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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_wp050_nsdp_v02

Request ID: cder_mpl1r_wp050_nsdp_v02

Request Description: This report contains estimates of the number of new pediatric users of leuprolide acetate depot, both with and without prior indication for centralized precocious puberty (CPP), and the length of their follow-up time within the Sentinel Distributed Database (SDD).

Sentinel Modular Program Tool Used: Cohort Identification and Descriptive Analysis (CIDA) tool, version 3.3.6

Data Source: Data from January 1, 2000 to the most recent available data from 16 Data Partners contributing to the SDD were included in this report. This request was distributed on April 4, 2017. See Appendix A for a list of dates of available data for each Data Partner.

Study Design: This request was designed to identify exposures and follow-up time. The number of eligible members and member-days with the exposures of interest were calculated.

Exposure of Interest: The exposure of interest was defined as use of leuprolide acetate depot. This was defined using National Drug Codes (NDCs) and Healthcare Common Procedure Coding System (HCPCS) codes. Please refer to Appendix B for generic and brand names of drugs and procedure codes used to define the exposure.

Cohort Eligibility Criteria: Patients were required to be continuously enrolled in plans with both medical and drug coverage for at least six months (183 days) before their index date, during which gaps in coverage of up to 45 days were allowed. Members with no evidence of use of leuprolide acetate depot within six months (183 days) prior to the leuprolide acetate depot use of interest were included (i.e., new users). For evaluation of all leuprolide acetate depot pediatric users with prior indication for CPP, members were included in the cohort if 1) they had a diagnosis of CPP in the six months (183 days) prior to an exposure episode or 2) if they had a diagnosis of CPP in the six months (183 days) prior to their first exposure episode. The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Edition, Clinical Modification (ICD-10-CM) codes defining CPP indication criteria can be found in Appendix C. The following age groups were included in the cohort: 0-4, 5-6, 7-8, 9-10, 11-12, and 13-18 years.

Follow-Up Time: Follow-up began on the day on which the first exposure of interest started and continued until end of enrollment. Follow-up time was categorized into these categories: <2, 2-<4, 4-<6, 6-<8, 8-<10, 10-<12, 12-<14, 14-<16, and ≥16 years. For a more detailed explanation of how the number of patients for each follow-up time category was determined by scenario comparison, please see Appendix D.

Please refer to Appendix E for detailed specifications of parameters used for this request.

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

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

Amount Supplied - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing. This is equivalent to the "RxAmt" value in the Sentinel Common Data Model.

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). 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: (1) 01: Cohort includes only the first valid treatment episode during the query period; (2) 02: Cohort includes all valid treatment episodes during the query period; (3) 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.

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

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

Event Deduplication - specifies how events are counted by the MP algorithm: (0) 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 (pre-existing condition) - 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.

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 Care Setting/PDX parameter.

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

Treatment Episode Truncation Indicator - indicates whether observation of the incident query code during follow-up requires truncation of valid treatment episodes. A value of Y indicates that the treatment episodes should be truncated at the first occurrence of an incident query code. A value of N indicates that the treatment episodes should not be truncated at the occurrence of the incident query code.

Users - number of members with exposure during the query period. Member must have no evidence of exposure(s) of interest (defined by incidence criteria) in the prior washout period. A user may only be counted once in a query period.

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

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

Tables 1-3. Summary of Follow-Up Time for New Users of Pediatric Leuprolide Acetate Depot in the Sentinel Distributed Database (SDD) between January 1, 2000 and the Most Recent Available Data, by Age Group and Sex

Table 1. Follow-up Time by Age, Female

Age at first exposure (years)	Individuals with follow-up (n):								
	<2 years	2-<4 years	4-<6 years	6-<8 years	8-<10 years	10-<12 years	12-<14 years	14-<16 years	≥16 years
0-4	116	53	39	22	16	5	2	0	0
5-6	234	107	50	30	24	16	1	4	0
7-8	874	410	220	106	63	23	11	5	0
9-10	527	286	120	79	42	14	6	7	0
11-12	165	79	50	28	17	12	6	4	0
13-18	586	276	168	77	29	15	6	2	0

Table 2. Follow-up Time by Age, Male

Age at first exposure (years)	Individuals with follow-up (n):								
	<2 years	2-<4 years	4-<6 years	6-<8 years	8-<10 years	10-<12 years	12-<14 years	14-<16 years	≥16 years
0-4	18	11	7	1	2	0	0	0	0
5-6	26	12	7	3	1	1	0	0	0
7-8	105	55	23	21	13	2	1	1	0
9-10	206	111	51	29	16	3	1	2	0
11-12	187	82	52	30	11	2	2	1	0
13-18	233	123	79	40	10	2	2	1	0

Table 3. Follow-up Time by Age, Ambiguous or Unknown Sex

Age at first exposure (years)	Individuals with follow-up (n):								
	<2 years	2-<4 years	4-<6 years	6-<8 years	8-<10 years	10-<12 years	12-<14 years	14-<16 years	≥16 years
0-4	0	0	0	0	0	0	0	0	0
5-6	0	0	0	0	0	0	0	0	0
7-8	0	0	0	0	0	0	0	0	0
9-10	0	0	0	0	0	0	0	0	0
11-12	0	0	0	0	0	0	0	0	0
13-18	1	0	1	0	0	0	0	0	0

Tables 4-6. Summary of New Users of Pediatric Leuprolide Acetate Depot with an Indication for Centralized Precocious Puberty (CPP) in the Sentinel Distributed Database (SDD) between January 1, 2000 and the Most Recent Available Data, by Age Group and Sex

Table 4. New Users of Pediatric Leuprolide Acetate Depot with an Indication for Centralized Precocious Puberty - Female

Age at first exposure (years)	Total exposed (n)	Individuals with diagnosis for CPP, Prior to <u>Any</u> Exposure:		Individuals with diagnosis for CPP, Prior to <u>First</u> Exposure:	
		(n)	Proportion of Patients over Total Exposed (%)	(n)	Proportion of Patients over Total Exposed (%)
0-4	253	238	94.1%	233	92.1%
5-6	466	445	95.5%	438	94.0%
7-8	1,712	1,669	97.5%	1,642	95.9%
9-10	1,081	971	89.8%	926	85.7%
11-12	361	182	50.4%	166	46.0%
13-18	1,159	60	5.2%	55	4.7%

Table 5. New Users of Pediatric Leuprolide Acetate Depot with an Indication for Centralized Precocious Puberty - Male

Age at first exposure (years)	Total exposed (n)	Individuals with diagnosis for CPP, Prior to <u>Any</u> Exposure:		Individuals with diagnosis for CPP, Prior to <u>First</u> Exposure:	
		(n)	Proportion of Patients over Total Exposed (%)	(n)	Proportion of Patients over Total Exposed (%)
0-4	39	27	69.2%	27	69.2%
5-6	50	49	98.0%	49	98.0%
7-8	221	209	94.6%	204	92.3%
9-10	419	381	90.9%	369	88.1%
11-12	367	255	69.5%	247	67.3%
13-18	490	96	19.6%	88	18.0%

Tables 4-6. Summary of New Users of Pediatric Leuprolide Acetate Depot with an Indication for Centralized Precocious Puberty (CPP) in the Sentinel Distributed Database (SDD) between January 1, 2000 and the Most Recent Available Data, by Age Group and Sex

Table 6. New Users of Pediatric Leuprolide Acetate Depot with an Indication for Centralized Precocious Puberty - Ambiguous or Unknown Sex

Age at first exposure (years)	Total exposed (n)	Individuals with diagnosis for CPP, Prior to <u>Any</u> Exposure:		Individuals with diagnosis for CPP, Prior to <u>First</u> Exposure:	
		(n)	Proportion of Patients over Total Exposed (%)	(n)	Proportion of Patients over Total Exposed (%)
0-4	0	0	---	0	---
5-6	0	0	---	0	---
7-8	0	0	---	0	---
9-10	0	0	---	0	---
11-12	0	0	---	0	---
13-18	2	0	0%	0	0%

Table 7. Summary of Follow-Up Time for New Users of Pediatric Leuprolide Acetate Depot in the Sentinel Distributed Database (SDD) between January 1, 2000 and the Most Recent Available Data for Users 18 Years of Age and Younger

	New Users	Eligible Members	Member-Years	New Users / 1K Eligible Members
Total Leuprolide Acetate Depot Users	6,620	32,374,572	84,752,022.6	0.20
Leuprolide Acetate Depot Users with 2 or More Years of Follow-Up	3,342	32,374,572	84,753,163.8	0.10
Leuprolide Acetate Depot Users with 4 or More Years of Follow-Up	1,737	32,374,572	84,755,398.9	0.05
Leuprolide Acetate Depot Users with 6 or More Years of Follow-Up	870	32,374,572	84,757,940.5	0.03
Leuprolide Acetate Depot Users with 8 or More Years of Follow-Up	404	32,374,572	84,759,961.0	0.01
Leuprolide Acetate Depot Users with 10 or More Years of Follow-Up	160	32,374,572	84,761,359.0	0.00
Leuprolide Acetate Depot Users with 12 or More Years of Follow-Up	65	32,374,572	84,761,978.1	0.00
Leuprolide Acetate Depot Users with 14 or More Years of Follow-Up	27	32,374,572	84,762,212.9	0.00
Leuprolide Acetate Depot Users with 16 or More Years of Follow-Up	0	32,374,572	84,762,393.0	0.00
Leuprolide Acetate Depot Users with Centralized Precocious Puberty (CPP) in 6 Months Prior to At Least One Exposure	4,582	143,824	93,091.8	31.86
Leuprolide Acetate Depot Users with Centralized Precocious Puberty (CPP) in 6 Months Prior to First Exposure	4,444	142,235	91,867.6	31.24

Table 8. Summary of Follow-Up Time for New Users of Pediatric Leuprolide Acetate Depot in the Sentinel Distributed Database (SDD) between January 1, 2000 and the Most Recent Available Data, by Age Group

	New Users	Eligible Members	Member-Years	New Users / 1K Eligible Members
Total Leuprolide Acetate Depot Users				
0-4 Years	292	10,998,431	18,457,329.7	0.03
5-6 Years	516	7,634,207	8,783,964.2	0.07
7-8 Years	1,933	7,826,526	9,051,881.1	0.25
9-10 Years	1,500	7,973,150	9,280,340.4	0.19
11-12 Years	728	8,097,205	9,504,914.7	0.09
13-18 Years	1,651	14,765,354	29,673,592.5	0.11
Leuprolide Acetate Depot Users with 2 or More Years of Follow-Up				
0-4 Years	158	10,998,431	18,457,357.4	0.01
5-6 Years	256	7,634,237	8,784,008.2	0.03
7-8 Years	954	7,826,611	9,052,034.5	0.12
9-10 Years	767	7,973,420	9,280,560.3	0.10
11-12 Years	376	8,097,445	9,505,100.0	0.05
13-18 Years	831	14,765,565	29,674,103.5	0.06
Leuprolide Acetate Depot Users with 4 or More Years of Follow-Up				
0-4 Years	94	10,998,431	18,457,404.7	0.01
5-6 Years	137	7,634,278	8,784,090.9	0.02
7-8 Years	489	7,826,724	9,052,265.7	0.06
9-10 Years	370	7,973,786	9,281,047.8	0.05
11-12 Years	215	8,097,983	9,505,619.4	0.03
13-18 Years	432	14,765,903	29,674,970.4	0.03
Leuprolide Acetate Depot Users with 6 or More Years of Follow-Up				
0-4 Years	48	10,998,431	18,457,457.8	0.00
5-6 Years	80	7,634,315	8,784,163.8	0.01
7-8 Years	246	7,826,800	9,052,426.4	0.03
9-10 Years	199	7,974,033	9,281,437.8	0.02
11-12 Years	113	8,098,409	9,506,235.7	0.01
13-18 Years	184	14,766,297	29,676,218.9	0.01
Leuprolide Acetate Depot Users with 8 or More Years of Follow-Up				
0-4 Years	25	10,998,431	18,457,470.9	0.00
5-6 Years	47	7,634,333	8,784,207.8	0.01
7-8 Years	119	7,826,844	9,052,522.1	0.02
9-10 Years	91	7,974,170	9,281,674.7	0.01
11-12 Years	55	8,098,664	9,506,655.6	0.01
13-18 Years	67	14,766,606	29,677,430.0	0.00
Leuprolide Acetate Depot Users with 10 or More Years of Follow-Up				
0-4 Years	7	10,998,431	18,457,483.2	0.00
5-6 Years	22	7,634,349	8,784,238.4	0.00
7-8 Years	43	7,826,881	9,052,585.1	0.01
9-10 Years	33	7,974,256	9,281,813.4	0.00
11-12 Years	27	8,098,828	9,506,915.6	0.00
13-18 Years	28	14,766,799	29,678,323.4	0.00
Leuprolide Acetate Depot Users with 12 or More Years of Follow-Up				



Table 8. Summary of Follow-Up Time for New Users of Pediatric Leuprolide Acetate Depot in the Sentinel Distributed Database (SDD) between January 1, 2000 and the Most Recent Available Data, by Age Group

	New Users	Eligible Members	Member-Years	New Users / 1K Eligible Members
0-4 Years	2	10,998,431	18,457,493.7	0.00
5-6 Years	5	7,634,354	8,784,248.6	0.00
7-8 Years	18	7,826,891	9,052,607.5	0.00
9-10 Years	16	7,974,293	9,281,863.9	0.00
11-12 Years	13	8,098,890	9,507,019.8	0.00
13-18 Years	11	14,766,876	29,678,744.6	0.00

Table 8. Summary of Follow-Up Time for New Users of Pediatric Leuprolide Acetate Depot in the Sentinel Distributed Database (SDD) between January 1, 2000 and the Most Recent Available Data, by Age Group

	New Users	Eligible Members	Member-Years	New Users / 1K Eligible Members
Leuprolide Acetate Depot Users with 14 or More Years of Follow-Up				
0-4 Years	0	10,998,431	18,457,493.7	0.00
5-6 Years	4	7,634,354	8,784,248.6	0.00
7-8 Years	6	7,826,892	9,052,609.5	0.00
9-10 Years	9	7,974,300	9,281,870.2	0.00
11-12 Years	5	8,098,912	9,507,058.9	0.00
13-18 Years	3	14,766,906	29,678,931.9	0.00
Leuprolide Acetate Depot Users with 16 or More Years of Follow-Up				
0-4 Years	0	10,998,431	18,457,493.7	0.00
5-6 Years	0	7,634,354	8,784,248.8	0.00
7-8 Years	0	7,826,893	9,052,611.5	0.00
9-10 Years	0	7,974,304	9,281,875.3	0.00
11-12 Years	0	8,098,929	9,507,086.2	0.00
13-18 Years	0	14,766,930	29,679,077.4	0.00
Leuprolide Acetate Depot Users with Centralized Precocious Puberty (CPP) in 6 Months Prior to At Least One Exposure				
0-4 Years	265	21,483	11,628.1	12.34
5-6 Years	494	22,116	10,242.1	22.34
7-8 Years	1,878	56,520	28,303.6	33.23
9-10 Years	1,352	49,127	23,507.7	27.52
11-12 Years	437	23,165	10,678.9	18.86
13-18 Years	156	17,391	8,731.4	8.97
Leuprolide Acetate Depot Users with Centralized Precocious Puberty (CPP) in 6 Months Prior to First Exposure				
0-4 Years	260	21,449	11,607.7	12.12
5-6 Years	487	22,046	10,199.1	22.09
7-8 Years	1,846	56,293	28,195.7	32.79
9-10 Years	1,295	48,546	23,231.0	26.68
11-12 Years	413	22,355	10,259.9	18.47
13-18 Years	143	16,879	8,374.2	8.47

Table 9. Summary of Follow-Up Time for New Users of Pediatric Leuprolide Acetate Depot in the Sentinel Distributed Database (SDD) between January 1, 2000 and the Most Recent Available Data for Users 18 Years of Age and Younger, by Sex

	New Users	Eligible Members	Member-Years	New Users / 1K Eligible Members
Total Leuprolide Acetate Depot Users				
Female	5,032	15,838,058	41,431,409.2	0.32
Male	1,586	16,534,660	43,317,716.4	0.10
Unknown	2	1,854	2,897.0	1.08
Leuprolide Acetate Depot Users with 2 or More Years of Follow-Up				
Female	2,530	15,838,058	41,432,302.3	0.16
Male	811	16,534,660	43,317,964.5	0.05
Unknown	1	1,854	2,897.0	0.54
Leuprolide Acetate Depot Users with 4 or More Years of Follow-Up				
Female	1,319	15,838,058	41,433,963.6	0.08
Male	417	16,534,660	43,318,538.3	0.03
Unknown	1	1,854	2,897.0	0.54
Leuprolide Acetate Depot Users with 6 or More Years of Follow-Up				
Female	672	15,838,058	41,435,822.2	0.04
Male	198	16,534,660	43,319,220.3	0.01
Unknown	0	1,854	2,897.9	0.00
Leuprolide Acetate Depot Users with 8 or More Years of Follow-Up				
Female	330	15,838,058	41,437,282.5	0.02
Male	74	16,534,660	43,319,780.6	0.00
Unknown	0	1,854	2,897.9	0.00
Leuprolide Acetate Depot Users with 10 or More Years of Follow-Up				
Female	139	15,838,058	41,438,403.2	0.01
Male	21	16,534,660	43,320,057.9	0.00
Unknown	0	1,854	2,897.9	0.00
Leuprolide Acetate Depot Users with 12 or More Years of Follow-Up				
Female	54	15,838,058	41,438,959.8	0.00
Male	11	16,534,660	43,320,120.4	0.00
Unknown	0	1,854	2,897.9	0.00
Leuprolide Acetate Depot Users with 14 or More Years of Follow-Up				
Female	22	15,838,058	41,439,162.9	0.00
Male	5	16,534,660	43,320,152.1	0.00
Unknown	0	1,854	2,897.9	0.00
Leuprolide Acetate Depot Users with 16 or More Years of Follow-Up				
Female	0	15,838,058	41,439,316.1	0.00
Male	0	16,534,660	43,320,179.0	0.00
Unknown	0	1,854	2,897.9	0.00
Leuprolide Acetate Depot Users with Centralized Precocious Puberty (CPP) in 6 Months Prior to At Least One Exposure				
Female	3,565	109,305	70,929.9	32.62
Male	1,017	34,515	22,160.0	29.47
Unknown	0	4	1.9	0.00
Leuprolide Acetate Depot Users with Centralized Precocious Puberty (CPP) in 6 Months Prior to First Exposure				
Female	3,460	108,034	69,992.6	32.03
Male	984	34,197	21,873.0	28.77
Unknown	0	4	1.9	0.00

Table 10. Summary of Follow-Up Time for New Users of Pediatric Leuprolide Acetate Depot in the Sentinel Distributed Database (SDD) between January 1, 2000 and the Most Recent Available Data for Users 18 Years of Age and Younger, by Year

	New Users	Eligible Members	Member- Years	New Users / 1K Eligible Members
Total Leuprolide Acetate Depot Users				
2000	26	1,979,209	896,562.9	0.01
2001	82	2,179,203	1,777,268.1	0.04
2002	71	2,202,170	1,777,131.7	0.03
2003	67	2,186,612	1,753,491.1	0.03
2004	120	2,285,775	1,806,833.0	0.05
2005	128	2,353,846	1,897,707.5	0.05
2006	235	5,279,338	3,209,290.5	0.04
2007	339	6,128,777	4,513,429.4	0.06
2008	571	11,445,570	7,054,143.0	0.05
2009	686	11,781,564	8,911,416.9	0.06
2010	666	11,083,022	8,472,359.3	0.06
2011	604	10,467,062	8,076,414.3	0.06
2012	631	10,261,243	7,829,619.8	0.06
2013	613	10,137,253	7,774,627.8	0.06
2014	683	9,977,847	7,597,788.4	0.07
2015	677	9,781,357	7,491,109.0	0.07
2016	421	7,574,869	3,912,253.3	0.06
2017	0	70,228	576.6	0.00
Leuprolide Acetate Depot Users with 2 or More Years of Follow-Up				
2000	17	1,979,209	896,562.9	0.01
2001	61	2,179,205	1,777,269.8	0.03
2002	53	2,202,180	1,777,136.5	0.02
2003	53	2,186,619	1,753,495.3	0.02
2004	92	2,285,787	1,806,839.3	0.04
2005	88	2,353,862	1,897,718.6	0.04
2006	172	5,279,363	3,209,303.0	0.03
2007	242	6,128,812	4,513,449.7	0.04
2008	371	11,445,633	7,054,177.1	0.03
2009	421	11,781,663	8,911,484.1	0.04
2010	386	11,083,179	8,472,459.2	0.03
2011	364	10,467,228	8,076,522.7	0.03
2012	383	10,261,414	7,829,730.1	0.04
2013	369	10,137,443	7,774,740.8	0.04
2014	270	9,978,056	7,597,917.1	0.03
2015	0	9,781,675	7,491,317.5	0.00
2016	0	7,575,331	3,912,463.4	0.00
2017	0	70,230	576.6	0.00

Table 10. Summary of Follow-Up Time for New Users of Pediatric Leuprolide Acetate Depot in the Sentinel Distributed Database (SDD) between January 1, 2000 and the Most Recent Available Data for Users 18 Years of Age and Younger, by Year

	New Users	Eligible Members	Member- Years	New Users / 1K Eligible Members
Leuprolide Acetate Depot Users with 4 or More Years of Follow-Up				
2000	12	1,979,209	896,562.9	0.01
2001	47	2,179,209	1,777,272.3	0.02
2002	42	2,202,190	1,777,142.4	0.02
2003	36	2,186,626	1,753,501.1	0.02
2004	76	2,285,811	1,806,850.7	0.03
2005	66	2,353,885	1,897,732.7	0.03
2006	128	5,279,389	3,209,319.3	0.02
2007	175	6,128,853	4,513,478.2	0.03
2008	243	11,445,701	7,054,223.9	0.02
2009	273	11,781,815	8,911,589.5	0.02
2010	248	11,083,415	8,472,632.9	0.02
2011	230	10,467,521	8,076,730.7	0.02
2012	161	10,261,714	7,829,948.8	0.02
2013	0	10,137,803	7,774,997.5	0.00
2014	0	9,978,562	7,598,285.2	0.00
2015	0	9,782,301	7,491,802.5	0.00
2016	0	7,575,862	3,912,751.8	0.00
2017	0	70,230	576.6	0.00
Leuprolide Acetate Depot Users with 6 or More Years of Follow-Up				
2000	11	1,979,209	896,562.9	0.01
2001	31	2,179,210	1,777,273.8	0.01
2002	26	2,202,204	1,777,149.7	0.01
2003	26	2,186,640	1,753,511.2	0.01
2004	59	2,285,830	1,806,864.9	0.03
2005	48	2,353,910	1,897,752.6	0.02
2006	93	5,279,428	3,209,349.6	0.02
2007	120	6,128,905	4,513,517.9	0.02
2008	183	11,445,780	7,054,282.2	0.02
2009	199	11,781,944	8,911,689.5	0.02
2010	74	11,083,595	8,472,774.3	0.01
2011	0	10,467,796	8,076,959.0	0.00
2012	0	10,262,138	7,830,300.1	0.00
2013	0	10,138,350	7,775,451.8	0.00
2014	0	9,979,100	7,598,739.9	0.00
2015	0	9,782,774	7,492,225.1	0.00
2016	0	7,576,213	3,912,959.4	0.00
2017	0	70,233	576.6	0.00

Table 10. Summary of Follow-Up Time for New Users of Pediatric Leuprolide Acetate Depot in the Sentinel Distributed Database (SDD) between January 1, 2000 and the Most Recent Available Data for Users 18 Years of Age and Younger, by Year

	New Users	Eligible Members	Member- Years	New Users / 1K Eligible Members
Leuprolide Acetate Depot Users with 8 or More Years of Follow-Up				
2000	8	1,979,209	896,562.9	0.00
2001	25	2,179,212	1,777,274.6	0.01
2002	24	2,202,207	1,777,150.9	0.01
2003	23	2,186,647	1,753,513.6	0.01
2004	45	2,285,836	1,806,870.7	0.02
2005	43	2,353,926	1,897,763.8	0.02
2006	77	5,279,447	3,209,365.2	0.01
2007	87	6,128,929	4,513,538.8	0.01
2008	72	11,445,827	7,054,317.7	0.01
2009	0	11,782,053	8,911,775.1	0.00
2010	0	11,083,858	8,472,980.1	0.00
2011	0	10,468,135	8,077,251.5	0.00
2012	0	10,262,497	7,830,625.9	0.00
2013	0	10,138,709	7,775,785.1	0.00
2014	0	9,979,429	7,599,048.8	0.00
2015	0	9,783,063	7,492,494.0	0.00
2016	0	7,576,408	3,913,065.7	0.00
2017	0	70,235	576.6	0.00
Leuprolide Acetate Depot Users with 10 or More Years of Follow-Up				
2000	6	1,979,209	896,562.9	0.00
2001	21	2,179,213	1,777,275.0	0.01
2002	22	2,202,209	1,777,151.9	0.01
2003	21	2,186,651	1,753,515.9	0.01
2004	38	2,285,843	1,806,876.1	0.02
2005	36	2,353,936	1,897,772.2	0.02
2006	15	5,279,459	3,209,378.3	0.00
2007	1	6,128,974	4,513,577.8	0.00
2008	0	11,445,936	7,054,402.9	0.00
2009	0	11,782,230	8,911,912.0	0.00
2010	0	11,084,051	8,473,145.4	0.00
2011	0	10,468,331	8,077,435.7	0.00
2012	0	10,262,700	7,830,814.5	0.00
2013	0	10,138,906	7,775,969.6	0.00
2014	0	9,979,610	7,599,219.8	0.00
2015	0	9,783,226	7,492,649.0	0.00
2016	0	7,576,500	3,913,123.5	0.00
2017	0	70,236	576.6	0.00

Table 10. Summary of Follow-Up Time for New Users of Pediatric Leuprolide Acetate Depot in the Sentinel Distributed Database (SDD) between January 1, 2000 and the Most Recent Available Data for Users 18 Years of Age and Younger, by Year

	New Users	Eligible Members	Member- Years	New Users / 1K Eligible Members
Leuprolide Acetate Depot Users with 12 or More Years of Follow-Up				
2000	5	1,979,209	896,562.9	0.00
2001	18	2,179,213	1,777,275.0	0.01
2002	14	2,202,210	1,777,152.8	0.01
2003	18	2,186,659	1,753,520.5	0.01
2004	10	2,285,853	1,806,884.9	0.00
2005	0	2,353,967	1,897,796.8	0.00
2006	0	5,279,508	3,209,415.4	0.00
2007	0	6,129,029	4,513,623.4	0.00
2008	0	11,446,004	7,054,460.2	0.00
2009	0	11,782,306	8,911,982.3	0.00
2010	0	11,084,133	8,473,220.8	0.00
2011	0	10,468,406	8,077,506.7	0.00
2012	0	10,262,767	7,830,879.8	0.00
2013	0	10,138,967	7,776,026.8	0.00
2014	0	9,979,666	7,599,272.2	0.00
2015	0	9,783,275	7,492,691.2	0.00
2016	0	7,576,509	3,913,129.7	0.00
2017	0	70,236	576.6	0.00
Leuprolide Acetate Depot Users with 14 or More Years of Follow-Up				
2000	4	1,979,209	896,562.9	0.00
2001	16	2,179,213	1,777,275.4	0.01
2002	7	2,202,212	1,777,154.3	0.00
2003	0	2,186,662	1,753,523.4	0.00
2004	0	2,285,864	1,806,894.2	0.00
2005	0	2,353,988	1,897,812.2	0.00
2006	0	5,279,534	3,209,437.3	0.00
2007	0	6,129,061	4,513,651.0	0.00
2008	0	11,446,037	7,054,491.4	0.00
2009	0	11,782,336	8,912,011.7	0.00
2010	0	11,084,162	8,473,247.3	0.00
2011	0	10,468,431	8,077,530.4	0.00
2012	0	10,262,787	7,830,898.3	0.00
2013	0	10,138,982	7,776,040.2	0.00
2014	0	9,979,677	7,599,280.6	0.00
2015	0	9,783,281	7,492,695.8	0.00
2016	0	7,576,509	3,913,129.7	0.00
2017	0	70,236	576.6	0.00

Table 10. Summary of Follow-Up Time for New Users of Pediatric Leuprolide Acetate Depot in the Sentinel Distributed Database (SDD) between January 1, 2000 and the Most Recent Available Data for Users 18 Years of Age and Younger, by Year

	New Users	Eligible Members	Member- Years	New Users / 1K Eligible Members
Leuprolide Acetate Depot Users with 16 or More Years of Follow-Up				
2000	0	1,979,209	896,562.9	0.00
2001	0	2,179,215	1,777,276.8	0.00
2002	0	2,202,221	1,777,160.4	0.00
2003	0	2,186,676	1,753,535.5	0.00
2004	0	2,285,883	1,806,908.5	0.00
2005	0	2,354,010	1,897,832.7	0.00
2006	0	5,279,556	3,209,458.8	0.00
2007	0	6,129,084	4,513,673.1	0.00
2008	0	11,446,061	7,054,514.8	0.00
2009	0	11,782,357	8,912,030.3	0.00
2010	0	11,084,180	8,473,263.0	0.00
2011	0	10,468,444	8,077,541.1	0.00
2012	0	10,262,797	7,830,906.0	0.00
2013	0	10,138,988	7,776,044.6	0.00
2014	0	9,979,680	7,599,281.9	0.00
2015	0	9,783,282	7,492,696.5	0.00
2016	0	7,576,509	3,913,129.7	0.00
2017	0	70,236	576.6	0.00
Leuprolide Acetate Depot Users with Centralized Precocious Puberty (CPP) in 6 Months Prior to At Least One Exposure				
2000	13	1,927	544.8	6.75
2001	42	2,717	1,076.6	15.46
2002	42	2,898	1,130.0	14.49
2003	31	3,040	1,199.3	10.20
2004	69	3,293	1,298.4	20.95
2005	82	3,302	1,274.8	24.83
2006	153	7,309	2,434.9	20.93
2007	234	9,935	3,665.2	23.55
2008	402	20,095	6,712.6	20.00
2009	493	24,913	9,669.9	19.79
2010	471	25,217	9,856.0	18.68
2011	451	25,342	9,927.5	17.80
2012	468	25,910	10,119.9	18.06
2013	465	26,191	10,218.3	17.75
2014	491	26,844	10,468.2	18.29
2015	432	25,149	10,031.4	17.18
2016	243	12,529	3,463.6	19.40
2017	0	47	0.4	0.00

Table 10. Summary of Follow-Up Time for New Users of Pediatric Leuprolide Acetate Depot in the Sentinel Distributed Database (SDD) between January 1, 2000 and the Most Recent Available Data for Users 18 Years of Age and Younger, by Year

	New Users	Eligible Members	Member- Years	New Users / 1K Eligible Members
Leuprolide Acetate Depot Users with Centralized Precocious Puberty (CPP) in 6 Months Prior to First Exposure				
2000	12	1,911	540.8	6.28
2001	40	2,685	1,063.8	14.90
2002	39	2,859	1,117.9	13.64
2003	29	3,011	1,188.3	9.63
2004	67	3,265	1,290.3	20.52
2005	80	3,266	1,263.1	24.49
2006	148	7,249	2,418.5	20.42
2007	228	9,837	3,628.6	23.18
2008	382	19,788	6,626.1	19.30
2009	473	24,419	9,484.2	19.37
2010	449	24,785	9,647.9	18.12
2011	437	24,975	9,760.2	17.50
2012	461	25,644	9,995.6	17.98
2013	456	25,945	10,112.4	17.58
2014	478	26,600	10,370.5	17.97
2015	425	24,921	9,934.8	17.05
2016	240	12,396	3,424.3	19.36
2017	0	47	0.4	0.00

Appendix A. Available Data in the Sentinel Distributed Database (SDD) for Each Data Partner as of Request End Date

DP ID	Start Date	End Date
DP0001	1/1/2008	11/30/2016
DP0002	1/1/2004	9/30/2016
DP0003	1/1/2006	7/31/2016
DP0004	1/1/2000	6/30/2016
DP0005	1/1/2000	10/31/2015
DP0006	6/1/2007	7/31/2016
DP0007	1/1/2000	11/30/2016
DP0008	1/1/2000	7/31/2016
DP0009	1/1/2005	10/31/2016
DP0010	1/1/2000	11/30/2016
DP0011	1/1/2000	12/31/2016
DP0012	1/2/2000	5/31/2015
DP0013	1/2/2000	10/31/2014
DP0014	1/1/2008	3/31/2016
DP0015	1/1/2000	12/31/2015
DP0016	1/1/2012	9/30/2015

**Appendix B. List of Generic Name, Brand Names, and Healthcare Common Procedure Coding System (HCPCS)
Codes used to Define the Exposure in this Request**

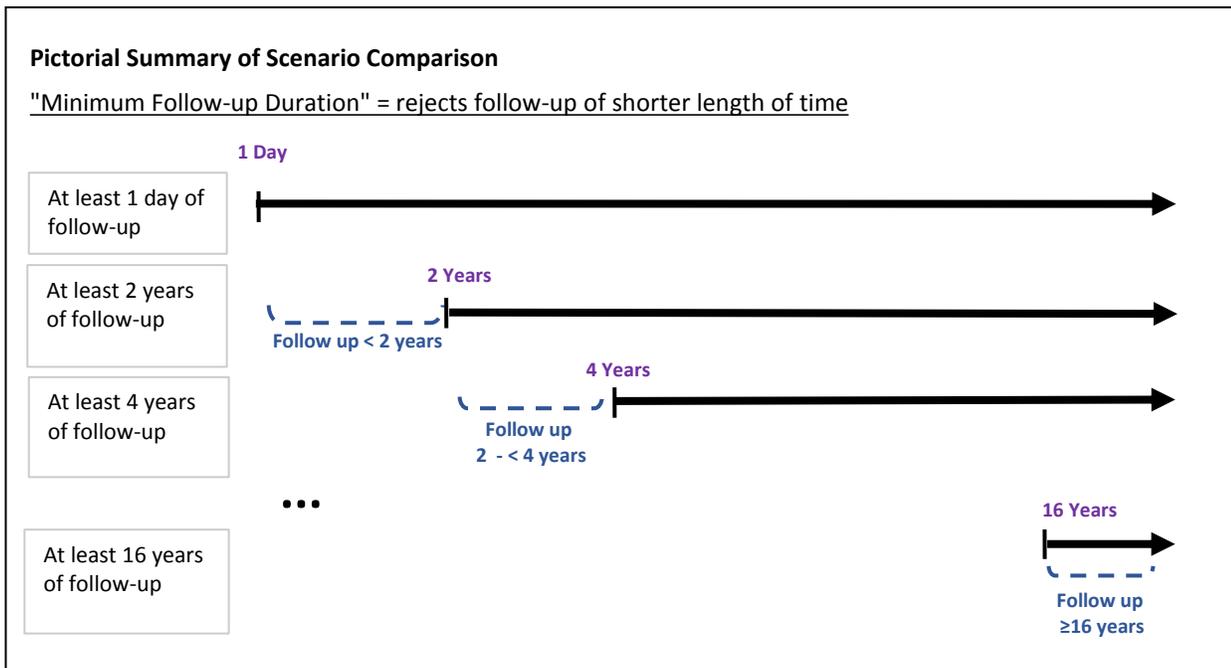
Brand Name	Generic Name
Lupron Depot-Ped (3 month)	LEUPROLIDE ACETATE
Lupron Depot-Ped	LEUPROLIDE ACETATE

Procedure	
J1950	Injection, leuprolide acetate (for depot suspension) per 3.75 mg
J9217	Leuprolide acetate (for depot suspension), 7.5 mg
J9218	Leuprolide acetate, per 1 mg
C9430	Leuprolide acetate, per 1 mg, brand name

Appendix C. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Edition, Clinical Modification (ICD-10-CM) Diagnosis Codes used to Define Indications in this Request

Indication	Code	Code Type	Long Description
Centralized Precocious Puberty	259.1	ICD-9-CM	Precocious sexual development and puberty, not elsewhere classified
Centralized Precocious Puberty	E30.1	ICD-10-CM	Precocious puberty

Appendix D. Pictorial Summary of How Follow-up Time was Calculated



Appendix E. Specifications for cder_mpl1r_wp050_nsdp_v02 - Pediatric Leuprolide Acetate Depot Feasibility

The Center for Drug Evaluation and Research (CDER) requested execution of the Cohort Identification and Descriptive Analysis (CIDA) tool, version 3.3.6, to provide exposure counts and follow-up data of children exposed to leuprolide acetate depot PED and the proportion of leuprolide acetate depot PED-exposed patients that had a diagnostic code for centralized precocious puberty during the baseline period.

Age Groups: 00-04 05-06 07-08 09-10 11-12 13-18
Query Period: January 1, 2000 - Most recent available data
Coverage Requirement: Medical and Drug Coverage
Enrollment Requirement: 183 days
Enrollment Gap: 45 days
Data Partners: All Data Partners

Scenario	Drug/Exposure					Inclusion Criteria				
	Exposure	Care Setting	Incident w/ respect to:	Washout (days)	Cohort Definition	Event	Type	Care Setting	Evaluation Start	Evaluation End
1	Leuprolide Depot PED	Any	Leuprolide Depot PED	183	First Incident Event					
2	Leuprolide Depot PED	Any	Leuprolide Depot PED	Entire history	First Incident Event	CPP	Include	Any	-183	0
3	Leuprolide Depot PED	Any	Leuprolide Depot PED	183	First Incident Event	CPP	Include	Any	-183	0
4	Leuprolide Depot PED	Any	Leuprolide Depot PED	183	First Incident Event	Dummy	Exclude (proxy for enrollment)	Any	0	2 years
5	Leuprolide Depot PED	Any	Leuprolide Depot PED	183	First Incident Event	Dummy	Exclude (proxy for enrollment)	Any	0	4 years
6	Leuprolide Depot PED	Any	Leuprolide Depot PED	183	First Incident Event	Dummy	Exclude (proxy for enrollment)	Any	0	6 years
7	Leuprolide Depot PED	Any	Leuprolide Depot PED	183	First Incident Event	Dummy	Exclude (proxy for enrollment)	Any	0	8 years
8	Leuprolide Depot PED	Any	Leuprolide Depot PED	183	First Incident Event	Dummy	Exclude (proxy for enrollment)	Any	0	10 years
9	Leuprolide Depot PED	Any	Leuprolide Depot PED	183	First Incident Event	Dummy	Exclude (proxy for enrollment)	Any	0	12 years
10	Leuprolide Depot PED	Any	Leuprolide Depot PED	183	First Incident Event	Dummy	Exclude (proxy for enrollment)	Any	0	14 years
11	Leuprolide Depot PED	Any	Leuprolide Depot PED	183	First Incident Event	Dummy	Exclude (proxy for enrollment)	Any	0	16 years

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

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

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

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