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

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

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

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Overview for Request cder_mpl1r_wp062

Request ID: cder_mpl1r_wp062_nsdp_v01

Request Description: In this report we examined drug utilization of oral and intranasal steroids in the Sentinel Distributed Database (SDD). We used the results from this request to characterize use of oral and intranasal steroids in a subsequent analysis (cder_mpl1r_wp061) which examined the association between sinus stents and oral and intranasal steroids with adverse ocular outcomes.

Sentinel Modular Program Tool Used: Cohort Identification and Descriptive Analysis (CIDA) tool, version 5.0.3

Data Source: We included data from August 1, 2011 to May 31, 2017 from 16 Data Partners contributing to the SDD were included in this report. We distributed this request on October 11, 2017. Please see Appendix A for a list of the dates of available data for each Data Partner.

Study Design: We designed this request to calculate summary statistics on length of treatment episodes and gaps between valid treatment episodes.

Exposures of Interest: We defined the exposures of interest, oral and intranasal steroids, using National Drug Codes (NDCs). Please see Appendix B for a list of generic and brand drug names we used to define exposures in this request. We included all qualifying incident dispensings that occurred between August 1, 2011 and May 31, 2017; cohort re-entry was allowed.

Cohort Eligibility Criteria: We required members included in the cohort to be continuously enrolled in health plans with medical and drug coverage for at least 183 days prior to their first valid dispensing (index) date, during which we allowed gaps in coverage of up to 45 days. We defined incident oral steroid use as no use of oral steroids or intranasal steroids and no evidence of stent implantation or sinus surgery in the 183 days preceding the index date. We defined incident intranasal steroid use as no use of intranasal steroids or evidence of stent implantation or sinus surgery in the 183 days preceding the index date. We excluded members from the cohort if they did not meet these incidence criteria. We defined stent implantation and sinus surgery using Current Procedural Terminology, Fourth Edition (CPT-4) and Healthcare Common Procedure Coding System (HCPCS) procedure codes. Please refer to Appendix C for specific CPT-4 and HCPCS codes we used to define these incidence criteria.
We additionally required individuals to have evidence of a nasal polyps diagnosis within 183 days of their index dispensing. We defined nasal polyps diagnoses using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes. Please refer to Appendix D for specific codes we used to define the inclusion criteria in this request.

Please see the Appendix E for the specifications of parameters to we used in the analyses for this request.

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

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

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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.

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 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.

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).

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” sequence.

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

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

Event Deduplication - specifies how events are counted by the 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 requests.

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

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

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 1. Descriptive Statistics for Cumulative Length of Treatment Episodes for Oral and Intranasal Steroids in the Sentinel Distributed Database (SDD) between August 1, 2011 and May 31, 2017

		Cumulative Episode Length (Days)				
	Number of Days	Q1	Median	Q3	Mean	Standard Deviation
Oral Steroids						
Episode 1	40,899	7	14	27	27.77	566.13
Episodes 1-2	20,003	17	25	44	46.14	536.70
Episodes 1-3	11,018	25	38	65	66.93	515.22
Episodes 1-4	6,602	35	52	86	88.41	447.26
Episodes 1-5	4,259	45	66	110	111.40	457.77
Episodes 1-6	2,934	56	80	135	134.51	438.79
Intranasal Steroids						
Episode 1	52,763	30	60	144	123.36	1159.80
Episodes 1-2	29,074	60	120	240	192.56	1021.33
Episodes 1-3	18,978	120	180	303	251.71	910.99
Episodes 1-4	13,362	150	225	379	304.29	817.15
Episodes 1-5	9,821	180	270	438	352.61	742.84
Episodes 1-6	7,473	218	319	480	395.14	679.62

Table 2. Descriptive Statistics for Length of Gap between Valid Treatment Episodes for Oral and Intranasal Steroids in the Sentinel Distributed Database (SDD) between August 1, 2011 and May 31, 2017, by Gap Number

	Gap Length (Days)					
	Number of Days	Q1	Median	Q3	Mean	Standard Deviation
Oral Steroids						
Gap 1	19,956	39	113	302	228.65	1,104.78
Gap 2	11,058	33	99	254	191.25	782.21
Gap 3	6,602	33	90	227	171.02	610.90
Gap 4	4,262	29	82	191	148.49	477.46
Gap 5	2,937	26	69	158	124.72	394.79
Intranasal Steroids						
Gap 1	29,072	20	56	170	145.49	1,074.53
Gap 2	18,979	19	48	131	116.34	794.28
Gap 3	13,361	18	43	109	96.41	621.65
Gap 4	9,823	17	39	94	83.71	503.82
Gap 5	7,472	15	37	87	74.19	433.18

Appendix A. Dates of Available Data for Each Data Partner (DP) as of Request Distribution Date (October 11, 2017)

DP ID	Start Date[1]	End Date[1]
DP01	8/1/2011	10/31/2014
DP02	8/1/2011	5/31/2015
DP03	8/1/2011	12/31/2015
DP04	8/1/2011	6/30/2016
DP05	8/1/2011	6/30/2016
DP06	8/1/2011	12/31/2016
DP07	8/1/2011	1/31/2017
DP08	8/1/2011	1/31/2017
DP09	8/1/2011	1/31/2017
DP10	8/1/2011	3/31/2017
DP11	8/1/2011	3/31/2017
DP12	8/1/2011	3/31/2017
DP13	8/1/2011	3/31/2017
DP14	8/1/2011	3/31/2017
DP15	8/1/2011	4/30/2017
DP16	8/1/2011	5/31/2017

[1]The 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

Generic Name	Brand Name
Oral Steroids	
BETAMETHASONE	Celestone
CORTISONE ACETATE	cortisone
DEFLAZACORT	Emflaza
DEXAMETHASONE	dexamethasone
DEXAMETHASONE	DexPak 6 Day
DEXAMETHASONE	ZonaCort
DEXAMETHASONE	LoCort
DEXAMETHASONE	DexPak 13 Day
DEXAMETHASONE	Zema-Pak
DEXAMETHASONE	Baycadron
DEXAMETHASONE	DexPak 10 day
DEXAMETHASONE	Dexamethasone Intensol
FLUDROCORTISONE ACETATE	fludrocortisone
HYDROCORTISONE	Cortef
HYDROCORTISONE	hydrocortisone
METHYLPREDNISOLONE	Medrol
METHYLPREDNISOLONE	methylprednisolone
METHYLPREDNISOLONE	Medrol (Pak)
PREDNISOLONE	prednisolone
PREDNISOLONE	Prelone
PREDNISOLONE	Millipred DP
PREDNISOLONE	Millipred
PREDNISOLONE ACETATE	Flo-Pred
PREDNISOLONE SOD PHOSPHATE	Orapred
PREDNISOLONE SOD PHOSPHATE	Orapred ODT
PREDNISOLONE SOD PHOSPHATE	Millipred
PREDNISOLONE SOD PHOSPHATE	prednisolone sodium phosphate
PREDNISOLONE SOD PHOSPHATE	Pediapred
PREDNISOLONE SOD PHOSPHATE	Veripred 20
PREDNISOLONE SODIUM PHOSPHATE/PEAK FLOW METER	Asmalpred Plus
PREDNISOLONE SODIUM PHOSPHATE/PEAK FLOW METER	Asmalpred
PREDNISONE	prednisone
PREDNISONE	Rayos
PREDNISONE	Deltasone
PREDNISONE	Prednisone Intensol
Intranasal Steroids	
AZELASTINE HCL/FLUTICASONE PROPIONATE	Dymista
AZELASTINE/FLUTICASONE/SODIUM CHLORIDE/SODIUM BICARBONATE	Ticalast
BECLOMETHASONE DIPROPIONATE	Beconase AQ
BECLOMETHASONE DIPROPIONATE	QNASL
BUDESONIDE	Rhinocort Aqua
BUDESONIDE	budesonide
BUDESONIDE	Rhinocort Allergy

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

Generic Name	Brand Name
FLUNISOLIDE	flunisolide
FLUTICASONE FUROATE	Flonase Sensimist
FLUTICASONE FUROATE	Veramyst
FLUTICASONE PROPIONATE	Allergy Relief (fluticasone)
FLUTICASONE PROPIONATE	fluticasone
FLUTICASONE PROPIONATE	Flonase Allergy Relief
FLUTICASONE PROPIONATE	Flonase
FLUTICASONE PROPIONATE	Children's Flonase Allergy Rlf
FLUTICASONE PROPIONATE	ClariSpray
FLUTICASONE PROPIONATE	24 Hour Allergy Relief
FLUTICASONE PROPIONATE	Aller-Flo
FLUTICASONE PROPIONATE/SODIUM CHLORIDE/SODIUM BICARBONATE	Ticaspray
FLUTICASONE PROPIONATE/SODIUM CHLORIDE/SODIUM BICARBONATE	Ticanase
MOMETASONE FUROATE	Nasonex
MOMETASONE FUROATE	mometasone
TRIAMCINOLONE ACETONIDE	Nasacort
TRIAMCINOLONE ACETONIDE	Nasacort AQ
TRIAMCINOLONE ACETONIDE	Nasal Allergy
TRIAMCINOLONE ACETONIDE	triamcinolone acetonide
TRIAMCINOLONE ACETONIDE	Children's Nasacort

Appendix C. List of Healthcare Common Procedure Coding System (HCPCS) and Current Procedural Terminology, Fourth Edition (CPT-4) Procedure Codes Used to Define Incidence Criteria in this Request

Code	Description	Code Type
	Stent Implant	
S1090	Mometasone furoate sinus implant, 370 micrograms	HCPCS
0406T	Nasal endoscopy, surgical, ethmoid sinus, placement of drug eluting implant;	CPT-4, Category III
0407T	Nasal endoscopy, surgical, ethmoid sinus, placement of drug eluting implant; with biopsy, polypectomy or debridement	CPT-4, Category III
31299	Unlisted procedure, accessory sinuses	CPT-4
	Sinus Surgery	
31237	Nasal/sinus endoscopy, surgical; with biopsy, polypectomy or debridement (separate procedure)	CPT-4
31238	Nasal/sinus endoscopy, surgical; with control of nasal hemorrhage	CPT-4
31239	Nasal/sinus endoscopy, surgical; with dacryocystorhinostomy	CPT-4
31240	Nasal/sinus endoscopy, surgical; with concha bullosa resection	CPT-4
31254	Nasal/sinus endoscopy, surgical; with ethmoidectomy, partial (anterior)	CPT-4
31255	Nasal/sinus endoscopy, surgical; with ethmoidectomy, total (anterior and posterior)	CPT-4
31256	Nasal/sinus endoscopy, surgical, with maxillary antrostomy;	CPT-4
31267	Nasal/sinus endoscopy, surgical, with maxillary antrostomy; with removal of tissue from maxillary sinus	CPT-4
31276	Nasal/sinus endoscopy, surgical with frontal sinus exploration, with or without removal of tissue from frontal sinus	CPT-4
31287	Nasal/sinus endoscopy, surgical, with sphenoidotomy;	CPT-4
31288	Nasal/sinus endoscopy, surgical, with sphenoidotomy; with removal of tissue from the sphenoid sinus	CPT-4
31290	Nasal/sinus endoscopy, surgical, with repair of cerebrospinal fluid leak; ethmoid region	CPT-4
31291	Nasal/sinus endoscopy, surgical, with repair of cerebrospinal fluid leak; sphenoid region	CPT-4
31292	Nasal/sinus endoscopy, surgical; with medial or inferior orbital wall decompression	CPT-4
31293	Nasal/sinus endoscopy, surgical; with medial orbital wall and inferior orbital wall decompression	CPT-4
31294	Nasal/sinus endoscopy, surgical; with optic nerve decompression	CPT-4
31295	Nasal/sinus endoscopy, surgical; with dilation of maxillary sinus ostium (eg, balloon dilation), transnasal or via canine fossa	CPT-4
31296	Nasal/sinus endoscopy, surgical; with dilation of frontal sinus ostium (eg, balloon dilation)	CPT-4
31297	Nasal/sinus endoscopy, surgical; with dilation of sphenoid sinus ostium (eg, balloon dilation)	CPT-4

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

Code	Description	Code Type
	Nasal Polyps	
471	Nasal polyps	ICD-9-CM
471.0	Polyp of nasal cavity	ICD-9-CM
471.1	Polypoid sinus degeneration	ICD-9-CM
471.8	Other polyp of sinus	ICD-9-CM
471.9	Unspecified nasal polyp	ICD-9-CM
J33	Nasal polyp	ICD-10-CM
J33.0	Polyp of nasal cavity	ICD-10-CM
J33.1	Polypoid sinus degeneration	ICD-10-CM
J33.8	Other polyp of sinus	ICD-10-CM
J33.9	Nasal polyp, unspecified	ICD-10-CM

Appendix E. Specifications for Parameters for this Request

This request used the Cohort Identification and Descriptive Analysis (CIDA) tool, version 5.0.3 to examine utilization of oral and intranasal steroids in the Sentinel Distributed Database (SDD).

Query Period: August 1, 2011 - May 31, 2017
Enrollment Requirement: 183 days
Enrollment Gap: 45 days
Coverage Requirement: Medical and drug coverage
Age Groups: 0-18, 19-24, 25-64, 65+ years

	Drugs of Interest							Inclusion/Exclusion Criteria		
	Exposure	Incident with respect to:	Washout Period (days)	Intent to Treat	Episode Gap Type	Episode Gap (days)	Censor due to Evidence of Death	Pre-Existing Conditions	Include/ Exclude	Lookback Period (days)
1	Oral steroids	Oral steroid, intranasal steroid, stent implant, or sinus surgery	183	N/A	Fixed	0	Yes	Nasal polyps	Include	-183, 0
2	Intranasal steroids	Intranasal steroid, stent implant, or sinus surgery	183	N/A	Fixed	0	Yes	Nasal polyps	Include	-183, 0

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