	30	51	105	1,561
2002	69	160.46	240.05	14	30	67	160	1,439
2003	76	259.55	410.26	20	30	92	246	1,967
2004	84	186.52	273.92	10	30	73	245	1,674
2005	59	167.08	303.08	10	30	60	171	1,555
2006	111	204.14	327.27	5	30	62	198	1,873
2007	156	161.87	272.81	5	30	41	168	1,736
2008	316	128.70	228.48	1	30	54	113	2,083
2009	398	175.01	331.60	1	30	62	151	2,828
2010	1,764	126.31	285.85	3	30	30	90	3,558
2011	1,640	155.11	378.71	1	30	30	108	3,509
2012	1,207	151.47	309.79	1	30	30	125	3,109
2013	1,188	151.96	289.40	1	30	31	129	2,774
2014	1,172	155.70	294.42	2	30	33	123	2,501
2015	1,219	151.84	277.73	1	30	45	132	2,063
2016	1,107	139.55	232.43	1	30	45	128	1,762
2017	1,052	131.15	202.56	1	30	40	136	1,361
2018	910	135.92	193.00	1	30	60	150	989
2019	947	118.24	133.78	1	30	60	150	642
2020	690	74.90	66.62	1	30	51	98	360

**Table 4e. Descriptive Statistics of First Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Year Group and Age Group**

Exposure	Total Episodes	Mean	Standard Deviation	Min	Q1	Median	Q3	Max
Hydroxyurea	<b>14,294</b>	<b>141.34</b>	<b>274.26</b>	<b>1</b>	<b>30</b>	<b>41</b>	<b>124</b>	<b>3,558</b>
<b>2000 - 2005</b>	417	177.88	304.83	5	30	61	171	1,967
0-17 Years	135	302.15	396.14	14	58	149	348	1,759
0-5 Years	12	373.75	576.55	26	45	83	541	1,759
6-11 Years	51	317.43	409.82	14	60	166	313	1,743
12-17 Years	72	279.39	353.32	30	51	148	363	1,727
18-49 Years	271	111.12	212.20	5	30	34	100	1,967
50+ Years	11	297.73	449.33	30	44	96	344	1,561
50-59 Years	*****	317.90	*****	*****	*****	*****	*****	*****
60+ Years	*****	96.00	*****	*****	*****	*****	*****	*****
<b>2006 - 2010</b>	2,745	138.81	288.80	1	30	30	108	3,558
0-17 Years	486	236.39	381.71	1	30	80	270	3,558
0-5 Years	84	363.92	568.83	15	30	135	382	3,558
6-11 Years	181	277.34	400.40	3	30	112	345	2,828
12-17 Years	221	154.38	231.58	1	30	61	157	1,498
18-49 Years	1,970	108.77	239.51	1	30	30	90	3,041
50+ Years	289	179.52	364.95	2	30	68	150	3,319
50-59 Years	*****	199.57	402.02	2	30	70	163	3,319
60+ Years	*****	122.31	220.61	12	30	66	127	1,664
<b>2011 - 2015</b>	6,426	153.33	317.01	1	30	30	122	3,509
0-17 Years	750	254.56	411.51	4	30	90	291	3,252
0-5 Years	175	307.05	532.16	6	30	102	312	3,252
6-11 Years	280	284.16	420.98	5	30	115	348	2,820
12-17 Years	295	195.34	299.39	4	30	84	233	2,399
18-49 Years	4,812	125.30	284.12	1	30	30	90	3,509
50+ Years	864	221.55	365.06	2	30	90	227	3,177
50-59 Years	574	221.81	393.01	2	30	80	205	3,177
60+ Years	290	221.02	302.84	2	43	93	253	1,992

**Table 4e. Descriptive Statistics of First Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Year Group and Age Group**

Exposure	Total Episodes	Mean	Standard Deviation	Min	Q1	Median	Q3	Max
<b>2016 - 2020</b>	4,706	123.20	183.75	1	30	60	131	1,762
0-17 Years	689	178.62	215.02	1	30	93	239	1,509
0-5 Years	146	232.40	267.42	1	46	132	329	1,509
6-11 Years	250	174.06	200.13	1	30	100	233	1,275
12-17 Years	293	155.71	193.09	1	30	84	195	1,199
18-49 Years	3,266	103.92	165.99	1	30	30	100	1,762
50+ Years	751	156.19	209.61	1	30	81	182	1,658
50-59 Years	427	163.37	225.25	2	30	80	182	1,658
60+ Years	324	146.73	186.94	1	30	83	182	1,173

\*\*\*\*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 5a. Distribution of All Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, Overall**

Exposure	All Hydroxyurea Exposure Episode Duration													
	Total Episodes		1-30 Days		31-60 Days		61-90 Days		91-183 Days		184-365 Days		366+ Days	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Hydroxyurea	67,309	100.0	34,318	51.0	5,284	7.9	9,946	14.8	8,438	12.5	5,385	8.0	3,938	5.9

**Table 5b. Distribution of All Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, by Age Group**

Exposure	All Hydroxyurea Exposure Episode Duration													
	Total Episodes		1-30 Days		31-60 Days		61-90 Days		91-183 Days		184-365 Days		366+ Days	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Hydroxyurea	<b>67,309</b>	<b>100.0</b>	<b>34,318</b>	<b>100.0</b>	<b>5,284</b>	<b>100.0</b>	<b>9,946</b>	<b>100.0</b>	<b>8,438</b>	<b>100.0</b>	<b>5,385</b>	<b>100.0</b>	<b>3,938</b>	<b>100.0</b>
0-17 Years	9,749	14.5	4,092	11.9	889	16.8	1,324	13.3	1,465	17.4	1,030	19.1	949	24.1
0-5 Years	1,634	2.4	617	1.8	141	2.7	201	2.0	272	3.2	184	3.4	219	5.6
6-11 Years	3,768	5.6	1,461	4.3	346	6.5	500	5.0	576	6.8	468	8.7	417	10.6
12-17 Years	4,347	6.5	2,014	5.9	402	7.6	623	6.3	617	7.3	378	7.0	313	7.9
18-49 Years	51,005	75.8	27,737	80.8	3,885	73.5	7,466	75.1	6,046	71.7	3,561	66.1	2,310	58.7
50+ Years	6,555	9.7	2,489	7.3	510	9.7	1,156	11.6	927	11.0	794	14.7	679	17.2
50-59 Years	4,514	6.7	1,858	5.4	307	5.8	737	7.4	614	7.3	529	9.8	469	11.9
60+ Years	2,041	3.0	631	1.8	203	3.8	419	4.2	313	3.7	265	4.9	210	5.3



**Table 5c. Distribution of All Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, by Race**

Exposure	All Hydroxyurea Exposure Episode Duration													
	Total Episodes		1-30 Days		31-60 Days		61-90 Days		91-183 Days		184-365 Days		366+ Days	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Hydroxyurea	67,309	100.0	34,318	100.0	5,284	100.0	9,946	100.0	8,438	100.0	5,385	100.0	3,938	100.0
Unknown	17,376	25.8	8,341	24.3	1,340	25.4	2,472	24.9	2,371	28.1	1,611	29.9	1,241	31.5
American Indian/Alaska Native	170	0.3	105	0.3	*****	*****	*****	*****	23	0.3	*****	*****	12	0.3
Asian	99	0.1	42	0.1	*****	*****	15	0.2	*****	*****	15	0.3	*****	*****
Black/African American	48,390	71.9	25,244	73.6	3,809	72.1	7,224	72.6	5,894	69.9	3,643	67.7	2,576	65.4
Native Hawaiian/Other Pacific Islander	35	0.1	17	0.0	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****
White	1,239	1.8	569	1.7	116	2.2	218	2.2	136	1.6	101	1.9	99	2.5

\*\*\*\*\*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 5d. Distribution of All Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, by Year**

Exposure	All Hydroxyurea Exposure Episode Duration													
	Total Episodes		1-30 Days		31-60 Days		61-90 Days		91-183 Days		184-365 Days		366+ Days	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Hydroxyurea	<b>67,309</b>	<b>100.0</b>	<b>34,318</b>	<b>100.0</b>	<b>5,284</b>	<b>100.0</b>	<b>9,946</b>	<b>100.0</b>	<b>8,438</b>	<b>100.0</b>	<b>5,385</b>	<b>100.0</b>	<b>3,938</b>	<b>100.0</b>
2000	462	0.7	232	0.7	50	0.9	58	0.6	69	0.8	28	0.5	25	0.6
2001	744	1.1	338	1.0	87	1.6	87	0.9	114	1.4	58	1.1	60	1.5
2002	694	1.0	332	1.0	73	1.4	91	0.9	94	1.1	55	1.0	49	1.2
2003	631	0.9	269	0.8	92	1.7	77	0.8	85	1.0	54	1.0	54	1.4
2004	715	1.1	342	1.0	82	1.6	92	0.9	100	1.2	53	1.0	46	1.2
2005	438	0.7	230	0.7	37	0.7	41	0.4	61	0.7	39	0.7	30	0.8
2006	635	0.9	284	0.8	43	0.8	95	1.0	88	1.0	71	1.3	54	1.4
2007	969	1.4	455	1.3	110	2.1	115	1.2	141	1.7	74	1.4	74	1.9
2008	1,775	2.6	940	2.7	159	3.0	251	2.5	214	2.5	124	2.3	87	2.2
2009	1,991	3.0	964	2.8	129	2.4	301	3.0	274	3.2	184	3.4	139	3.5
2010	13,471	20.0	7,359	21.4	929	17.6	2,012	20.2	1,526	18.1	947	17.6	698	17.7
2011	10,447	15.5	5,510	16.1	787	14.9	1,572	15.8	1,198	14.2	813	15.1	567	14.4
2012	6,820	10.1	3,548	10.3	482	9.1	994	10.0	847	10.0	536	10.0	413	10.5
2013	5,792	8.6	2,944	8.6	426	8.1	859	8.6	730	8.7	468	8.7	365	9.3
2014	5,159	7.7	2,621	7.6	375	7.1	772	7.8	654	7.8	411	7.6	326	8.3
2015	4,748	7.1	2,316	6.7	368	7.0	724	7.3	618	7.3	411	7.6	311	7.9
2016	3,786	5.6	1,834	5.3	337	6.4	566	5.7	497	5.9	329	6.1	223	5.7
2017	3,100	4.6	1,498	4.4	236	4.5	444	4.5	438	5.2	281	5.2	203	5.2
2018	2,251	3.3	1,038	3.0	206	3.9	365	3.7	310	3.7	204	3.8	128	3.3
2019	1,824	2.7	843	2.5	172	3.3	293	2.9	239	2.8	191	3.5	86	2.2
2020	857	1.3	421	1.2	104	2.0	137	1.4	141	1.7	54	1.0	0	0.0

\*\*\*\*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 5e. Distribution of All Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, by Year Group and Age Group**

Exposure	All Hydroxyurea Exposure Episode Duration													
	Total Episodes		1-30 Days		31-60 Days		61-90 Days		91-183 Days		184-365 Days		366+ Days	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Hydroxyurea	67,309	100.0	34,318	100.0	5,284	100.0	9,946	100.0	8,438	100.0	5,385	100.0	3,938	100.0
<b>2000 - 2005</b>	3,684	100.0	1,743	100.0	421	100.0	446	100.0	523	100.0	287	100.0	264	100.0
0-17 Years	1,680	45.6	731	41.9	****	****	****	****	****	****	151	52.6	168	63.6
0-5 Years	133	3.6	44	2.5	****	****	****	****	****	****	15	5.2	24	9.1
6-11 Years	647	17.6	254	14.6	84	20.0	80	17.9	91	17.4	63	22.0	75	28.4
12-17 Years	900	24.4	433	24.8	81	19.2	124	27.8	120	22.9	73	25.4	69	26.1
18-49 Years	1,952	53.0	991	56.9	235	55.8	224	50.2	283	54.1	****	****	****	****
50+ Years	52	1.4	21	1.2	****	****	****	****	****	****	****	****	****	****
50-59 Years	37	1.0	****	****	****	****	****	****	****	****	****	****	****	****
60+ Years	15	0.4	****	****	****	****	0	0.0	****	****	0	0.0	0	0.0
<b>2006 - 2010</b>	18,841	100.0	10,002	100.0	1,370	100.0	2,774	100.0	2,243	100.0	1,400	100.0	1,052	100.0
0-17 Years	3,140	16.7	1,419	14.2	****	****	****	****	****	****	310	22.1	284	27.0
0-5 Years	558	3.0	228	2.3	****	****	****	****	****	****	68	4.9	65	6.2
6-11 Years	1,262	6.7	515	5.1	108	7.9	176	6.3	178	7.9	151	10.8	134	12.7
12-17 Years	1,320	7.0	676	6.8	109	8.0	204	7.4	155	6.9	91	6.5	85	8.1
18-49 Years	14,108	74.9	7,868	78.7	1,012	73.9	2,071	74.7	1,623	72.4	****	****	****	****
50+ Years	1,593	8.5	715	7.1	****	****	****	****	****	****	****	****	****	****
50-59 Years	1,258	6.7	****	****	****	****	****	****	****	****	****	****	****	****
60+ Years	335	1.8	****	****	****	****	61	2.2	****	****	35	2.5	25	2.4
<b>2011 - 2015</b>	32,966	100.0	16,939	100.0	2,438	100.0	4,921	100.0	4,047	100.0	2,639	100.0	1,982	100.0
0-17 Years	3,273	9.9	1,362	8.0	262	10.7	437	8.9	520	12.8	347	13.1	345	17.4
0-5 Years	667	2.0	262	1.5	51	2.1	88	1.8	115	2.8	61	2.3	90	4.5
6-11 Years	1,231	3.7	481	2.8	87	3.6	162	3.3	194	4.8	152	5.8	155	7.8
12-17 Years	1,375	4.2	619	3.7	124	5.1	187	3.8	211	5.2	134	5.1	100	5.0
18-49 Years	26,383	80.0	14,383	84.9	1,912	78.4	3,891	79.1	3,049	75.3	1,897	71.9	1,251	63.1
50+ Years	3,310	10.0	1,194	7.0	264	10.8	593	12.1	478	11.8	395	15.0	386	19.5
50-59 Years	2,300	7.0	929	5.5	162	6.6	383	7.8	316	7.8	256	9.7	254	12.8
60+ Years	1,010	3.1	265	1.6	102	4.2	210	4.3	162	4.0	139	5.3	132	6.7

**Table 5e. Distribution of All Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, by Year Group and Age Group**

Exposure	All Hydroxyurea Exposure Episode Duration													
	Total Episodes		1-30 Days		31-60 Days		61-90 Days		91-183 Days		184-365 Days		366+ Days	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
<b>2016 - 2020</b>	11,818	100.0	5,634	100.0	1,055	100.0	1,805	100.0	1,625	100.0	1,059	100.0	640	100.0
0-17 Years	1,656	14.0	580	10.3	181	17.2	228	12.6	293	18.0	222	21.0	152	23.8
0-5 Years	276	2.3	83	1.5	26	2.5	38	2.1	49	3.0	40	3.8	40	6.3
6-11 Years	628	5.3	211	3.7	67	6.4	82	4.5	113	7.0	102	9.6	53	8.3
12-17 Years	752	6.4	286	5.1	88	8.3	108	6.0	131	8.1	80	7.6	59	9.2
18-49 Years	8,562	72.4	4,495	79.8	726	68.8	1,280	70.9	1,091	67.1	624	58.9	346	54.1
50+ Years	1,600	13.5	559	9.9	148	14.0	297	16.5	241	14.8	213	20.1	142	22.2
50-59 Years	919	7.8	347	6.2	70	6.6	149	8.3	142	8.7	122	11.5	89	13.9
60+ Years	681	5.8	212	3.8	78	7.4	148	8.2	99	6.1	91	8.6	53	8.3

\*\*\*\*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 6a. Descriptive Statistics of All Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, Overall**

<b>Exposure</b>	<b>Total Episodes</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
Hydroxyurea	67,309	111.53	209.94	1	30	30	100	5,494

**Table 6b. Descriptive Statistics of All Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Age Group**

<b>Exposure</b>	<b>Total Episodes</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
Hydroxyurea	<b>67,309</b>	<b>111.53</b>	<b>209.94</b>	<b>1</b>	<b>30</b>	<b>30</b>	<b>100</b>	<b>5,494</b>
0-17 Years	9,749	147.72	257.99	1	30	60	144	3,558
0-5 Years	1,634	188.62	339.61	1	30	70	179	3,558
6-11 Years	3,768	164.48	274.46	1	30	66	174	3,379
12-17 Years	4,347	117.82	197.20	1	30	44	113	2,399
18-49 Years	51,005	98.21	186.28	1	30	30	90	5,494
50+ Years	6,555	161.40	278.92	1	30	73	166	3,335
50-59 Years	4,514	161.16	290.65	1	30	66	159	3,335
60+ Years	2,041	161.93	251.10	1	30	89	180	2,723

**Table 6c. Descriptive Statistics of All Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Race**

<b>Exposure</b>	<b>Total Episodes</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
Hydroxyurea	<b>67,309</b>	<b>111.53</b>	<b>209.94</b>	<b>1</b>	<b>30</b>	<b>30</b>	<b>100</b>	<b>5,494</b>
Unknown	17,376	122.18	217.24	1	30	41	120	3,558
American Indian/Alaska Native	170	102.52	175.48	3	30	30	100	1,535
Asian	99	157.22	332.59	5	30	60	170	2,849
Black/African American	48,390	107.16	206.06	1	30	30	91	5,494
Native Hawaiian/Other Pacific Islander	35	123.66	157.96	15	30	32	185	637
White	1,239	130.20	240.55	1	30	50	101	2,150

**Table 6d. Descriptive Statistics of All Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Year**

<b>Exposure</b>	<b>Total Episodes</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
Hydroxyurea	<b>67,309</b>	<b>111.53</b>	<b>209.94</b>	<b>1</b>	<b>30</b>	<b>30</b>	<b>100</b>	<b>5,494</b>
2000	462	113.85	263.45	1	30	30	100	3,406
2001	744	139.60	312.09	1	30	50	111	5,494
2002	694	122.46	249.00	6	30	40	108	3,335
2003	631	138.29	256.44	4	30	50	116	2,058
2004	715	117.43	226.17	3	30	33	100	2,124
2005	438	127.86	259.55	2	30	30	101	2,773
2006	635	140.32	249.50	1	30	60	140	2,729
2007	969	128.68	261.87	1	30	35	107	3,379
2008	1,775	99.53	176.18	1	30	30	90	2,083
2009	1,991	126.71	236.16	1	30	42	120	2,927
2010	13,471	104.27	208.33	1	30	30	90	3,580
2011	10,447	112.30	237.50	1	30	30	90	3,509
2012	6,820	115.96	228.11	1	30	30	100	3,109
2013	5,792	114.95	208.03	1	30	30	104	2,774
2014	5,159	112.75	197.33	1	30	30	100	2,501
2015	4,748	117.08	199.94	1	30	40	110	2,063
2016	3,786	107.84	169.63	1	30	35	109	1,762
2017	3,100	110.35	161.02	1	30	43	120	1,361
2018	2,251	105.73	146.51	1	30	54	111	989
2019	1,824	97.14	112.80	1	30	51	114	642
2020	857	68.07	62.62	1	30	33	90	360



**Table 6e. Descriptive Statistics of All Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Year Group and Age Group**

Exposure	Total Episodes	Mean	Standard Deviation	Min	Q1	Median	Q3	Max
Hydroxyurea	<b>67,309</b>	<b>111.53</b>	<b>209.94</b>	<b>1</b>	<b>30</b>	<b>30</b>	<b>100</b>	<b>5,494</b>
<b>2000 - 2005</b>	3,684	127.22	263.17	1	30	38	101	5,494
0-17 Years	1,680	149.59	265.53	2	30	56	129	2,124
0-5 Years	133	226.47	349.82	5	30	83	256	1,759
6-11 Years	647	162.15	268.55	4	30	60	148	1,743
12-17 Years	900	129.21	245.93	2	30	38	109	2,124
18-49 Years	1,952	103.56	240.47	1	30	30	95	5,494
50+ Years	52	292.38	634.57	30	30	57	188	3,335
50-59 Years	37	390.14	731.92	30	30	100	344	3,335
60+ Years	15	51.27	42.44	30	30	30	54	169
<b>2006 - 2010</b>	18,841	108.66	213.48	1	30	30	90	3,580
0-17 Years	3,140	141.97	265.72	1	30	54	130	3,558
0-5 Years	558	184.55	362.59	1	30	63	171	3,558
6-11 Years	1,262	163.44	289.49	1	30	62	168	3,379
12-17 Years	1,320	103.45	172.34	1	30	30	92	2,162
18-49 Years	14,108	96.45	188.37	1	30	30	90	3,580
50+ Years	1,593	151.22	283.49	1	30	60	144	3,319
50-59 Years	1,258	155.38	299.32	2	30	60	146	3,319
60+ Years	335	135.61	213.49	1	30	63	142	1,664
<b>2011 - 2015</b>	32,966	114.28	219.30	1	30	30	99	3,509
0-17 Years	3,273	158.00	280.20	1	30	62	149	3,252
0-5 Years	667	189.11	355.88	1	30	66	170	3,252
6-11 Years	1,231	180.99	304.16	1	30	71	183	2,820
12-17 Years	1,375	122.33	201.36	1	30	60	119	2,399
18-49 Years	26,383	101.18	194.68	1	30	30	90	3,509
50+ Years	3,310	175.46	303.84	1	30	82	180	3,177
50-59 Years	2,300	168.82	305.67	1	30	68	161	3,177
60+ Years	1,010	190.57	299.24	1	30	90	194	2,723

**Table 6e. Descriptive Statistics of All Hydroxyurea Exposure Episode Durations in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Year Group and Age Group**

Exposure	Total Episodes	Mean	Standard Deviation	Min	Q1	Median	Q3	Max
<b>2016 - 2020</b>	11,818	103.56	149.89	1	30	43	109	1,762
0-17 Years	1,656	136.40	175.94	1	30	70	169	1,509
0-5 Years	276	177.41	228.69	1	30	86	224	1,509
6-11 Years	628	136.61	164.07	1	30	75	181	1,275
12-17 Years	752	121.18	160.44	1	30	62	138	1,199
18-49 Years	8,562	90.74	134.90	1	30	30	90	1,762
50+ Years	1,600	138.20	182.64	1	30	78	164	1,658
50-59 Years	919	140.69	186.85	1	30	74	168	1,658
60+ Years	681	134.84	176.89	1	30	83	158	1,260

**Table 7a. Descriptive Statistics of the Length of All Gaps Between Hydroxyurea Exposure Episodes in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days**

<b>Exposure</b>	<b>Total Gaps</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
Hydroxyurea	53,015	162.75	270.90	31	46	75	157	4,927

**Table 7b. Descriptive Statistics of the Length of All Gaps Between Hydroxyurea Exposure Episodes in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Age Group**

<b>Exposure</b>	<b>Total Gaps</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
Hydroxyurea	<b>53,015</b>	<b>162.75</b>	<b>270.90</b>	<b>31</b>	<b>46</b>	<b>75</b>	<b>157</b>	<b>4,927</b>
0-17 Years	7,689	136.29	268.58	31	42	63	117	4,699
0-5 Years	1,217	144.86	343.00	31	40	58	102	4,699
6-11 Years	3,006	125.75	252.42	31	41	60	104	3,915
12-17 Years	3,466	142.42	251.67	31	44	68	134	3,208
18-49 Years	40,686	172.09	276.45	31	48	81	171	4,927
50+ Years	4,640	124.66	213.22	31	41	61	115	3,549
50-59 Years	3,289	130.93	230.29	31	42	62	118	3,549
60+ Years	1,351	109.38	163.51	31	41	59	108	2,015

**Table 7c. Descriptive Statistics of the Length of All Gaps Between Hydroxyurea Exposure Episodes in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Race**

<b>Exposure</b>	<b>Total Gaps</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
Hydroxyurea	<b>53,015</b>	<b>162.75</b>	<b>270.90</b>	<b>31</b>	<b>46</b>	<b>75</b>	<b>157</b>	<b>4,927</b>
Unknown	12,648	144.07	270.08	31	43	67	130	4,757
American Indian/Alaska Native	141	130.01	152.59	31	46	86	132	1,080
Asian	73	191.99	321.24	31	46	86	187	2,471
Black/African American	39,176	169.33	272.11	31	48	79	168	4,927
Native Hawaiian/Other Pacific Islander	30	122.60	266.04	31	35	52	72	1,471
White	947	143.52	224.80	31	44	72	135	2,160

**Table 7d. Descriptive Statistics of the Length of All Gaps Between Hydroxyurea Exposure Episodes in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Year**

<b>Exposure</b>	<b>Total Gaps</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
Hydroxyurea	<b>53,015</b>	<b>162.75</b>	<b>270.90</b>	<b>31</b>	<b>46</b>	<b>75</b>	<b>157</b>	<b>4,927</b>
2000	406	201.79	350.56	31	46	80	188	2,671
2001	671	166.85	351.65	31	43	67	153	4,757
2002	625	180.00	356.95	31	45	73	167	4,927
2003	555	197.33	443.09	31	46	76	185	4,765
2004	631	171.44	303.69	31	47	75	153	3,223
2005	379	172.48	363.09	31	44	71	141	3,216
2006	524	213.40	515.31	31	44	66	142	4,699
2007	813	179.81	385.94	31	45	68	137	3,549
2008	1,459	158.60	312.18	31	44	68	126	3,117
2009	1,593	153.96	311.59	31	43	67	131	3,791
2010	11,707	163.26	273.42	31	47	76	154	3,562
2011	8,807	175.69	283.54	31	47	81	172	3,311
2012	5,613	172.45	278.28	31	47	77	168	2,772
2013	4,604	176.53	277.11	31	47	81	177	2,650
2014	3,987	164.64	234.06	31	47	76	171	2,148
2015	3,529	146.94	203.15	31	46	75	150	1,840
2016	2,679	140.07	176.42	31	46	72	152	1,617
2017	2,048	130.70	149.64	31	46	74	146	1,261
2018	1,341	114.22	108.89	31	46	72	139	829
2019	877	94.18	78.09	31	44	65	114	567
2020	167	65.44	35.85	31	40	55	78	286

**Table 7e. Descriptive Statistics of the Length of All Gaps Between Hydroxyurea Exposure Episodes in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Year Group and Age Group**

<b>Exposure</b>	<b>Total Gaps</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
<b>Hydroxyurea</b>	<b>53,015</b>	<b>162.75</b>	<b>270.90</b>	<b>31</b>	<b>46</b>	<b>75</b>	<b>157</b>	<b>4,927</b>
<b>2000 - 2005</b>	3,267	180.42	362.59	31	45	73	159	4,927
0-17 Years	1,545	156.48	309.99	31	44	68	142	4,500
0-5 Years	121	270.53	654.37	31	44	62	168	4,500
6-11 Years	596	133.32	238.98	31	43	68	131	3,223
12-17 Years	828	156.48	271.84	31	45	70	146	3,159
18-49 Years	1,681	204.07	406.97	31	47	79	182	4,927
50+ Years	41	113.10	136.74	32	44	54	100	594
50-59 Years	27	144.59	160.19	32	46	60	151	594
60+ Years	14	52.36	13.42	36	40	51.5	62	81
<b>2006 - 2010</b>	16,096	164.39	298.41	31	46	74	149	4,699
0-17 Years	2,654	139.38	298.14	31	42	62	113	4,699
0-5 Years	474	133.46	337.53	31	40	59	94	4,699
6-11 Years	1,081	132.88	301.80	31	41	56	102	3,915
12-17 Years	1,099	148.33	275.60	31	46	69	135	3,208
18-49 Years	12,138	174.85	304.58	31	48	80	164	4,453
50+ Years	1,304	117.85	224.56	31	40	59	102	3,549
50-59 Years	1,044	120.78	233.65	31	41	60	104	3,549
60+ Years	260	106.10	183.48	31	38	57	90	2,015
<b>2011 - 2015</b>	26,540	169.67	264.91	31	47	79	169	3,311
0-17 Years	2,523	135.82	247.49	31	42	62	117	2,958
0-5 Years	492	136.75	258.24	31	40	57	103	2,072
6-11 Years	951	121.57	235.18	31	40	58	96	2,958
12-17 Years	1,080	147.95	252.57	31	45	70	143	2,607
18-49 Years	21,571	177.48	269.74	31	48	83	181	3,311
50+ Years	2,446	135.71	232.00	31	41	63	127	2,940
50-59 Years	1,726	144.38	250.32	31	42	66	137	2,940
60+ Years	720	114.93	179.11	31	41	59	110	1,969

**Table 7e. Descriptive Statistics of the Length of All Gaps Between Hydroxyurea Exposure Episodes in the Sentinel Distributed Database (SDD) between January 1, 2000 and December 31, 2020, in Days, by Year Group and Age Group**

<b>Exposure</b>	<b>Total Gaps</b>	<b>Mean</b>	<b>Standard Deviation</b>	<b>Min</b>	<b>Q1</b>	<b>Median</b>	<b>Q3</b>	<b>Max</b>
<b>2016 - 2020</b>	7,112	125.09	146.63	31	45	71	140	1,617
0-17 Years	967	96.77	119.26	31	41	60	101	1,316
0-5 Years	130	100.19	146.83	31	41	58.5	98	1,189
6-11 Years	378	103.96	129.18	31	41	60	102	1,132
12-17 Years	459	89.88	100.47	31	40	60	103	1,316
18-49 Years	5,296	133.67	153.94	31	47	76	154	1,617
50+ Years	849	103.81	119.57	31	42	62	112	992
50-59 Years	492	104.54	126.85	31	42	61	106	992
60+ Years	357	102.80	108.90	31	42	64	116	896



**Appendix A. Start and End Dates for Each Data Partner as of Request Distribution Date (July 27, 2021)**

Masked ID	DP Start Date <sup>1</sup>	DP End Date <sup>1</sup>
DP01	01/01/2008	12/31/2020
DP02	01/01/2007	10/31/2020
DP03	01/01/2006	08/31/2020
DP04	01/01/2000	12/31/2018
DP05	01/01/2000	07/31/2019
DP06	01/01/2008	08/31/2020
DP07	01/01/2010	09/30/2020

<sup>1</sup>Start and end dates are based on the minimum and maximum dates within each DP. The month with the maximum date must have at least 80% of the number of records in the previous month.

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

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<b>Generic Name</b>	<b>Brand Name</b>
	<b>Hydroxyurea</b>
hydroxyurea	Hydrea
hydroxyurea	Droxia
hydroxyurea	hydroxyurea
hydroxyurea	Mylocel
hydroxyurea	Siklos

**Appendix C. List of Healthcare Common Procedure Coding System (HCPCS) Codes Used to Define Exposures in this Request**

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<b>Code</b>	<b>Description</b>	<b>Code Type</b>	<b>Code Category</b>
<b>Hydroxyurea</b>			
S0176	Hydroxyurea, oral, 500 mg	HCPCS	Procedure

**Appendix D. List of International Classification of Diseases, Ninth and Tenth Revisions, Clinical Modification (ICD-9-CM and ICD-10-CM) Diagnosis Codes Used to Define Inclusion/Exclusion Criteria in this Request**

Code	Description	Code Type	Code Category
<b>Sickle Cell Disease (SCD) Diagnosis Codes</b>			
282.6	Sickle-cell disease	ICD-9-CM	Diagnosis
282.60	Sickle-cell disease, unspecified	ICD-9-CM	Diagnosis
282.61	Hb-SS disease without crisis	ICD-9-CM	Diagnosis
282.62	Hb-SS disease with crisis	ICD-9-CM	Diagnosis
282.63	Sickle-cell/Hb-C disease without crisis	ICD-9-CM	Diagnosis
282.64	Sickle-cell/Hb-C disease with crisis	ICD-9-CM	Diagnosis
282.68	Other sickle-cell disease without crisis	ICD-9-CM	Diagnosis
282.69	Other sickle-cell disease with crisis	ICD-9-CM	Diagnosis
D57.0	Hb-SS disease with crisis	ICD-10-CM	Diagnosis
D57.00	Hb-SS disease with crisis, unspecified	ICD-10-CM	Diagnosis
D57.01	Hb-SS disease with acute chest syndrome	ICD-10-CM	Diagnosis
D57.02	Hb-SS disease with splenic sequestration	ICD-10-CM	Diagnosis
D57.03	Hb-SS disease with cerebral vascular involvement	ICD-10-CM	Diagnosis
D57.09	Hb-SS disease with crisis with other specified complication	ICD-10-CM	Diagnosis
D57.1	Sickle-cell disease without crisis	ICD-10-CM	Diagnosis
D57.2	Sickle-cell/Hb-C disease	ICD-10-CM	Diagnosis
D57.20	Sickle-cell/Hb-C disease without crisis	ICD-10-CM	Diagnosis
D57.21	Sickle-cell/Hb-C disease with crisis	ICD-10-CM	Diagnosis
D57.211	Sickle-cell/Hb-C disease with acute chest syndrome	ICD-10-CM	Diagnosis
D57.212	Sickle-cell/Hb-C disease with splenic sequestration	ICD-10-CM	Diagnosis
D57.213	Sickle-cell/Hb-C disease with cerebral vascular involvement	ICD-10-CM	Diagnosis
D57.218	Sickle-cell/Hb-C disease with crisis with other specified complication	ICD-10-CM	Diagnosis
D57.219	Sickle-cell/Hb-C disease with crisis, unspecified	ICD-10-CM	Diagnosis
D57.8	Other sickle-cell disorders	ICD-10-CM	Diagnosis
D57.80	Other sickle-cell disorders without crisis	ICD-10-CM	Diagnosis
D57.81	Other sickle-cell disorders with crisis	ICD-10-CM	Diagnosis
D57.811	Other sickle-cell disorders with acute chest syndrome	ICD-10-CM	Diagnosis
D57.812	Other sickle-cell disorders with splenic sequestration	ICD-10-CM	Diagnosis
D57.813	Other sickle-cell disorders with cerebral vascular involvement	ICD-10-CM	Diagnosis
D57.818	Other sickle-cell disorders with crisis with other specified complication	ICD-10-CM	Diagnosis
D57.819	Other sickle-cell disorders with crisis, unspecified	ICD-10-CM	Diagnosis
<b>Specific Cancers which may be Treated with Hydroxyurea Diagnosis Codes</b>			
171.0	Malignant neoplasm of connective and other soft tissue of head, face, and neck	ICD-9-CM	Diagnosis
173.42	Squamous cell carcinoma of scalp and skin of neck	ICD-9-CM	Diagnosis
173.92	Squamous cell carcinoma of skin, site unspecified	ICD-9-CM	Diagnosis
192.1	Malignant neoplasm of cerebral meninges	ICD-9-CM	Diagnosis
192.3	Malignant neoplasm of spinal meninges	ICD-9-CM	Diagnosis
195.0	Malignant neoplasm of head, face, and neck	ICD-9-CM	Diagnosis
205.1	Chronic myeloid leukemia	ICD-9-CM	Diagnosis
205.10	Chronic myeloid leukemia, without mention of having achieved remission	ICD-9-CM	Diagnosis
205.11	Chronic myeloid leukemia in remission	ICD-9-CM	Diagnosis
205.12	Chronic myeloid leukemia, in relapse	ICD-9-CM	Diagnosis
238.4	Neoplasm of uncertain behavior of polycythemia vera	ICD-9-CM	Diagnosis
238.71	Essential thrombocythemia	ICD-9-CM	Diagnosis

**Appendix D. List of International Classification of Diseases, Ninth and Tenth Revisions, Clinical Modification (ICD-9-CM and ICD-10-CM) Diagnosis Codes Used to Define Inclusion/Exclusion Criteria in this Request**

<b>Code</b>	<b>Description</b>	<b>Code Type</b>	<b>Code Category</b>
289.0	Polycythemia, secondary	ICD-9-CM	Diagnosis
289.6	Familial polycythemia	ICD-9-CM	Diagnosis
C44.42	Squamous cell carcinoma of skin of scalp and neck	ICD-10-CM	Diagnosis
C44.92	Squamous cell carcinoma of skin, unspecified	ICD-10-CM	Diagnosis
C49.0	Malignant neoplasm of connective and soft tissue of head, face and neck	ICD-10-CM	Diagnosis
C70	Malignant neoplasm of meninges	ICD-10-CM	Diagnosis
C70.0	Malignant neoplasm of cerebral meninges	ICD-10-CM	Diagnosis
C70.1	Malignant neoplasm of spinal meninges	ICD-10-CM	Diagnosis
C70.9	Malignant neoplasm of meninges, unspecified	ICD-10-CM	Diagnosis
C76.0	Malignant neoplasm of head, face and neck	ICD-10-CM	Diagnosis
C92.1	Chronic myeloid leukemia, BCR/ABL-positive	ICD-10-CM	Diagnosis
C92.10	Chronic myeloid leukemia, BCR/ABL-positive, not having achieved remission	ICD-10-CM	Diagnosis
C92.11	Chronic myeloid leukemia, BCR/ABL-positive, in remission	ICD-10-CM	Diagnosis
C92.12	Chronic myeloid leukemia, BCR/ABL-positive, in relapse	ICD-10-CM	Diagnosis
C92.2	Atypical chronic myeloid leukemia, BCR/ABL-negative	ICD-10-CM	Diagnosis
C92.20	Atypical chronic myeloid leukemia, BCR/ABL-negative, not having achieved	ICD-10-CM	Diagnosis
C92.21	Atypical chronic myeloid leukemia, BCR/ABL-negative, in remission	ICD-10-CM	Diagnosis
C92.22	Atypical chronic myeloid leukemia, BCR/ABL-negative, in relapse	ICD-10-CM	Diagnosis
D45	Polycythemia vera	ICD-10-CM	Diagnosis
D47.3	Essential (hemorrhagic) thrombocythemia	ICD-10-CM	Diagnosis

**Appendix E. Specifications Defining Parameters for this Request**

This report executed the Cohort Identification and Descriptive Analysis (CIDA) tool [10.3.3] to examine the use of hydroxyurea among patients with sickle cell disease in the Sentinel Distributed Database (SDD).

**Query period:** 01/01/2000 - current data completeness  
**Coverage requirement:** Medical & Drug Coverage  
**Pre-index enrollment requirement:** 183 days  
**Post-index enrollment requirement:** 0 days  
**Enrollment gap:** 45 days  
**Age groups:** 0-5, 6-11, 12-17, 18-49, 50-59, 60+; collapsed 0-17, 50+ years  
**Stratifications:** Age Group, Calendar Year, Race, Year- Age Group

Scenario	Exposure				Inclusion/Exclusion Criteria								
	Index Exposure	Cohort definition	Incident exposure washout period	Treatment episode gap	Censor treatment episode at evidence of:	Inclusion/Exclusion group	Criteria	Care setting	Principal diagnosis position	Evaluation period start	Evaluation period end	Exclude evidence of days supply if inclusion/exclusion evaluation period includes dispensings	Number of instances the criteria should be found in evaluation period
1	Hydroxyurea	Include all valid exposure episodes during query period	0 days	30 days	Death; DP end date; Query end date;	Sickle cell disease	Inclusion	Any care setting	Any	All patient history	0 days	N/A	1
						Specified cancers potentially treated with hydroxyurea <sup>1</sup>	Exclusion	Any care setting	Any	-183 days	0 days	N/A	1

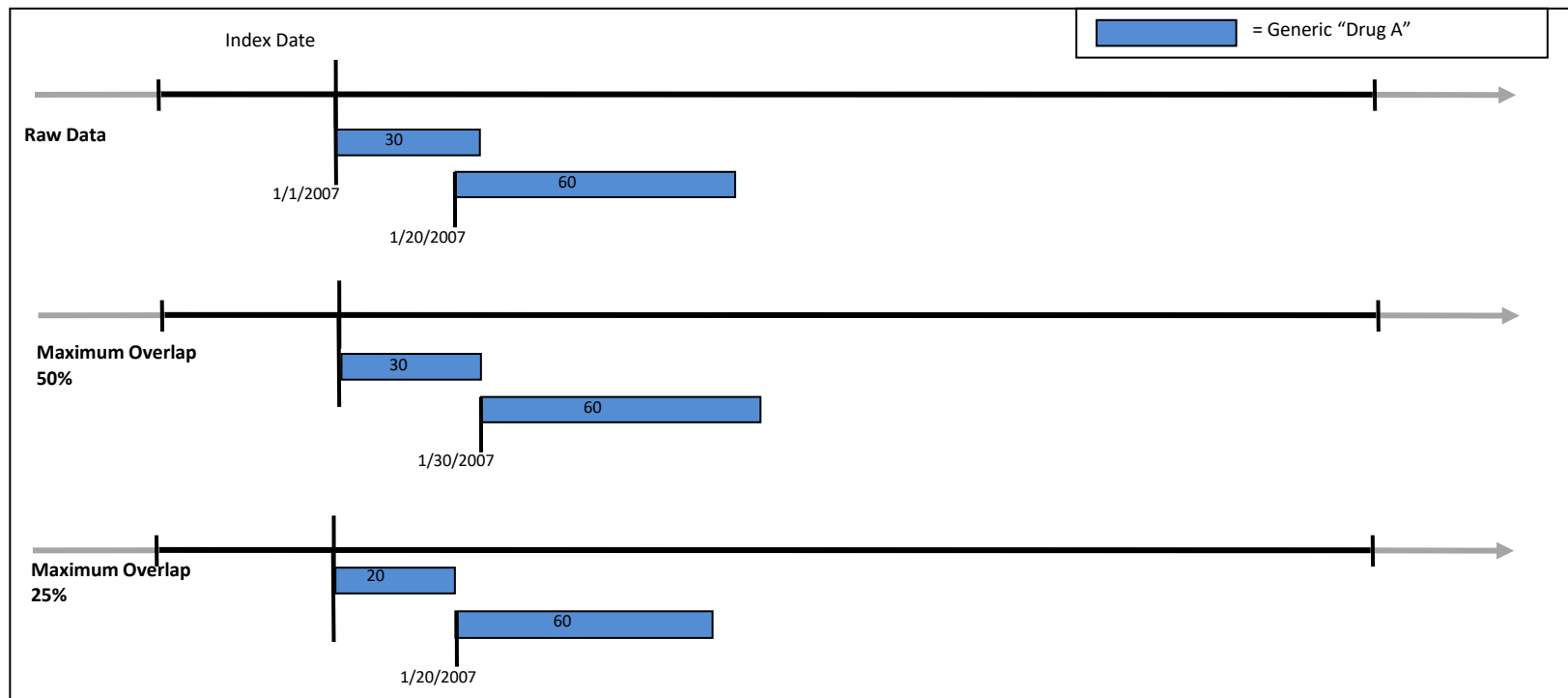
<sup>1</sup>See Appendix D for a list of codes used to define specified cancers for which hydroxyurea may have been used to treat.

International Classification of Diseases, Ninth Revision (ICD-9), International Classification of Diseases, Tenth Revision (ICD-10), Healthcare Common Procedure Coding System (HCPCS), and Current Procedural Terminology, Fourth Edition (CPT-4) codes are provided by Optum360. National Drug Codes (NDC) codes are checked against First Data Bank's "FDB MedKnowledge®."

Appendix F. Specifications for Stockpiling

Stockpiling

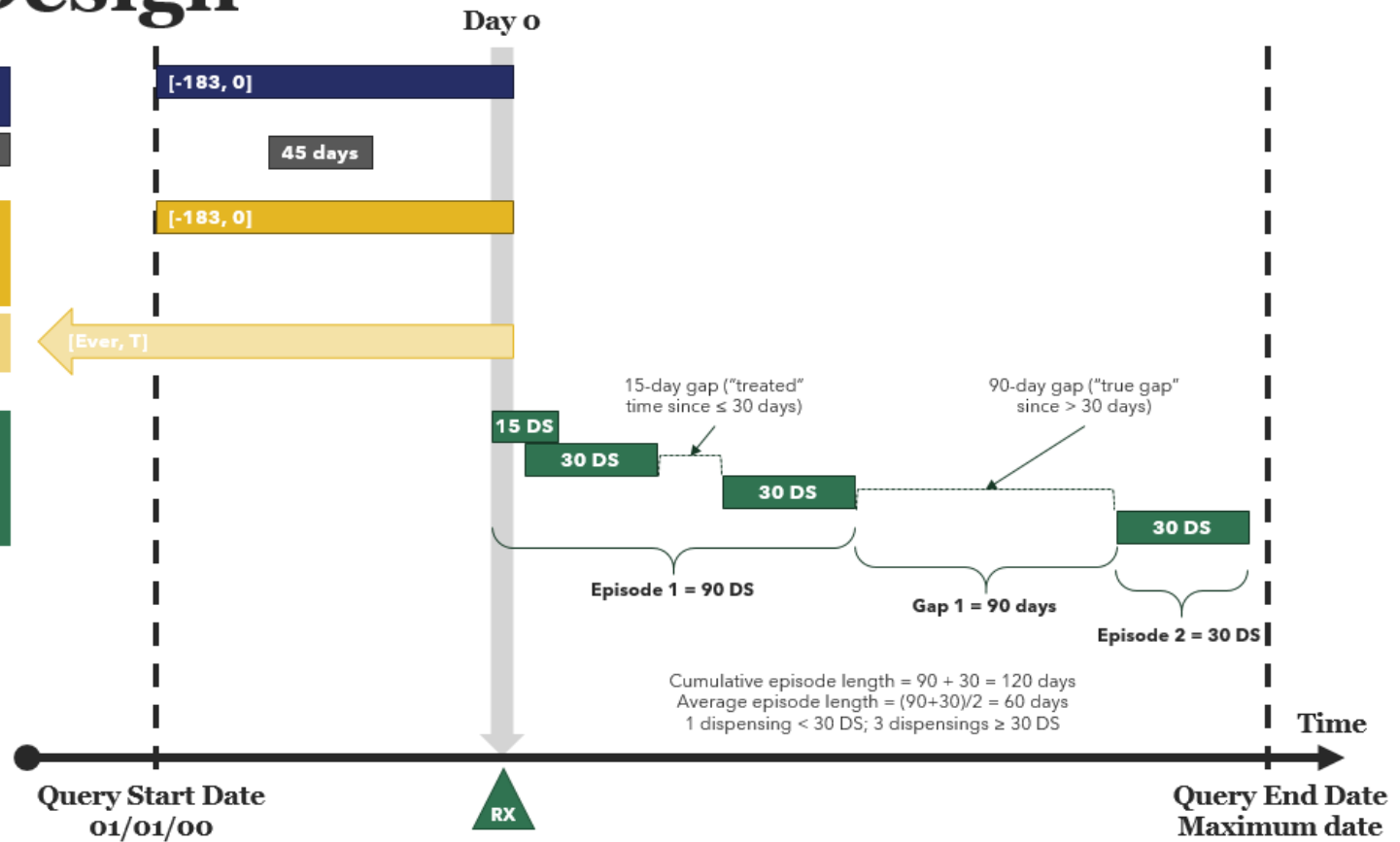
Group	Stockpiling group	Same day dispensing processing for days supplied	Same day dispensing processing for amount supplied	Range of allowable days supplied values	Range of allowable amount supplied values	Overlap percentage*
hydroxyurea	Default: stockpiling by generic name	Default: Adds all days supplied values for dispensings in the same stockgroup on the same day	Default: Adds all amount values for dispensings in the same stockgroup on the same day	Default: Does not consider days supplied values of 0 or less	Default: Does not consider days supplied values of 0 or less	50%



# Type 5 Design

## Hydroxyurea Dispensing

- Enrollment requirement**  
Medical & drug coverage
- Allowed coverage gap**  
45 days
- Exclusion criteria**  
[-183, 0]  
  - Chronic myeloid leukemia
  - Advanced squamous cell carcinoma of the head and neck
- Inclusion criteria**  
[Ever, T]  
  - Sickle cell disease
- Episode length**  
Truncated at earliest of:
  - Gap > 30 days
  - Disenrollment
  - Data completeness date
  - Death



DS = Days supplied