South Dakota
Department of Social Services

Medicaid P&T Committee Meeting

September 20, 2024

South Dakota Department of Social Services

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South Dakota Department of Social Services

SOUTH DAKOTA
MEDICAID P&T COMMITTEE MEETING
AGENDA

September 20, 2024
1:00 – 3:00 PM CT
12:00 – 2:00 PM MT

Meeting Link:
https://teams.microsoft.com/l/meetup-join/19%3ameeting_YzAzMzk0NDUtYmExOC00Y2M3LWI1NDEtM2NlMmI2ZDRmNDhi%40thread.v2/0?context=%7b%22Tid%22%3a%22db05faca-c82a-4b9d-b9c5-0f64b6755421%22%2c%22Oid%22%3a%22b6efd724-b34e-4a86-b34c-e34f07dd4ceb%22%7d

Join with a video conferencing device
425899727@t.plcm.vc
Video Conference ID: 118 229 989 73

Join by phone
+1 952-222-7450
Phone Conference ID: 939 317 70#

Call to order

Approval of previous meeting minutes

PA update
Review of top 15 therapeutic categories/top 50 drugs
Old business
- **GCM review**
- **Veozah**
- **Zurvuvae**
- **Opioid update**

New business
- **GLP-1 review**
- **ADHD review**
- **Daybue**

Public input accepted after individual topic discussion
Next meeting date December 13, 2024 & adjournment

South Dakota Department of Social Services, Division of Medicaid Services
Pharmacy & Therapeutics (P&T) Committee Meeting Minutes

Friday, June 7, 2024
1:00 – 3:00 pm CT

Members and DSS Staff

Michelle Baack, MD	X	Brandi Tackett, PharmD	X
Bill Ladwig, RPh	X	Deidra Van Gilder, PharmD, Chair	X
Kelley Oehlke, PharmD	X	Clarissa Barnes, MD, DSS Staff	X
Lenny Petrik, PharmD	X	Mike Jockheck, DSS Staff	X
Heather Preuss, MD		Taylor Koerner, DSS Staff	X
Matthew Stanley, DO	X	Heather Petermann, DSS Staff	X

Administrative Business

Van Gilder called the meeting to order at 1:01 pm. Jockheck introduced new committee member Brandi Tackett, pharmacist at Monument Health in Rapid City. The minutes of the March meeting were presented. Ladwig made a motion to approve. Baack seconded the motion. The motion was approved unanimously.

Prior Authorization Update (PA) and Statistics

The committee reviewed the PA activity report from January 1, 2024, to March 31, 2024. A total of 3,498 PAs were reviewed of which 175 requests (5%) were received via telephone, 148 requests (4.2%) were received via fax, 1,316 (37.6%) were reviewed electronically, and 1,853 requests (53%) were received via ePA. There was a 23% increase in PAs received compared to the previous quarter. The therapeutic class Medical Devices comprising of continuous glucose monitors (CGMs) debut on the Top Classes for PAs reviewed. Jockheck explained, traditionally CGMs had been covered on the medical side for Type 1 diabetics only. Coverage was moved to the pharmacy side with some expanded coverage. Ladwig requested outcomes data on CGMs in the future.

Analysis of the Top 15 Therapeutic Classes and Drug Spend

The committee reviewed the top 15 therapeutic classes by total cost of claims from January 1, 2024, to March 31, 2024. The top five therapeutic classes based on paid amount were atypical antipsychotics, skin and mucous membrane agents, disease-modifying anti-rheumatic agents, incretin mimetics, and antineoplastic agents. These top 15 therapeutic classes comprise 22.28% of total claims. The committee also reviewed the top 50 drugs based on amount paid and number of claims. The top 50 drugs by amount paid constitute 7.96% of total claims.

Old Business

Vijoice PA reviews

Committee reviewed the PA approvals and utilization of Vijoice. There were 2 patients utilizing Vijoice with appropriate diagnosis.

Linzess PA reviews

Committee had requested an in-depth review of Linzess PA appeals. The increase in appeals was due to Linzess 72mcg approved for pediatric patients 6 to 17 years old. The PA criteria has been updated to

include the expanded age indication. The appeals for Linzess should decrease.

Van Gilder inquired if there were any public comment on agenda items covered thus far. There were none.

Opioid Update
The committee reviewed 1Q2024 opioid outcomes compared to the previous quarter from the opioid initiatives. There was an increase in opioid utilization and utilizers during 1Q2024 with corresponding increase in total eligibility and utilizers. The committee also reviewed the average MME/day/utilizer graph. Ladwig requested additional utilization data for trend tracking.

Van Gilder inquired if there was any public comment. There was none.

New Business
Committee reviewed low volume requests with high approval rates. Most of the reviews were on antibiotic quantity limit reviews, antihypertensive and beta blocker quantity limits. The Committee agreed to the DSS request to adjust quantity limits for inexpensive generic products in order to decrease the number of quantity limit prior authorization requests.

Van Gilder inquired if there was any public comment. There was none.

Rezdiffra
Rezdiffra clinical information was presented for review. Baack said this disease state is being seen in younger patients including the pediatric population. Baack is in favor of having a specialist involved in and following the patient's care. Tara McKinely, Health System Scientific Director at Madrigal Pharmaceutics, provided public comment. Baack made a motion to adopt the PA criteria from State A, but remove criteria 3a to 3d (confirming the diagnostic testing); only requiring documented chart notes confirming diagnosis. Ladwig seconded the motion. Jockheck requested a roll call vote. The following committee members replied with a yes response: Van Gilder, Oehlke, Stanley, Petrik, Tackett, Ladwig, Baack. The motion carried. Ladwig requested to evaluate utilization in 3 to 6 months, review PA approval rate, and what other states have done and been successful.

Auvelity
Auvelity clinical information was presented for review. Stanley provided clinical comment. Ronnie DePue, Senior Director at Axsome Therapeutics, provided public comment. After discussion, Stanley made a motion to add State B's PA criteria with 3-year lookback for three other drugs to try first except for trial of esketamine. Ladwig seconded the motion. The motion was approved unanimously.

Exxua
Exxua clinical information was presented for review. Stanley provided clinical comment. There was no public comment. Stanley made the motion to add the same PA recommended for Auvelity. Oehkle seconded the motion. The motion was approved unanimously.

Lybalvi
Lybalvi clinical information was presented for review. Stanley appreciated new approaches to treating chronic psychiatric diseases. Paul Thompson, psychiatric pharmacist and Medical Science Liaison from Alkermes, provided public comment. Stanley made the motion to add PA criteria similar to the

commercial criteria with 3-year lookback for two other drugs to try first for diagnosis of schizophrenia and bipolar disorder 1. Ladwig seconded the motion. The motion was approved unanimously.

Veozah

Veozah clinical information was presented for review. Baack inquired on the number of patients using non-hormonal agents (i.e., SSRI, SNRI, gabapentin, etc) for menopause. After discussion, Ladwig asked how long the patients currently using Veozah have been on therapy. Baack inquired when patients would stop therapy. Committee requested more information.

Adjournment

The next meeting is scheduled on September 20, 2024. The December meeting is scheduled for December 13, 2024. Ladwig motioned to adjourn the meeting and Baack seconded the motion. The motion to adjourn the meeting was unanimous and the meeting adjourned at 2:55 pm CT.

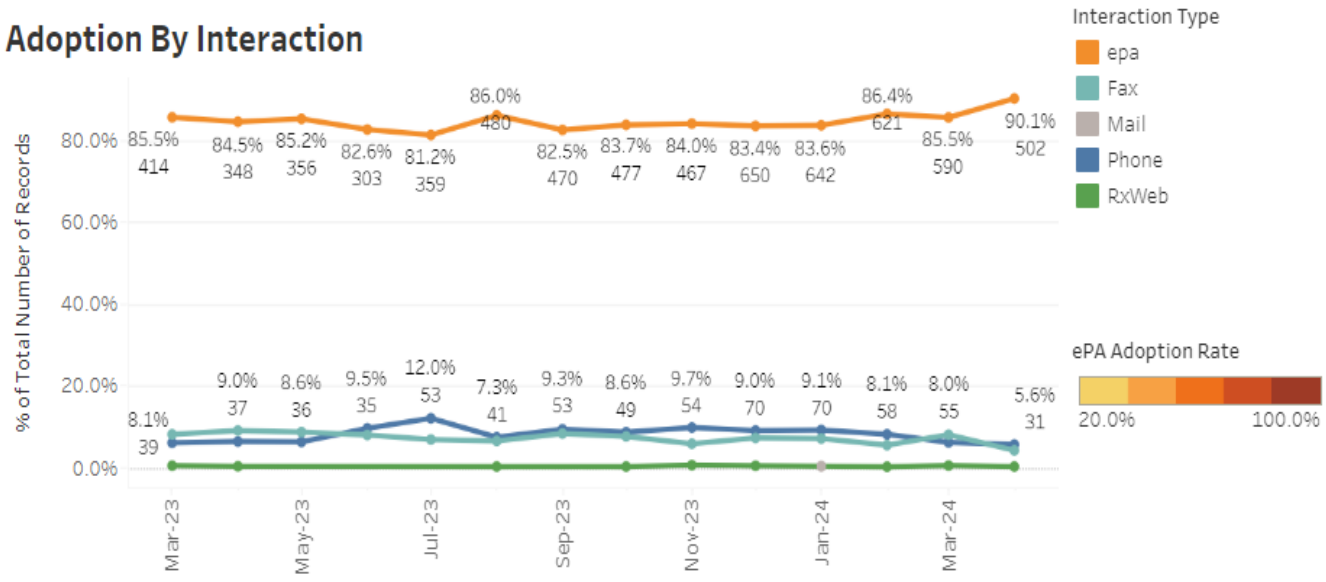
PA Report
4/1/2024 – 6/30/2024

Compliance Summary

Priority	Total PAs	PAs Compliant	PAs Not Compliant	% PAs Compliant	% PAs Not Compliant
Standard	3,028	3,028	0	100.00%	0.00%
Urgent	380	380	0	100.00%	0.00%
Grand Total	**3,408**	**3,408**	**0**		

Priority	Standard	Urgent
ePA	1,431	358
Fax	95	7
Phone	112	14
Real-Time	1,389	0
RxWeb	1	1

Request Summary	Total # of Requests	Phone Requests		Fax Requests		Real-Time PA		ePA PA	
		#	%	#	%	#	%	#	%
Total	**3,408**	**126**	**3.7%**	**102**	**3%**	**1,389**	**40.7%**	**1,789**	**52.5%**



This graph shows the adoption of Interaction Types in percentage. This graph considers all resolved cases (Approved + Denied).

PA Initial Requests Summary

Month	Approved	Denied	Total
Apr-24	1,051	202	1,253
May-24	952	175	1,127
Jun-24	881	148	1,028
2Q24	**2,884**	**525**	**3,408**
Percent of Total	**84.6%**	**18.07%**	

Top Therapeutic Classes for PA

Drug Class	Approved	Denied	Total	Approval Rate	% of Total Requests	Most Requested Products
ANTIDIABETICS	592	47	639	92.64%	18.74%	, OZEMPIC
ANTIPSYCHOTICS/ANTIMANIC	468	31	499	93.79%	14.64%	, VRAYLAR
MEDICAL DEVICES & SUPPLIES	316	62	378	83.60%	11.09%	, DEXCOM G7 SENSOR
ANALGESICS - OPIOID	277	59	336	82.44%	9.86%	HYDROCODONE/APAP
DERMATOLOGICALS	209	36	245	85.31%	7.19%	DUPIXENT, EUCRISA
OTHERS -	1022	290	1312	77.90%	38.49%	
2Q24	2,884	525	3409	84.60%		

PA Appeals Summary

Month	Approved	Approved %	Denied	Denied %	Total
Apr-24	19	70.37%	8	29.63%	27
May-24	22	91.67%	2	8.33%	24
Jun-24	13	65.00%	7	35.00%	20
2Q24	**54**	76.06%	17	23.94%	71

PA Drug Class Summary

Drug Class	Approved	Denied	Total	Approval Rate
27 - ANTIDIABETICS*	592	47	639	92.64%
59 - ANTIPSYCHOTICS/ANTIMANIC AGENTS*	468	31	499	93.79%
97 - MEDICAL DEVICES AND SUPPLIES*	316	62	378	83.60%
65 - ANALGESICS - OPIOID*	277	59	336	82.44%
90 - DERMATOLOGICALS*	209	36	245	85.31%
58 - ANTIDEPRESSANTS*	195	31	226	86.28%
67 - MIGRAINE PRODUCTS*	123	28	151	81.46%
52 - GASTROINTESTINAL AGENTS - MISC.*	109	15	124	87.90%
49 - ULCER DRUGS/ANTISPASMODICS/ANTICHOLINERG	93	31	124	75.00%
61 - ADHD/ANTI-NARCOLEPSY/ANTI-OBESITY/ANOREX	86	50	136	63.24%
66 - ANALGESICS - ANTI-INFLAMMATORY*	74	20	94	78.72%
41 - ANTIHISTAMINES*	50	8	58	86.21%
16 - ANTI-INFECTIVE AGENTS - MISC.*	41	4	45	91.11%
12 - ANTIVIRALS*	29	15	44	65.91%
62 - PSYCHOTHERAPEUTIC AND NEUROLOGICAL AGENT	25	1	26	96.15%
72 - ANTICONVULSANTS*	25	3	28	89.29%
21 - ANTINEOPLASTICS AND ADJUNCTIVE THERAPIES	23	1	24	95.83%
44 - ANTIASTHMATIC AND BRONCHODILATOR AGENTS*	22	8	30	73.33%
54 - URINARY ANTISPASMODICS*	18	7	25	72.00%
60 - HYPNOTICS/SEDATIVES/SLEEP DISORDER AGENT	15	16	31	48.39%
83 - ANTICOAGULANTS*	15	2	17	88.24%
30 - ENDOCRINE AND METABOLIC AGENTS - MISC.*	14	13	27	51.85%
28 - THYROID AGENTS*	11	4	15	73.33%
33 - BETA BLOCKERS*	7	9	16	43.75%
50 - ANTIEMETICS*	7	1	8	87.50%
75 - MUSCULOSKELETAL THERAPY AGENTS*	6	5	11	54.55%
34 - CALCIUM CHANNEL BLOCKERS*	4	6	10	40.00%
39 - ANTIHYPERLIPIDEMICS*	4	0	4	100.00%
99 - MISCELLANEOUS THERAPEUTIC CLASSES*	4	0	4	100.00%
02 - CEPHALOSPORINS*	3	0	3	100.00%
36 - ANTIHYPERTENSIVES*	3	2	5	60.00%
40 - CARDIOVASCULAR AGENTS - MISC.*	3	0	3	100.00%
42 - NASAL AGENTS - SYSTEMIC AND TOPICAL*	3	6	9	33.33%
86 - OPHTHALMIC AGENTS*	3	1	4	75.00%
19 - PASSIVE IMMUNIZING AND TREATMENT AGENTS*	2	0	2	100.00%
82 - HEMATOPOIETIC AGENTS*	2	0	2	100.00%
01 - PENICILLINS*	1	0	1	100.00%
15 - ANTHELMINTICS*	1	0	1	100.00%
79 - MINERALS & ELECTROLYTES*	1	0	1	100.00%
03 - MACROLIDES*	0	1	1	0.00%
38 - VASOPRESSORS*	0	1	1	0.00%
85 - HEMATOLOGICAL AGENTS - MISC.*	0	1	1	0.00%
2Q24	**2,884**	**525**	**3,409**	
Percent of Total	**84.60%**	**15.4%**		

Appeals Detail

Drug Class	Approved	Denied	Total	Approval Rate
LINZESS	4	1	5	80.00%
MAVYRET	4	1	5	80.00%
AIMOVIG	3	0	3	100.00%
DEXCOM G7 SENSOR	3	1	4	75.00%
DEXLANSOPRAZOLE	3	0	3	100.00%
HYDROCODONE BITARTRATE/APAP	3	1	4	75.00%
NORDITROPIN FLEXPRO	3	1	4	75.00%
BELSOMRA	2	0	2	100.00%
EMGALITY	2	0	2	100.00%
HUMATROPE	2	0	2	100.00%
RINVOQ	2	0	2	100.00%
VRAYLAR	2	1	3	66.67%
ADDERALL XR	1	0	1	100.00%
AJOVY	1	0	1	100.00%
AMBIEN CR	1	0	1	100.00%
BUPRENORPHINE HCL	1	0	1	100.00%
DEXCOM G6 SENSOR	1	0	1	100.00%
DEXCOM G7 RECEIVER	1	0	1	100.00%
ESCITALOPRAM OXALATE	1	0	1	100.00%
EUCRISA	1	0	1	100.00%
FREESTYLE LIBRE 2/SENSOR	1	0	1	100.00%
GATTEX	1	0	1	100.00%
HUMIRA PEN	1	1	2	50.00%
INVEGA SUSTENNA	1	0	1	100.00%
MOUNJARO	1	0	1	100.00%
MYDAYIS	1	0	1	100.00%
MYRBETRIQ	1	1	2	50.00%
OXYCODONE HYDROCHLORIDE	1	0	1	100.00%
SOFOSBUVIR/VELPATASVIR	1	0	1	100.00%
STELARA	1	1	2	50.00%
TRAMADOL HYDROCHLORIDE	1	1	2	50.00%
TRAMADOL HYDROCHLORIDE ER	1	0	1	100.00%
XELJANZ XR	1	0	1	100.00%
CLINDAMYCIN/BENZOYL PEROXIDE	0	1	1	0.00%
QELBREE	0	3	3	0.00%
QUVIVIQ	0	1	1	0.00%
TETRABENAZINE	0	1	1	0.00%
2Q24	**54**	**17**	**71**	

Top 15 Therapeutic Classes & Top 50 Drugs

TOP 15 THERAPEUTIC CLASSES BASED ON NUMBER OF CLAIMS FROM 4/1/2024 – 6/30/2024					
	AHFS Description	**Total Rxs**	**Plan Paid Amount**	**Paid/Rx**	**% Total Claims**
1	SELECTIVE-SEROTONIN REUPTAKE INHIBITORS	16,726	$199,373.00	$11.92	6.11%
2	ANTICONVULSANTS, MISCELLANEOUS	15,386	$1,183,278.75	$76.91	5.62%
3	ATYPICAL ANTIPSYCHOTICS	11,298	$3,966,069.16	$351.04	4.13%
4	PROTON-PUMP INHIBITORS	8,723	$211,822.69	$24.28	3.19%
5	SELECTIVE BETA-2-ADRENERGIC AGONISTS	8,561	$440,169.49	$51.42	3.13%
6	SECOND GENERATION ANTIHISTAMINES	8,252	$92,639.88	$11.23	3.01%
7	AMPHETAMINES	7,951	$1,061,115.10	$133.46	2.90%
8	AMINOPENICILLIN ANTIBIOTICS	7,721	$112,698.40	$14.60	2.82%
9	ADRENALS	7,516	$873,824.08	$116.26	2.74%
10	RESPIRATORY AND CNS STIMULANTS	7,514	$811,430.99	$107.99	2.74%
11	OPIOID AGONISTS (28:08)	7,061	$211,320.04	$29.93	2.58%
12	ANXIOLYTICS,SEDATIVES,AND HYPNOTICS,MISC	6,952	$87,284.23	$12.56	2.54%
13	HMG-COA REDUCTASE INHIBITORS	5,905	$67,291.25	$11.40	2.16%
14	SEL.SEROTONIN,NOREPI REUPTAKE INHIBITOR	5,363	$99,889.31	$18.63	1.96%
15	ANTIDEPRESSANTS, MISCELLANEOUS	5,230	$166,735.76	$31.88	1.91%
Total		**130,159**	**$9,584,942.13**	**$73.64**	**47.54%**

TOP 15 THERAPEUTIC CLASSES BASED ON AMOUNT PAID FROM 4/1/2024 – 6/30/2024					
	AHFS Description	**Total Rxs**	**Plan Paid Amount**	**Paid/Rx**	**% Total Claims**
1	ATYPICAL ANTIPSYCHOTICS	11,298	$3,966,069.16	$351.04	4.13%
2	DISEASE-MODIFYING ANTIRHEUMATIC AGENTS	474	$3,339,263.80	$7,044.86	0.17%
3	SKIN AND MUCOUS MEMBRANE AGENTS, MISC.	749	$2,867,286.79	$3,828.15	0.27%
4	INCRETIN MIMETICS	2,542	$2,408,807.53	$947.60	0.93%
5	ANTINEOPLASTIC AGENTS	459	$1,780,132.92	$3,878.29	0.17%
6	CYSTIC FIBROSIS (CFTR) CORRECTORS	66	$1,501,250.42	$22,746.22	0.02%
7	HEMOSTATICS	58	$1,393,957.00	$24,033.74	0.02%
8	ANTICONVULSANTS, MISCELLANEOUS	15,386	$1,183,278.75	$76.91	5.62%
9	AMPHETAMINES	7,951	$1,061,115.10	$133.46	2.90%
10	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	4,258	$1,058,356.42	$248.56	1.56%
11	HIV INTEGRASE INHIBITOR ANTIRETROVIRALS	261	$951,869.05	$3,647.01	0.10%
12	ADRENALS	7,516	$873,824.08	$116.26	2.74%
13	SODIUM-GLUC COTRANSPORT 2 (SGLT2) INHIB	1,559	$845,766.06	$542.51	0.57%
14	RESPIRATORY AND CNS STIMULANTS	7,514	$811,430.99	$107.99	2.74%
15	IMMUNOMODULATORY AGENTS (84:06)	200	$717,985.99	$3,589.93	0.07%
Total		**60,291**	**$24,760,394.06**	**$410.68**	**22.02%**

Total Rx Claims from 4/1/2024 – 6/30/2024	**273,813**

TOP 50 DRUGS BASED ON NUMBER OF CLAIMS FROM 4/1/2024 – 6/30/2024						
	Therapeutic Class Name	**Drug Label Name**	**Total Rxs**	**Plan Paid Amount**	**Paid/Rx**	**% Total Claims**
1	Antidepressants	**FLUOXETINE**	**5,721**	**$64,010.15**	$11.19	2.09%
2	Penicillins	AMOXICILLIN	5,590	$73,511.61	$13.15	2.04%
3	Antidepressants	**SERTRALINE**	**5,211**	**$61,652.57**	$11.83	1.90%
4	Proton Pump Inhibitors	**OMEPRAZOLE**	**5,034**	**$55,316.12**	$10.99	1.84%
5	Inhaled Bronchodilator	ALBUTEROL SULFATE HFA	4,966	$168,604.93	$33.95	1.81%
6	Anticonvulsants - 2nd Generation	GABAPENTIN	4,920	$76,216.16	$15.49	1.80%
7	ADHD & Narcolepsy Medications	METHYLPHENIDATE	4,725	$256,858.08	$54.36	1.73%
8	Antihistamines	**CETIRIZINE**	**4,469**	**$47,345.03**	$10.59	1.63%
9	Antidepressants	TRAZODONE	4,443	$46,513.55	$10.47	1.62%
10	Thyroid Hormones	LEVOTHYROXINE	4,267	$44,706.61	$10.48	1.56%
11	Antidepressants	ESCITALOPRAM	4,132	$49,286.02	$11.93	1.51%
12	ADHD & Narcolepsy Medications	AMPHETAMINE/DEXTROAMP	4,116	$108,322.96	$26.32	1.50%
13	Antidepressants	**BUPROPION**	**3,537**	**$60,796.40**	$17.19	1.29%
14	Biguanides & Combos	**METFORMIN**	**3,534**	**$39,415.21**	$11.15	1.29%
15	ACE Inhibitors & Combos	LISINOPRIL	3,454	$31,025.99	$8.98	1.26%
16	Statins & Combos	ATORVASTATIN	3,388	$37,897.07	$11.19	1.24%
17	Antiadrenergic Antihypertensives	**CLONIDINE**	**3,215**	**$39,658.00**	$12.34	1.17%
18	Leukotriene Modulators	MONTELUKAST	3,045	$38,037.91	$12.49	1.11%
19	Antidepressants	**DULOXETINE**	**2,911**	**$41,259.64**	$14.17	1.06%
20	Opioid Agonists & Combos	HYDROCODONE BIT/AC	2,753	$46,106.17	$16.75	1.01%
21	Antianxiety Agents	**HYDROXYZINE**	**2,539**	**$30,287.50**	$11.93	0.93%
22	Atypical Antipsychotics	ARIPIPRAZOLE	2,398	$33,582.82	$14.00	0.88%
23	Antianxiety Agents	**BUSPIRONE**	**2,269**	**$27,003.70**	$11.90	0.83%
24↑	Angiotensin II Receptor Antagonists & Combo	LOSARTAN	2,223	$23,591.79	$10.61	0.81%
25	Glucocorticosteroids	PREDNISONE	2,173	$20,796.48	$9.57	0.79%
26	Calcium Channel Blockers	AMLODIPINE	2,169	$19,716.93	$9.09	0.79%
27	Penicillins	AMOXICILLIN/CLAVULANATE	2,131	$39,186.79	$18.39	0.78%
28	Atypical Antipsychotics	QUETIAPINE	2,127	$26,906.59	$12.65	0.78%
29	Anticonvulsants - 2nd Generation	LAMOTRIGINE	2,070	$26,809.24	$12.95	0.76%
30	Cephalosporins	CEPHALEXIN	2,065	$31,273.73	$15.14	0.75%
31	Antiemetics	ONDANSETRON ODT	2,007	$27,101.50	$13.50	0.73%
32	Proton Pump Inhibitors	PANTOPRAZOLE	1,981	$23,962.14	$12.10	0.72%
33	Muscle Relaxants & Combos	CYCLOBENZAPRINE	1,897	$18,492.82	$9.75	0.69%
34	Atypical Antipsychotics	RISPERIDONE	1,891	$22,127.24	$11.70	0.69%
35	Beta Blockers & Combos	METOPROLOL SUCCINATE ER	1,829	$21,516.35	$11.76	0.67%
36	ADHD & Narcolepsy Medications	VYVANSE	1,827	$645,361.56	$353.24	0.67%
37	Anticonvulsants - 2nd Generation	CLONAZEPAM	1,823	$19,715.60	$10.81	0.67%
38	Anticonvulsants - 2nd Generation	TOPIRAMATE	1,817	$21,917.26	$12.06	0.66%
39	Statins & Combos	ROSUVASTATIN	1,807	$21,056.40	$11.65	0.66%
40	ADHD & Narcolepsy Medications	LISDEXAMFETAMINE	1,780	$267,367.54	$150.21	0.65%
41	Nasal Steroids	FLUTICASONE PROPIONATE	1,674	$27,183.61	$16.24	0.61%
42	Antidepressants	VENLAFAXINE	1,667	$23,943.59	$14.36	0.61%
43↓	Inhaled Bronchodilator	ALBUTEROL SULFATE	1,649	$33,054.39	$20.05	0.60%
44	Nonsteroidal Anti-Inflammatory Agents	MELOXICAM	1,647	$15,825.47	$9.61	0.60%
45↓	Macrolides	AZITHROMYCIN	1,640	$23,868.46	$14.55	0.60%
46	Antihistamines	**LORATADINE**	**1,637**	**$18,263.06**	$11.16	0.60%
47↓	ADHD & Narcolepsy Medications	GUANFACINE ER	1,622	$24,975.69	$15.40	0.59%
48	Anticonvulsants - 2nd Generation	LEVETIRACETAM	1,585	$30,245.77	$19.08	0.58%
49	Antidepressants	MIRTAZAPINE	1,523	$19,273.41	$12.65	0.56%
50	Corticosteroids - Topical	TRIAMCINOLONE ACETONIDE	1,508	$21,785.79	$14.45	0.55%
	Total Top 50 Drugs		**140,406**	**$2,992,733.40**	**$21.31**	**51.28%**

TOP 50 DRUGS BASED ON AMOUNT PAID FROM 4/1/2024 – 6/30/2024						
	Therapeutic Class Name	**Drug Label Name**	**Total Rxs**	**Plan Paid Amount**	**Paid/Rx**	**% Total Claims**
1	Chronic Inflammatory Disease	DUPIXENT	418	$1,604,916.97	$3,839.51	0.15%
2	Cystic Fibrosis	TRIKAFTA	66	$1,501,250.42	$22,746.22	0.02%
3	Chronic Inflammatory Disease	**HUMIRA**	**161**	**$1,492,245.65**	$9,268.61	0.06%
4	Atypical Antipsychotics	INVEGA **SUSTENNA**-TRINIZA-HAFYERA	**382**	**$1,367,018.32**	$3,578.58	0.14%
5	Chronic Inflammatory Disease	STELARA	54	$1,305,707.90	$24,179.78	0.02%
6	GLP-1 Receptor Agonists	OZEMPIC	1,340	$1,245,378.80	$929.39	0.49%
7	GLP-1 Receptor Agonists	MOUNJARO	850	$854,314.07	$1,005.08	0.31%
8	Atypical Antipsychotics	VRAYLAR	660	$851,407.13	$1,290.01	0.24%
9	Rett Syndrome Agent	DAYBUE	16	$770,028.47	$48,126.78	0.01%
10	ADHD & Narcolepsy Medications	VYVANSE	1,827	$645,361.56	$353.24	0.67%
11	HIV-Multiclass Combo	BIKTARVY	165	$640,045.86	$3,879.07	0.06%
12	Chronic Inflammatory Disease	**COSENTYX SENSOREADY/UNOREADY**	**69**	**$628,062.30**	$9,102.35	0.03%
13	SGLT-2 Inhibitors & Combos	JARDIANCE	995	$559,381.08	$562.19	0.36%
14↑	Antihemophilic Products	HEMLIBRA	17	$554,308.03	$32,606.35	0.01%
15	Atypical Antipsychotics	ARISTADA/INITIO	**175**	**$505,098.54**	$2,886.28	0.06%
16	Chronic Inflammatory Disease	TALTZ	60	$464,601.21	$7,743.35	0.02%
17	Anticonvulsants - 2nd Generation	EPIDIOLEX	151	$450,667.46	$2,984.55	0.06%
18↓	Chronic Inflammatory Disease	SKYRIZI PEN	22	$446,060.69	$20,275.49	0.01%
19	Chronic Inflammatory Disease	ENBREL/MINI/**SURECLICK**	**59**	**$425,529.79**	$7,212.37	0.02%
20*	Diabetes Monitoring and Testing	DEXCOM	1,166	$401,865.74	$344.65	0.43%
21	Oral Anticoagulants	**ELIQUIS**/ STARTER PACK	**619**	**$332,746.57**	$537.56	0.23%
22↑	Spinal Muscular Atrophy (SMA)	EVRYSDI	12	$307,681.32	$25,640.11	0.00%
23	Atypical Antipsychotics	REXULTI	234	$302,386.47	$1,292.25	0.09%
24	Movement Disorder Drug Therapy	INGREZZA	42	$294,642.52	$7,015.30	0.02%
25	Hepatitis C	SOFOSBUVIR/VELPATASVIR	37	$289,813.76	$7,832.80	0.01%
26	Anti-Infective Agents - Misc.	XIFAXAN	98	$277,772.52	$2,834.41	0.04%
27	Atypical Antipsychotics	CAPLYTA	180	$269,516.23	$1,497.31	0.07%
28	ADHD & Narcolepsy Medications	LISDEXAMFETAMINE	1,780	$267,367.54	$150.21	0.65%
29	ADHD & Narcolepsy Medications	**METHYLPHENIDATE**	**4,744**	**$260,486.80**	$54.91	1.73%
30↑	Antihemophilic Products	ALPROLIX	10	$253,150.16	$25,315.02	0.00%
31	Antihemophilic Products	NOVOSEVEN RT	3	$241,231.65	$80,410.55	0.00%
32	Oncology	SPRYCEL	17	$240,063.80	$14,121.40	0.01%
33	Inhaled Asthma/COPD Combo	TRELEGY ELLIPTA	380	$239,065.02	$629.12	0.14%
34	Chronic Inflammatory Disease	RINVOQ	35	$235,786.73	$6,736.76	0.01%
35↓	Hepatitis C	MAVYRET	18	$230,801.88	$12,822.33	0.01%
36↓	Oncology	KOSELUGO	14	$227,631.05	$16,259.36	0.01%
37	Chronic Inflammatory Disease	TREMFYA	16	$216,027.72	$13,501.73	0.01%
38	Growth Hormones	NORDITROPIN FLEXPRO	61	$209,741.37	$3,438.38	0.02%
39	Irritable Bowel Syndrome (IBS)	LINZESS	390	$202,920.90	$520.31	0.14%
40	Pulmonary Arterial Hypertension	OPSUMIT	16	$195,364.91	$12,210.31	0.01%
41	Metabolic Modifiers	PALYNZIQ	3	$189,031.65	$63,010.55	0.00%
42↑	Oncology	KISQALI	12	$187,561.77	$15,630.15	0.00%
43↓	Glucagon-Like Peptide-2 (GLP-2)	GATTEX	4	$182,149.72	$45,537.43	0.00%
44	Cystic Fibrosis	PULMOZYME	37	$181,877.22	$4,915.60	0.01%
45	HIV-Multiclass Combo	GENVOYA	46	$178,410.00	$3,878.48	0.02%
46	Asthma	NUCALA	48	$177,517.44	$3,698.28	0.02%
47	Inhaled Bronchodilator	ALBUTEROL SULFATE HFA	4,966	$168,604.93	$33.95	1.81%
48↑	Psychotherapeutic And Neurological	LYBALVI	122	$167,774.88	$1,375.20	0.04%
49↓	GLP-1 Receptor Agonists	TRULICITY	175	$167,245.86	$955.69	0.06%
50↑	PIK3CA-Related Overgrowth	VIJOICE	5	$162,552.75	$32,510.55	0.00%
	Total Top 50 Drugs		**22,777**	**$23,570,175.13**	**$1,034.82**	**8.32%**

Old Business

Continuous Glucose Monitoring (CGM)

Time Period: 1/1/2024 – 6/30/2024

CGM Utilizers by Diagnosis

Diagnosis	Members
Type I diabetes mellitus (E10)	303
Type II diabetes mellitus (E11)	311
Gestational diabetes (O24)	39
Total	653

CGM Prescribers

Taxonomy Description	Members
Ambulatory Health Care Facilities/Clinic/Center/Urgent Care	16
Emergency Medicine	15
Endocrinology, Diabetes & Metabolism	58
Endocrinology, Pediatric	14
Family Medicine, Obesity Medicine	3
Family Practice	47
Geriatric Medicine, Family Practice	1
Hospitalist	5
Internal Medicine	105
Multi-Specialty/Group	3
Neonatal/Perinatal Medicine	1
Neurology, Pediatric	1
Neuromusculoskeletal Medicine, Sports Medicine	2
Nuclear Medicine, In Vitro & In Vivo	19
Nurse Midwife	1
Nurse Practitioner	218
Obstetrics & Gynecology	11
Pediatrics	40
Physician Assistant	61
Psychiatry & Neurology, Addiction Psychiatry	1
Pulmonology, Pediatric	5
Registered Nurse, Ambulatory Care	6
Registered Nurse, Diabetes Educator	2
Single Specialty/Group	3
Sports Medicine, Family Practice	1
Student in an Organized Health Care Education/Training Program/Student, Health Care	14
Total	653

CGM Compliance

CGM utilizers during Jan24-Apr24	CGM utilizers during both Jan24-Apr24 and May24-June24	Members NOT receiving CGM during May24-June24
535	448	87

Diagnosis Code	CGM utilizers during Jan24-Apr24 but NOT during May24-June24
Type I diabetes mellitus (E10)	34
Type II diabetes mellitus (E11)	44
Gestational diabetes (O24)	9

*15 members off Medicaid

CGM and Glucose Test Strip Utilization

- CGM Utilization Time Period: 1/1/2024 – 6/30/2024
- Glucose Test Strip Utilization Time Period: 7/1/2023 – 6/30/2024

Total Members receiving CGM	653
Total Members receiving CGM & glucose test strips	404
Members receiving 200 or more glucose test strips	104

Members receiving 200 or more glucose test strips

	Members	Percentage
Glucose test strip use decreased or member is no longer using	66	63.46%
Glucose test strip use with little to no change or has increased	38	36.54%
Total	104	

CGM average fill per month

Glucose test strip use: Summary of 38 Members with little to no change or increased use			
Date Filled YYYY-MM	**Total Quantity**	**Total Rxs**	**Avg Qty/ Rx**
2023-07	3,350	19	176.3
2023-08	4,600	23	200
2023-09	4,600	20	230
2023-10	3,850	16	240.6
2023-11	3,500	15	233.3
2023-12	4,250	17	250
	24,150	**110**	**219.5**
2024-01	4,950	20	247.5
2024-02	5,000	20	250
2024-03	4,850	20	242.5
2024-04	3,700	14	264.3
2024-05	6,600	26	253.
2024-06	7,950	30	265
	33,050	**130**	**254.2**

Veozah (fezolinetant) for the treatment of moderate to severe vasomotor symptoms due to menopause

Time Period 8/1/2023 to 8/9/2024

	Drug Name	Total Rx	Paid Amount	Paid/Rx	Avg Quantity/DS	Utilizers	Age Range
Non-hormonal agents	VEOZAH tab 45mg	53	$28,096.96	$530.13	29.7 per 29.7 days	13	33 – 64

Compliance based on claims review:

	Mbr A	Mbr B	Mbr C	Mbr D	Mbr E	Mbr F	Mbr G	Mbr H	Mbr I	Mbr J	Mbr K	Mbr L	Mbr M
Aug-23				*									
Sep-23				*									
Oct-23				*	*								
Nov-23	*			*	*							*	
Dec-23	*			*	*							*	*
Jan-24	*			*	*							*	*
Feb-24			*	*	*	*					*	*	
Mar-24	*	*	*		*	*				*	*		
Apr-24	*		*		*	*			*		*		
May-24			*		*	*			*		*		
Jun-24			*		*	*			*				
Jul-24			*		*	*	*	*					
Aug-24			*		*				*	*			

State A

Must meet all of the following:

1. Diagnosis of moderate to severe vasomotor symptoms due to menopause
2. Trial and failure, contraindication, or intolerance to TWO of the following:
    - Gabapentin
    - Menopausal hormone therapy (e.g., estrogen monotherapy or estrogen + progesterone)
    - Oxybutynin
    - SSRI (e.g., paroxetine, escitalopram, citalopram)
    - SNRI (e.g., venlafaxine and desvenlafaxine)

State B

Initial Criteria

Must meet all of the following:

1. Diagnosis of moderate to severe vasomotor symptoms due to menopause
2. Member has tried and failed to achieve an adequate response with at least TWO preferred oral estrogen or estrogen/progestin products

Reauthorization: Documentation of positive clinical response to therapy (e.g., decrease in frequency and severity of vasomotor symptoms from baseline, etc.)

State C

Initial Authorization
Must meet all of the following:
1. Diagnosis of moderate to severe vasomotor symptoms due to menopause
2. Member is 18 years of age or older
3. One of the following:
    - Member has tried and failed at least 90 days of therapy with ONE hormonal agent (e.g., oral, injectable, topical, transdermal, or vaginal), confirmed by claims history or chart documentation
    - Member has contraindication to hormonal therapy (must submit supporting chart documentation) and has tried and failed at least 90 days of therapy with ONE non-hormonal agent (e.g., gabapentin, paroxetine, venlafaxine, oxybutynin), confirmed by claims history or chart documentation
    - Prescriber has submitted valid medical justification for the use of Veozah (fezolinetant) over hormonal therapy AND other non-hormonal therapy
4. Prescriber attests to the following:
    - Member does not have cirrhosis
    - Member does not have severe renal impairment or end-stage renal disease (ESRD)
    - Member is not currently utilizing a CYP1A2 inhibitor and will not be initiated on CYP1A2 inhibitor therapy while on concomitant Veozah (fezolinetant) therapy
5. Dose requested does not exceed 45 mg (1 tablet) per day

Reauthorization
Must meet all of the following:
1. History of the requested agent for at least 90 days of the past 120 days, confirmed by claims history or chart documentation
2. One of the following:
    - Member has previously tried and failed at least 90 days of therapy with ONE hormonal agent (e.g., oral, injectable, topical, transdermal, or vaginal), confirmed by claims history or chart documentation
    - Member has contraindication to hormonal therapy and has previously tried and failed at least 90 days of therapy with ONE non-hormonal agent (e.g., gabapentin, paroxetine, venlafaxine, oxybutynin), confirmed by claims history or chart documentation
    - Prescriber has submitted valid medical justification for the use of Veozah (fezolinetant) over hormonal therapy AND other non-hormonal therapy
3. Prescriber attests to the following:
    - Member does not have cirrhosis
    - Member does not have severe renal impairment or end-stage renal disease (ESRD)
    - Member is currently not on a CYP1A2 inhibitor and will not be initiated on a CYP1A2 inhibitor while on concomitant Veozah (fezolinetant) therapy
4. Dose requested does not exceed 45 mg (1 tablet) per day

Commercial

Must meet all of the following:
1. Diagnosis of moderate to severe vasomotor symptoms due to menopause
2. Submission of medical records (e.g., chart notes, paid claims history) documenting trial and failure, contraindication, or intolerance to both of the following (document drug, date, and duration of trial):
    - Menopausal hormone therapy (e.g., Premarin, Bijuva, Estrogel, etc.)
    - Non-hormonal therapy (e.g. paroxetine mesylate, venlafaxine, clonidine, etc.)

Reauthorization: Documentation of positive clinical response to therapy (e.g., decrease in frequency and severity of vasomotor symptoms from baseline, etc.)

Zurzuvae (zuranolone) first oral medication for the treatment of postpartum depression (PPD) in adults

Time Period February 2024 to July 2024

Drug Name	Total Rx	Paid Amount	Paid/Rx	Avg Quantity/DS	Utilizers	Age Range
ZURZUVAE cap 25mg	5	$79,546.15	$15,909.23	28 per 14 days	5	22 – 32

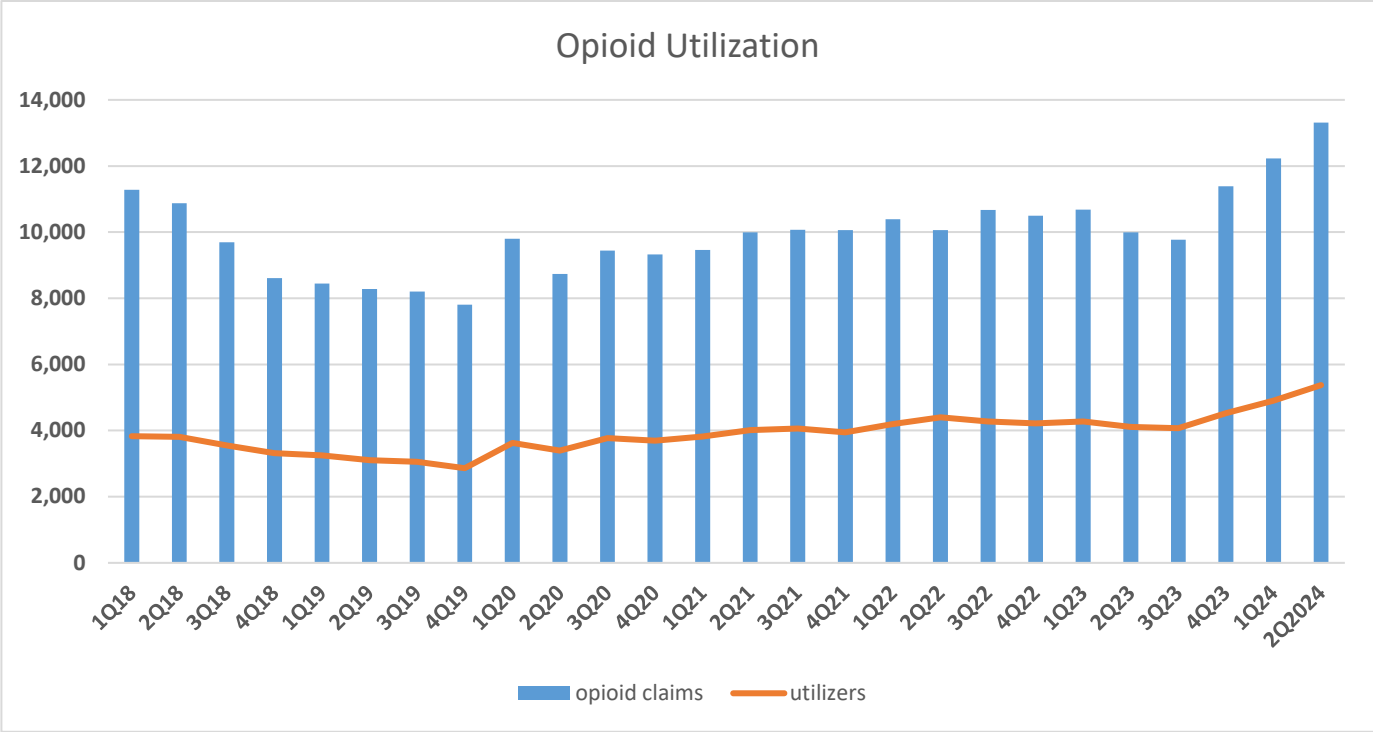
*Red font denotes drug is on PA

PA effective 5/1/2024
Fill Dates:

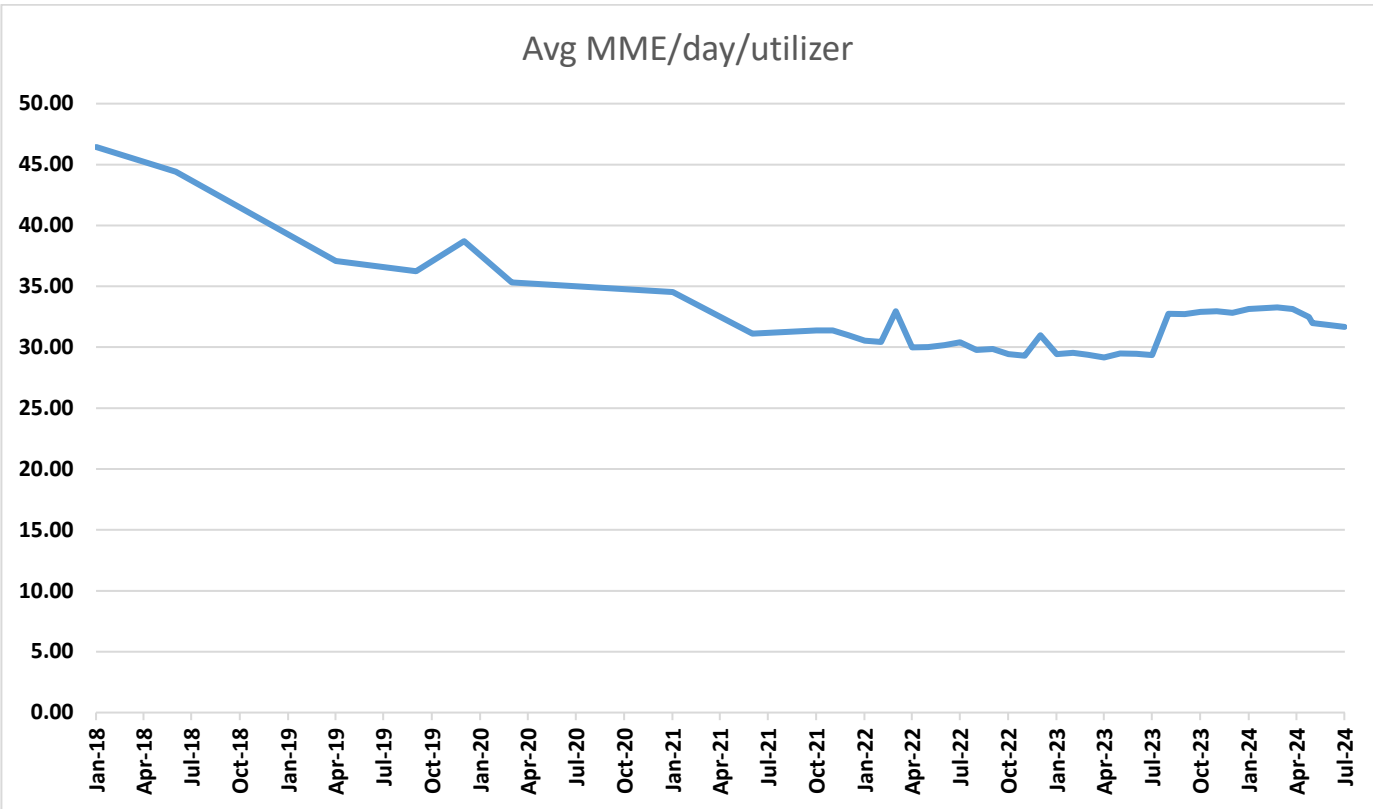
- Feb 14, 2024 – Nurse Practitioner, Psychiatric/Mental Health
- Feb 26, 2024 – Obstetrics & Gynecology
- April 3, 2024 – Nurse Practitioner, Family Health
- April 12, 2024 – Nurse Practitioner, Psychiatric/Mental Health
- July 23, 2024 (PA review) – Obstetrics & Gynecology

PA Type	Month	Approved	Denied	Total
High Dollar	February 2024 March 2024 April 2024	4		4
Clinical Review	June 2024 July 2024	1	3	4

Opioid Summary



- 1Q18 to 4Q19 excludes IHS
- 1Q20 to current includes IHS
- March 13, 2020 – Pandemic Closure



Opioid Initiatives:

1. June 1, 2018 – early refill threshold for controlled substance changed from 75% to 85%
2. July 1, 2028 – PA for more than one LAO and one SAO
3. August 1, 2018 – opioid Naïve PA (initial 7-day supply and 60 MED limit)
4. October 1, 2018 to October 1, 2019 – decrease from 300 MED to 90 MED (cancer diagnosis excluded)

Other Initiatives:

- Buprenorphine PA (Bunavail/Suboxone/Zubsolv/Subutex) and ST (Belbuca/Butrans) removed 10/14/2019
- Lidoderm PA removed 8/1/2020

Total Eligibles and Utilizers

Quarter	Avg eligible members	Avg utilizing members of all drugs	% utilizing members of all drugs
1Q2020	123,573	27,090	21.9%
2Q2020	126,777	20,746	16.4%
3Q2020	132,373	23,417	17.7%
4Q2020	136,262	23,489	17.2%
1Q2021	139,748	24,407	17.5%
2Q2021	142,872	26,206	18.3%
3Q2021	146,023	27,933	19.1%
4Q2021	149,034	29,317	19.7%
1Q2022	151,735	29,092	19.2%
2Q2022	154,608	28,370	18.3%
3Q2022	157,627	29,167	18.5%
4Q2022	160,060	32,124	20.1%
1Q2023	162,684	31,612	19.4%
2Q2023	142,001	27,296	19.2%
3Q2023	131,292	26,218	19.9%
4Q2023	134,270	29,320	21.8%
1Q2024	141,162	32,891	23.3%
2Q2024	149,613	32,686	21.8%

SDM 2Q2024
Mar 24 to Jun 24

Opioid Utilization Snapshot

1Q2024
Dec 23 to Jan 24

Opioid Claims **13,315**

3.1% prescription claims filled for an opioid

1.2% higher than Medicaid FFS benchmark

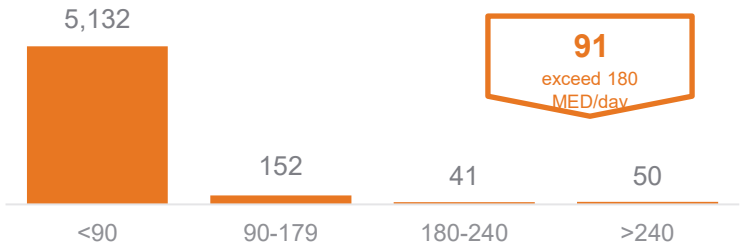
Utilizers **5,375**

30.2% are high utilizers [1]

2.8% higher than high utilizers Medicaid FFS

Utilizers by Cumulative MED[4]

Current CDC Guidelines[5] urge doses of 90 MME[6] or less in chronic opioid utilizers[5]



Shoppers: Poly Pharmacy

77 opioid utilizing members with 3+ pharmacies

450 Shoppers: Poly Prescriber

opioid utilizing members with 3+ prescribers

Opioid Claims **12,230**

3.2% prescription claims filled for an opioid

1.3% higher than Medicaid FFS benchmark

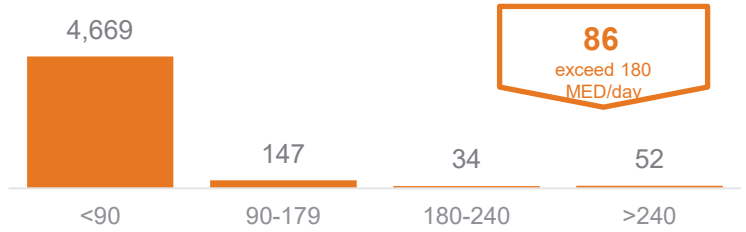
Utilizers **4,902**

31.4% are high utilizers [1]

3.5% higher than high utilizers Medicaid FFS

Utilizers by Cumulative MED[4]

Current CDC Guidelines[5] urge doses of 90 MME[6] or less in chronic opioid utilizers[5]



Shoppers: Poly Pharmacy

66 opioid utilizing members with 3+ pharmacies

403 Shoppers: Poly Prescriber

opioid utilizing members with 3+ prescribers

OPTUMRx®

[1]Defined as 3+ opioid scripts within 120 days period; [4]**MED** – Morphine Equivalent Dose is a relative potency of an opioid to standard of a morphine; Cumulative MED is daily MED or narcotic load across all active opioid prescriptions in a members profile within a 120 day period; [5]JAMA. 2016 Apr 19;315(15):1624-45. [6]MME – Morphine Milligram Equivalent represents a relative potency of an opioid to a morphine dose.

Opioid Utilization

SDM 2Q2024
Opportunities date range: Mar - Jun 2024
Benchmark: MEDICAID FEE FOR SERVICE

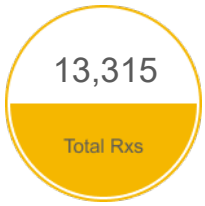
Utilizers: 5,375

3.1% of all Rx claims are filled for an Opioid

Opioid dependence can start in just a few days, and the risk of chronic opioid use increases with each additional day of opioid supplied, starting with the third day. Our Opioid Risk Management program, which includes point of sale, utilization management and retrospective drug utilization edits, are tightly aligned with CDC opioid prescribing guidelines which can help reduce exposure to excessive doses and prevent more members from transitioning from acute to chronic use.

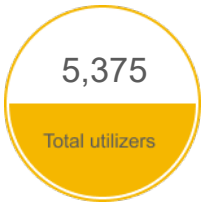
- Opioid prescriptions account for 3.1% of all prescriptions this period, which is 1.2% higher than the benchmark
- 1,622 high opioid utilizers were identified this period, which is 2.8% higher than the benchmark

Opioid claims



PERCENT NON-COMPLIANT
11.0%

Opioid utilizers

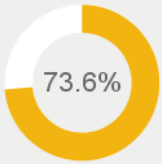


HIGH UTILIZERS
30.2%
1,622 high utilizers

2.8% over benchmark

High utilizers – view definition

Claim breakdown



short acting opioids

73.6% of all opioid Rxs were filled for short acting opioids. **2,714** Rxs were for medication assisted therapy (MAT) and **106** were for rescue therapy. CDC guidelines advise prescribers to manage pain with the lowest effective dose and to avoid or carefully justify doses for chronic users >90mg MME/day.

MAT – view definition
Overdose rescue therapy – view definition
MME – view definition

Utilizers by cumulative MED

91 utilizers exceed 180 MED/day

MED Scores	<90	90-179	180-240	>240
Utilizers	5,132	152	41	50

MED – view definition

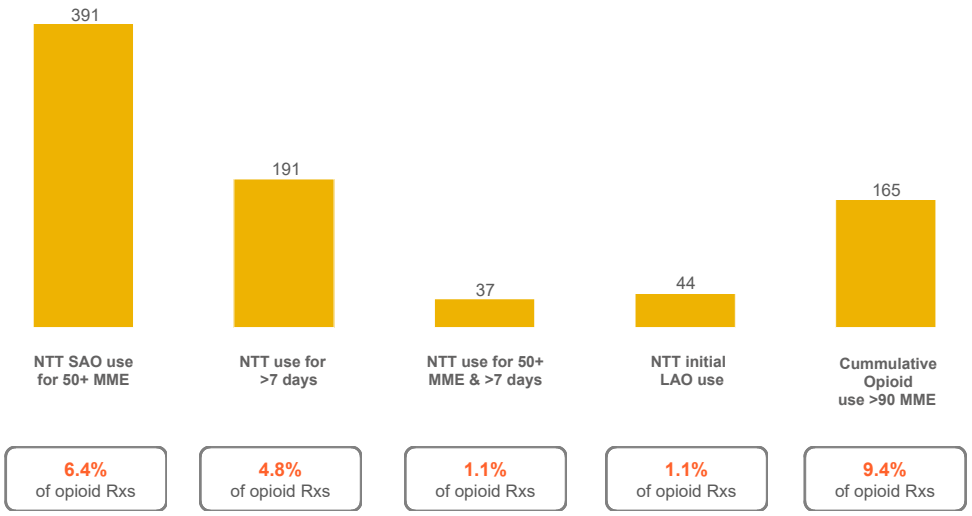
Opioid Opportunity Assessment

SDM 2Q2024
Opportunities date range: Mar - Jun 2024
Benchmark: MEDICAID FEE FOR SERVICE

Percent non-compliant: 11.0%

Utilizers non-compliant to opioid Rx CDC guidelines

(new to therapy and chronic use)



NTT - view definition | SAO - view definition | LAO - view definition | MME - view definition

DID YOU KNOW?

77 opioid utilizing members use 3 or more pharmacies and 450 opioid utilizing members use 3 or more prescribers.

Identification, management and prevention of fraudulent or potential abuse of opioid medications are monitored and addressed by OptumRx through various means in pharmacy network audit capabilities and high touch clinical programs that include care coordination with opioid prescribers.

Opioid utilizers with potentially contraindicated medication use

SKELETAL MUSCLE RELAXANTS	BENZODIAZEPINES	ANTICONVULSANTS	MEDICATION ASSISTED THERAPY	PRENATAL
1,066	747	989	502	161

Anticonvulsants –view definition

New Business

Glucagon-like peptide-1 receptor agonist (GLP-1) Review

Time Frame 2Q2024

Drug Name	Total Rx	Paid Amount	Paid/ Rx	Avg Qty/DS	Mbr	Age Range	Net Cost
BYETTA (exenatide) inj	0						$
BYDUREON BC (exenatide) inj	15	$12,058.34	$803.89	3.4 per 28 days	6	14-64	$$$
MOUNJARO (tirzepatide) inj	850	$854,314.07	$1,005.08	2 per 28 days	331	10-68	$$$$
OZEMPIC (semaglutide) inj	1,342	$1,247,262.03	$929.41	3 per 28.3 days	560	10-65	$$$
RYBELSUS (semaglutide) tab	103	$95,998.27	$932.02	30 per 30 days	49	32-64	$$
TRULICITY (dulaglutide) inj	175	$167,245.86	$955.69	2 per 28 days	81	32-64	$$
VICTOZA (liraglutide) inj	59	$33,812.19	$573.08	6.4 per 28 days	32	14-62	$
TOTAL	2,544	$2,410,690.76	$947.60		1,010	10-68	

*Red font denotes drug is on PA; Excludes IHS

GLP Prescribers

Taxonomy Description	Members
Ambulatory Health Care Facilities/Clinic/Center/Urgent Care	97
Dermatology	1
Dietitian, Registered, Nutrition, Obesity and Weight Management	**1**
Emergency Medicine	72
Endocrinology, Diabetes & Metabolism	**48**
Family Medicine, Obesity Medicine	**10**
Family Practice	168
Geriatric Medicine	5
Homeopathic Physician	1
Hospitalist	8
Internal Medicine	87
Internal Medicine, Hospice and Palliative Medicine	2
Internal Medicine, Obesity Medicine	**19**
Nuclear Medicine, In Vitro & In Vivo	1
Nurse Midwife	1
Nurse Practitioner	249
Obstetrics & Gynecology	6
Osteopathic Manipulative Medicine, Neuromusculoskeletal Medicine	3
Pediatrics	12
Physical Medicine & Rehabilitation, Brain Injury Medicine	1
Physician Assistant, Medical	109
Psychiatry & Neurology	5
Pulmonology, Pediatric	20
Sports Medicine, Family Practice	1
Student/Training Program/Student, Health Care	80
Surgery, Transplant	3

Indication	**Byetta** (exenatide)	**Bydureon BCise** (exenatide ER)	**Mounjaro** (tirzepatide)	**Ozempic** (semaglutide)	**Rybelsus** (semaglutide)	**Symlin** (pramlintide)	**Trulicity** (dulaglutide)	**Victoza** (liraglutide)
T1DM, as an adjunctive treatment in patients who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy						✔		
T2DM, as an adjunctive treatment in patients who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy						✔		
Adjunct to diet and exercise to improve glycemic control in adults with T2DM	✔	✔	✔	✔	✔		✔	✔
Adjunct to diet and exercise to improve glycemic control in patients 10 years and older with T2DM		✔					✔	✔
Reduce the risk of major adverse cardiovascular (CV) events (MACE; CV death, non-fatal myocardial infarction [MI], or non-fatal stroke) in adults with T2DM and established CV disease (CVD)				✔				✔
Reduce the risk of MACE (CV death, non-fatal MI, or non-fatal stroke) in adults with T2DM who have established CVD or multiple CV risk factors							✔	
Not recommended as first-line therapy for patients inadequately controlled on diet and exercise because of the uncertain relevance of the rodent C-cell tumor findings to humans. Prescribe only to patients for whom the potential benefits are considered to outweigh the potential risk.		✔						
Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in these patients.	✔	✔	✔	✔	✔		✔	
Not indicated in treatment of patients with T1DM.	✔	✔	✔	✔	✔		✔	✔
Has not been studied in patients with severe gastrointestinal (GI) disease, including severe gastroparesis. Not recommended in patients with pre-existing severe GI disease.							✔	
Has not been studied in patients with gastroparesis. Not recommended in patients with gastroparesis.								
Should not be used with other products containing the active ingredient.	✔	✔						✔

Indication	Saxenda (liraglutide)	Wegovy (semaglutide)	Zepbound (tirzepatide)
Indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in: • Adult patients with an initial BMI of ≥ 30 kg/m^2 (obese) or ≥ 27 kg/m^2 (overweight) in the presence of ≥ 1 weight-related comorbid condition (e.g., hypertension, T2DM, dyslipidemia, OSA, or CVD)	✓		✓
Indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in: • Pediatric patients ≥ 12 years of age with: o Body weight > 60 kg and o An initial BMI corresponding to ≥ 30kg/m^2 for adults (obese) by international cut-offs	✓		
Indicated in combination with a reduced calorie diet and increased physical activity: • To reduce the risk of MACE (i.e., cardiovascular death, non-fatal myocardial infarction [MI], or non-fatal stroke) in adults with established CVD and either obesity or overweight • To reduce excess body weight and maintain weight long term in adults with overweight in the presence of ≥ 1weight-related comorbid condition • To reduce excess body weight and maintain weight long term in adults and pediatric patients ≥ 12 years of age with obesity		✓	

Abbreviations: BMI = body mass index; CVD = cardiovascular disease; MACE = major adverse cardiovascular events; OSA = obstructive sleep apnea; T2DM = type 2 diabetes mellitus; T1DM = type 1 diabetes mellitus

MACE Criteria

Criteria A

Initial Criteria – Approval Duration: 12 months

For reduction of MACE in members without diabetes

- Member is ages of ≥ 55 and < 75
- Member does not have diabetes, as evidenced by A1c within normal range without diabetes medication
- Member has an initial BMI of ≥ 27 kg/m^2 and < 35 kg/m^2
- Member has one of the following:
  - Prior myocardial infarction
  - Prior stroke and peripheral arterial disease (PAD)
- Member is concurrently taking lipid-lowering and antiplatelet therapy
- If member is a current tobacco user, member must receive tobacco cessation counseling
- If member qualifies for Wegovy, a dose escalation to 2mg of Ozempic (semaglutide) must be tolerated before Wegovy will be authorized (2.4mg is the only strength indicated for reduction of MACE)

Criteria B

Approval Criteria – 12 months

1. Patient is 21 years of age or older
2. Treatment is being requested to reduce the risk of major adverse cardiovascular events
3. Submission medical records (e.g. chart notes) of initial body mass index (BMI) of ≥ 27 kg/m2
4. Submission of medical records (e.g. chart notes) of ONE of the following:
   - Prior myocardial infarction
   - Prior stroke (ischemic and hemorrhagic stroke)

- Symptomatic peripheral arterial disease as evidenced by intermittent claudication with ankle–brachial index < 0.85, peripheral arterial revascularization procedure, or amputation due to atherosclerotic disease

5. Submission of medical records (e.g. chart notes, labs) of HbA1C ≤ 6.5%*
6. Prescriber attests patient is participating in a supervised comprehensive weight management program that encourages behavioral modification, reduced calorie diet, and increased physical activity
7. Patient does not have any of the following:
   - Diagnosis of type 1 or type 2 diabetes
   - New York Heart Association class IV heart failure
   - Personal or family history of medullary thyroid carcinoma (MTC) OR Multiple Endocrine Neoplasia syndrome type 2 (MEN 2);
   - History or presence of chronic pancreatitis
   - End-stage renal disease or currently receiving dialysis
8. For female patients of reproductive potential, all of the following has been addressed:
   - Patient is not pregnant or breastfeeding
   - Patient has been counseled to use highly effective contraceptive method during treatment
9. Medication is not being co-administered with another GLP-1 receptor agonists (e.g. Byetta, Ozempic, and Victoza)

Reauthorization – 12 months
1. Patient continues to meet initial criteria
2. Submission of medical records (e.g., chart notes) documenting a positive clinical response to therapy (e.g., patient has not had a major cardiovascular event within the past 12 months, decreased body weight or waist circumference from baseline, decrease blood pressure, total cholesterol, LDL, or triglyceride levels from baseline);
3. Patient must not have any contraindications or serious adverse effects (e.g., acute gallbladder disease, acute kidney injury, acute pancreatitis);

Criteria C

Initial Authorization – 12 months
1. Treatment is being requested to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke)
2. Patient is 18 years of age or older
3. Patient has established cardiovascular disease as evidenced by one of the following:
   - Prior myocardial infarction (MI)
   - Prior stroke (i.e., ischemic or hemorrhagic stroke)
   - Peripheral arterial disease (i.e., intermittent claudication with ankle-brachial index < 0.85, peripheral arterial revascularization procedure, or amputation due to atherosclerotic disease)
4. Used in as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program)
5. BMI greater than or equal to 27 kg/m2
6. Medication is not being co-administered with any of the following:
   - GLP-1 receptor agonists (e.g., Victoza, Ozempic, Rybelsus, Trulicity)
   - Tirzepatide-containing products (e.g., Mounjaro)

Reauthorization – 12 months
1. Patient is currently on a maintenance dose of 1.7mg or 2.4mg once weekly
2. Used in as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program)

3. Medication is not being co-administered with any of the following:
    - GLP-1 receptor agonists (e.g., Victoza, Ozempic, Rybelsus, Trulicity)
    - Tirzepatide-containing products (e.g., Mounjaro)

Criteria D

Initial Approval – 12 months

1. Treatment is being requested to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke)
2. Patient is 45 years of age or older
3. Submission of medical records (e.g., chart notes) documenting patient has established cardiovascular disease as evidenced by one of the following:
    - Prior myocardial infarction (MI)
    - Prior stroke (i.e., ischemic or hemorrhagic stroke)
    - Peripheral arterial disease (i.e., intermittent claudication with ankle-brachial index < 0.85, peripheral arterial revascularization procedure, or amputation due to atherosclerotic disease)
4. Submission of medical records (e.g., chart notes) documenting that medication is being used in combination with a program supporting a reduced calorie diet of at least 500 kcal/day and patient can be active for at least 150 minutes per week
5. Submission of medical records (e.g., chart notes) documenting BMI greater than or equal to 27 kg/m2
6. Submission of medical records (e.g., chart notes) documenting HbA1c less than 6.5% in the past 12 months
7. Submission of medical records (e.g., chart notes) documenting patient does not have any of the following:
    - Diagnosis of type 1 or type 2 diabetes (excluding gestational diabetes)
    - NY Heart Association functional class IV heart failure
8. Submission of medical records (e.g., chart notes) or absence of paid claims confirming medication is not being co-administered with any of the following:
    - GLP-1 receptor agonists (e.g., Victoza, Ozempic, Rybelsus, Trulicity)
    - Tirzepatide-containing products (e.g., Mounjaro)

Reauthorization – 12 months

1. Submission of medical records (e.g., chart notes) documenting that patient demonstrated medication adherence (e.g., 80% adherence to treatment) over prior 6 months
2. Submission of medical records (e.g., chart notes) documenting that medication is being used in combination with a program supporting a reduced calorie diet of at least 500 kcal/day and patient can be active for at least 150 minutes per week
3. Paid claims or submission of medical records (e.g., chart notes) documenting patient is receiving a dose of 1.7mg or 2.4mg per week
4. Submission of medical records (e.g., chart notes) documenting HbA1c less than 6.5% in the past 12 months
5. Submission of medical records (e.g., chart notes) documenting patient does not have any of the following:
    - Diagnosis of type 1 or type 2 diabetes (excluding gestational diabetes)
    - NY Heart Association functional class IV heart failure
6. Submission of medical records (e.g., chart notes) or absence of paid claims confirming medication is not being co-administered with any of the following:
    - GLP-1 receptor agonists (e.g., Victoza, Ozempic, Rybelsus, Trulicity)
    - Tirzepatide-containing products (e.g., Mounjaro)

ADHD Review of Cotempla, Daytrana, Jornay, Relexxi, Aptensio, Azstarys

Time Frame 2Q2024

Drug Name	Tota l Rx	Paid Amount	Paid/ Rx	Avg Qty/DS	Mbr	Age Range	Net Cost
methylphenidate							
methylphenidate **CAP** 10mg, 20mg, 30mg 50mg, 60mg	523	$21,213.23	$40.56	29.8/29.5 days	257	4 - 64	$
methylphenidate **CAP ER** 10mg, 15mg, 20mg, 30mg, 40mg	335	$25,328.30	$75.61	29.4/29.2 days	163	5 - 59	$
methylphenidate **TAB** 5mg, 10mg, 20mg	973	$20,330.39	$20.89	46.9/29.3 days	466	4 - 64	$
methylphenidate **TAB ER** 10mg, 18mg, 20mg, 27mg, 36mg, 45mg, 54mg, 63mg, 72mg	2941	$260,721.75	$88.65	31.1/29.3 days	1288	4 - 60	$
CONCERTA TAB 18mg, 27mg, 36mg, 54mg	39	$7,270.41	$186.42	32/30 days	20	5 - 37	$
COTEMPLA XR ODT 8.6mg 8.6mg, 17.3mg, 29.9mg	**6**	**$3,014.16**	**$502.36**	**30/30 days**	**2**	**8**	**$$$$**
JORNAY PM CAP ER 24HR 20mg, 40mg, 60mg, 80mg, 100mg	**302**	**$131,429.61**	**$435.20**	**29.9/29.6 days**	**132**	**5 - 40**	**$$$$**
RELEXXII TAB 45mg ER 18mg, 27mg, 36mg, 45mg	**1**	**$646.62**	**$646.62**	**30/30 days**	**1**	**12**	**$$$$**
RITALIN TAB [5mg & 10mg]	3	$1,452.14	$484.05	28.3/28.3 days	3	8 - 14	$
RITALIN LA CAP [10mg & 20mg]	2	$146.66	$73.33	30/30 days	2	8 - 9	$
APTENSIO XR CAP 24 HR 10mg, 15mg, 20mg, 30mg, 40mg, 50mg, 60mg	0						**$$$**
DAYTRANA DIS transdermal patch 10mg/9HR, **30mg /9HR**	**4**	**$1,002.60**	**$250.65**	**30/30 days**	**2**	**16 - 32**	**$$$**
methylphenidate PAD 10mg/9HR, 15mg/9HR, 20mg/9HR, 30mg/9HR	19	$3,628.72	$190.99	26.1/30 days	10	3 - 32	**$$$**
QUILLICHEW CHW ER 20mg, 30mg, 40mg	213	$84,643.71	$397.39	33.2/29.6 days	96	4 - 18	$$
methylphenidate CHW 2.5mg, 5mg, 10mg	79	$10,222.78	$129.40	60.4/29.5 days	41	4 - 16	$
QUILLIVANT SUSP 25mg/5ml	231	$95,267.30	$412.41	158/29.4 days	104	4 - 31	$$
methylphenidate SOL 5mg/5ml, 10mg/5ml	35	$1,170.69	$33.45	234/29.5 days	20	4 - 12	$
serdexmethylphenidate/dexmethylphenidate							
AZSTARYS CAP 26.1-5.2mg, 39.2-7.8mg, 52.3-10mg	**417**	**$159,829.36**	**$383.28**	**29.5/29.5days**	**175**	**2 - 51**	**$$$**
dexmethylphenidate							
dexmethylphenidate TAB 2.5mg, 5mg, 10mg	280	$5,675.29	$20.27	43.6/29.1 days	136	4 - 59	$
dexmethylphenidate CAP ER 5mg, 10mg, 15mg, 20mg 25mg, 30mg, 35mg, 40mg	1222	$60,859.13	$49.80	30.3/29 days	504	4 - 53	$
FOCALIN XR CAP 5mg, 10mg, 15mg, 20mg, 25mg, 40mg	28	$1,903.15	$67.97	30.4/29.3 days	21	5 - 19	$

Daybue (trofinetide) indicated for the treatment of Rett syndrome in adults and pediatric patients 2 years of age and older

	June-Dec 2023					Jan-July 2024				
Drug Name	**Total Rx**	**Paid Amount**	**Paid/ Rx**	**Mbr**	**Age Range**	**Total Rx**	**Paid Amount**	**Paid/ Rx**	**Mbr**	**Age Range**
Daybue	29	$1,199,862.41	$41,374.57	8	5 - 30	41	$1,769,709.61	$43,163.65	6	5 - 43

State A

Initial Authorization – 12 months
1. Patient is 2 years of age or older
2. Diagnosis of Rett Syndrome
3. Prescribed by, or in consultation with, a neurologist, clinical geneticist, or developmental pediatrician

Reauthorization – 12 months
1. Documentation of positive clinical response to Daybue® (e.g. improvement or stabilization in purposeful hand skills, spoken language, repetitive hand movements, and gait abnormalities)

State B

Initial Authorization – 6 months
1. Prescribed by or in consultation with one of the following:
   a. Geneticist
   b. Neurologist
   c. Developmental pediatrician experienced in the treatment of Rett syndrome
2. Patient is 2 years of age or older
3. Diagnosis of Rett syndrome
4. The member has mutation(s) in the *methyl CpG binding protein 2 (MECP2)* gene confirmed by molecular genetic testing.
5. Member has documentation of one of the following baseline assessment scores (for verification of benefit on renewal request):
   a. Rett Syndrome Behavioral Questionnaire (RSBQ) score
   b. Clinical Global Impression-Severity (CGI-S) score

Reauthorization – 12 months
1. Member has experienced a positive clinical response to therapy as demonstrated by an improvement or stabilization of RSBQ or CGI-S score compared to baseline

State C

Initial Authorization: 6 months
Must meet all of the following:
1. Member is 2 years of age or older
2. Member weighs 9 kg or more [PAS note- add a field for submitter to provide member weight]
3. Diagnosis of Rett syndrome (RTT) with both of the following:
   a. Genetic analysis demonstrating mutation(s) in the methyl-CpG binding protein-2 (MECP2) gene (documentation of genetic confirmation required)
   b. Diagnosis of Typical or Classic Rett syndrome with a period of regression followed by recovery or stabilization, confirmed by ALL of the following:
      - Partial or complete loss of acquired purposeful hand skills

- Partial or complete loss of acquired spoken language
- Gait abnormalities: impaired or absence of ability to walk
- Hand wringing/squeezing/clapping/tapping, mouthing, and/or washing/rubbing that seems habitual or uncontrollable

4. Prescribed by, or in consultation with, a neurologist or specialist with expertise in the management of RTT
5. Prescriber attests that member does not have any of the following:
   - Brain injury secondary to trauma (peri-or postnatally), neurometabolic disease, or severe infection that causes neurological problems
   - Moderate to severe renal impairment (eGFR < 45 mL/minute/1.73 m2)
6. Requested quantity does not exceed 120 mL per day or 8 bottles (450 mL) per 30 days

Reauthorization – 12 months
Must meet all of the following:
1. History of the requested agent for at least 90 days of the past 120 days, as confirmed by claims history or chart documentation (excluding claims with an emergency supply indicator)
2. Prescriber has submitted clinical documentation demonstrating ONE of the following (documentation must be provided):
   - Member has achieved disease stability
   - Member has achieved clinically significant improvement in core symptoms
   - Member has experienced less than expected decline in disease progression
3. Prescriber attests that member does NOT have any of the following:
   - Brain injury secondary to trauma (peri-or postnatally), neurometabolic disease, or severe infection that causes neurological problems
   - Moderate to severe renal impairment (eGFR < 45 mL/minute/1.73 m2)
4. Requested quantity does not exceed 120 mL per day or 8 bottles (450 mL) per 30 days

Commercial

Initial Authorization – 3 months
1. Diagnosis of Rett syndrome [submission of medical records (e.g., chart notes)]
2. Patient is 2 years of age or older
3. One of the following:
   a. Submission of medical records (e.g., chart notes) confirming presence of ALL of the following clinical signs and symptoms:
      - A pattern of development, regression, then recovery or stabilization
      - Partial or complete loss of purposeful hand skills such as grasping with fingers, reaching for things, or touching things on purpose
      - Partial or complete loss of spoken language
      - Repetitive hand movements, such as wringing the hands, washing, squeezing, clapping, or rubbing
      - Gait abnormalities, including walking on toes or with an unsteady, wide-based, stiff-legged gait
   b. Submission of medical records (e.g., chart notes) documenting molecular genetic testing confirms mutations in the MECP2 gene
4. Prescribed by or in consultation with one of the following:
   a. Geneticist
   b. Neurologist

Reauthorization – 12 months
1. Submission of medical records (e.g., chart notes) documenting positive clinical response to therapy

Optum Rx®

Therapeutic Class Overview

Insulin- Like Growth Factor-1 agents

Introduction

- Insulin-like growth factor 1 (IGF-1) is a hormone that plays a pivotal role in fetal development, adolescent growth, and adult tissue homeostasis. Imbalance in IGF production is associated with various pathologic conditions such as short stature, insufficient skeletal acquisition, alternations in body composition, metabolic disorders and reduced mental and physical capacity (*Yakar and Adamo 2012*).
- Growth hormone insensitivity (GHI) is a group of rare autosomal recessive disorders in which there is a reduction in or absence of the biologic effects of GH despite normal levels of GH. This is generally caused by loss-of-function mutations in the GH receptor gene or its downstream mediators, namely *IGF-1*, *STAT5b*, or *IGFALS*. In affected children, IGF-1 levels are abnormally low, referred to as primary IGF-1 deficiency, in that, no chronic medical condition can be identified causing the low levels. The most common form is known as Laron's syndrome; where abnormal GH receptor gene makes patients resistant to GH, resulting in low levels of IGF-1. There are less than 500 known cases of Laron Syndrome worldwide; 65% have Middle Eastern ancestry or are of Ecuadorian decent (*Food and Drug Administration [FDA] medical review 2005, National Organization for Rare Diseases [NORD] 2016*, *Richmond and Rogol 2022*).
- Severe primary IGF-1 deficiency is defined as both height and serum IGF-1 levels ≤ -3 standard deviations (SD) despite normal or elevated GH levels. Guidelines indicate basing diagnosis primary IGF deficiency on a combination of factors (eg, abnormally low serum IGF-1, secondary causes excluded, presence of characteristic features [eg, microcephaly, protruding forehead, saddle nose, small chin, high pitched voice]) (*Grimberg et al 2016)*.
- Increlex (mecasermin) is a recombinant IGF-1 recommended for children with severe primary IGF-1 deficiency who are 2 years of age or older with open epiphyses and height and basal IGF-1 SD both ≤-3 due to GH gene deletion or who have developed neutralizing antibodies to GH (*Daybue prescribing information 2023*). Once diagnosed, patients should be treated chronically until epiphyseal plate closure (ie, until no further linear growth is possible) (*FDA Medical Review 2005*). If the cause of GHI has not been established, a trial of GH therapy may be recommended prior to initiating recombinant IGF-1 (*Grimberg et al 2016*).
- Rett syndrome is a neurodevelopmental disorder that affects mainly girls, and most cases result from mutations in the *MECP2* gene, but a small group are caused by mutations in *CDKL5* or *FOXG1* genes. Symptoms typically present between 6 and 18 months of age. Rett syndrome presents as loss of speech and hand use, stereotypic hand movements, and gait abnormalities. Additional features include deceleration of head growth, seizures, autistic features, and breathing abnormalities. There are 2 phenotypic types of Rett syndrome (*NORD 2023, Schultz and Suter 2022[a-b]*):
  - Typical (classic) form: Affected patients initially develop normally and then experience loss of speech and purposeful hand use and onset of stereotypic hand movement and gait abnormalities. Deceleration of head growth can be one of the first signs. Additional manifestations can include seizures, autistic features, intermittent breathing abnormalities, autonomic nervous system dysfunction, cardiac abnormalities, and sleep disturbances.
  - Atypical form: Often presents similarly to the typical form but may not have all of the clinical features of the typical form.
- Rett syndrome is the second most common cause of severe intellectual disability after Down syndrome. The incidence of Rett syndrome in the United States is estimated to be 1 in 10,000 girls by age 12. In a report from a large population-based registry in Texas, the prevalence of classic Rett syndrome was estimated as 1 per 22,800 females ages 2 through 18 years, or 0.44 per 10,000. The prevalence per 10,000 girls was 0.56 in France, 0.65 in Sweden and Scotland, and 0.72 in Australia (*NORD 2023, Schultz and Suter 2023[a-b]*).
- Daybue (Trofinetide) is the first therapy FDA-approved for Rett syndrome. Trofinetide is a synthetic analog of the amino-terminal tripeptide of IGF-1, which occurs naturally in the brain. The mechanism by which trofinetide exerts its therapeutic effect in Rett syndrome is unknown (*Daybue prescribing information 2023*). Currently, the mainstay of treatment includes symptomatic treatment. Specific issues that commonly require attention include growth failure and nutrition, bone quality, epilepsy, breathing dysfunction, cardiac abnormalities, scoliosis, sleep disturbance, and motor dysfunction. Therapy in areas of communication, physical and occupational disciplines may be warranted (*Schultz and Suter 2023[a-b]*).
- The marketing and distribution of mecasermin rinfabate (Iplex) was discontinued in the United States due to legal reasons between manufacturers (*Pollack 2007*).
- Medispan Class: Insulin-Like Growth Factors (Somatomedins)

Table 1. Medications Included Within Class Review

Drug	Alternative Available (same molecular entity)*
Daybue (trofinetide) oral solution	-
Increlex (mecasermin) injection	-

*For example, authorized generic, branded generic (unless not considered therapeutically equivalent by the Orange Book), generic, unbranded biologic, or interchangeable biologic.

(*Drugs@FDA 2024, Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations 2024*)

Indications

Table 2. Food and Drug Administration Approved Indications

Indication	Daybue (trofinetide)	Increlex (mecasermin)
Treatment of growth failure in pediatric patients 2 years of age and older with severe primary IGF-1 deficiency* or with GH gene deletion who have developed neutralizing antibodies to GH. †		✔
Treatment of Rett syndrome in adults and pediatric patients 2 years of age and older	✔	

*Defined as height SD score and basal IGF-1 SD score ≤ -3 with normal or elevated GH.
†Limitations of use: not a substitute to GH for approved GH indications, and not indicated for use in patients with secondary forms of IGF-1 deficiency, such as GH deficiency, malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory corticosteroids

(*Prescribing information: Daybue 2023, Increlex 2024*)

- Information on indications, mechanism of action, pharmacokinetics, dosing, and safety has been obtained from the prescribing information for the individual products, except where noted otherwise.

Clinical Efficacy Summary

- The FDA-approval of mecasermin was based on pooled efficacy analysis of 5 clinical studies (4 open-label [OL] and 1 double-blind [DB], placebo-controlled [PC] trials) in pediatric patients with severe primary IGF-1 deficiency. Patients were enrolled in the trials based on extreme short stature, slow growth rates, low IGF-1 serum concentrations, and normal GH levels. This study integrated 23 patients from 4 preceding OL clinical studies (treated with mecasermin twice daily for up to 2 years) into a single study named 1419 (N = 48) for a total of 71 patients. The primary endpoint was the increase in height velocity (*FDA medical review 2005, Increlex prescribing information 2024*).
  - Sixty-one patients had at least 1 year of treatment. Fifty-three (87%) had Laron Syndrome; 7 (11%) had GH gene deletion, and 1 (2%) had neutralizing antibodies to GH. Thirty-seven (61%) were male; forty-eight (79%) were Caucasian. Fifty-six (92%) patients were prepubertal at baseline.
  - Annual height results showed a statistically significant improvement in height velocity (cm/year) compared to baseline for years 1 to 6, but not year 7 or 8.
    - Year 1: + 5.2 cm/year, n = 58, p < 0.0001
    - Year 2: + 2.9 cm/year, n = 48, p < 0.0001
    - Year 3: + 2.3 cm/year, n = 38, p < 0.0001
    - Year 4: + 1.5 cm/year, n = 23, p = 0.0045
    - Year 5: + 1.5 cm/year, n = 21, p = 0.0015
    - Year 6: + 1.5 cm/year, n = 20, p = 0.0009
    - Year 7: + 1.0 cm/year, n = 16, p = 0.0897
    - Year 8: + 0.7 cm/year, n = 13, p = 0.3059
  - The major secondary analysis was the assessment of change in height SD score. The mean SD scores increased from -6.7 at baseline to a mean of -5.9 at year 1 and maintained through year 8. Bone maturation rate was also assessed in 49 patients, with bone age increasing 8.1% faster than chronological age (5.3 vs 4.9 years, respectively). Of note, approximately 42% of patients reported at least one hyperglycemic episode during their course of therapy.

- A multicenter, OL study evaluated the long-term efficacy of mecasermin in 76 children (treated for up to 12 years) with IGF-1 deficiency due to GH insensitivity. Inclusion criteria included patients over the age of 2 years old with SD scores for height and circulating IGF-I concentration less than - 2 for age and sex, and evidence of resistance to GH. The primary outcome was the increase in height velocity (*Chernausek et al 2007*).
  - The baseline height velocity (2.8 cm/year on average) increased to 8.0 cm/year during the first year of treatment ($p < 0.0001$). The median increment in first-year height velocity over baseline was 5.3 cm/year (mean 5.2 cm/year; range -2.8 to 10.4).
  - The first-year growth was dose dependent, with those patients receiving 120 ug/kg twice daily growing the fastest ($p < 0.001$). For patients receiving an average dose of at least 100 ug/kg twice daily for 2 years (N = 19), first- and second year mean height velocities were 8.7 ± 1.7 and 6.1 ± 1.6 cm/year, respectively, significantly greater ($p < 0.0001$) than the baseline height velocity (2.8 ± 1.3 cm/year). Treatment effects persisted and remained above baseline up to year 8.
- A 1-year, randomized, OL trial evaluated the safety and efficacy of mecasermin in 136 pediatric patients aged 3 or older with SD scores for height and circulating IGF-I concentration less than - 2 and stimulated GH ≥ 7 ng/mL. Patients were randomized to observation or 1 of 2 doses of mecasermin; Initially, the 2 dose groups were 40 and 80 ug/kg. However, 40 ug/kg was replaced with 120 ug/kg by trial amendment when it was determined that the 40 ug/kg dose did not normalize serum IGF-I. The primary endpoint was the increase in first-year height velocity (centimeters per year, cm/year) (*Midyett et al 2010*).
  - Mean first-year height velocities were significantly increased for the 80 and 120 ug/kg groups vs the untreated group using the intention to treat population (N = 136; 6.9 ± 1.0, 7.7 ± 1.5, and 5.2 ± 1.0 cm/yr, respectively; $p < 0.0001$ vs the untreated group). Results were consistent with those patients who completed the study (N = 124; $p < 0.0001$ vs untreated group), and first-year height velocities were also significantly greater for the 120 vs the 80 g/kg group (1.0 cm/year; $p < 0.0002$).
- The approval of trofinetide was supported by results from the DB, PC, Phase 3, LAVENDER (N = 187) study that tested the efficacy and safety of trofinetide vs placebo in female patients with Rett syndrome, aged 5 to 20 years of age. A total of 93 patients were randomly assigned to trofinetide twice daily and 94 patients received placebo for 12 weeks. After 12 weeks, trofinetide showed a statistically significant improvement from baseline compared with placebo on both the caregiver-assessed Rett Syndrome Behavior Questionnaire (RSBQ; Least square mean difference [LSMD] vs placebo, -3.1; 95% confidence interval [CI], -5.7 to -0.6; p = 0.0175) and 7-point Clinical Global Impression-Improvement (CGI-I; LSMD, -0.3; 95% CI, -0.5 to -0.1; p = 0.003) scale (*Neul et al 2022, Neul et al 2023*).

Clinical Guidelines

- The 2016 Pediatric Endocrine Society guidelines for GH and IGF-1 treatment in children and adolescents: GH deficiency, idiopathic short stature, and primary insulin-like growth factor-1 deficiency recommends the use of IGF-1 therapy to increase height in patients with severe primary IGF-1 deficiency (*Grimberg et al 2016*).
  - Diagnosis of primary IGF-1 deficiency or GHI should be based on a combination of 4 factors including 1) screening (eg, growth parameters and low IGF-1 concentrations, 2) excluding causes of secondary IGF-1 deficiencies (eg, poor nutrition, hepatic disease, and GH deficiency), 3) circulating levels of GH binding protein (low levels suggesting Laron's Syndrome and normal levels considered non-informative), and 4) IGF-1 generation test and mutation analysis (limited usefulness).
  - A trial of GH therapy is recommended in patients with unexplained IGF-1 deficiency.
  - Patients with hormone signaling defects known to be unresponsive to GH treatment can start directly on IGF-1 replacement, including:
    - Very low or undetectable levels of GH binding protein and/or proven GH receptor gene mutations know to be associated with Laron Syndrome/GHI, GH-neutralizing antibodies, *STAT5b* gene mutations, and IGF1 gene deletion or mutation.
  - The guideline recommends a starting dose of 80 to 120 ug/kg 2 times daily, given after a carbohydrate containing meal. Patients and families should be educated on the symptoms and risks of hypoglycemia associated with treatment.
- The International Rett Syndrome Foundation published guidance and best practices to assist health professionals and families in care. The guidelines include a checklist and detailed references for guidance developed by consensus. The International Rett Syndrome Foundation states given the median life expectancy well into the sixth decade, guidance is provided to health professionals to achieve current best possible outcomes for these special-needs individuals.

Treatment is supportive and focuses on gastrointestinal, respiratory, neurological, cardiology, dermatological, orthopedics, urology, development and behavioral, sleep, pain, and physical symptoms and systems (*Fu et al 2020*).

Safety Summary

- Pediatric use: The safety and effectiveness of mecasermin or trofinetide have not been established in children less than 2 years of age.

Daybue (trofinetide)

- Warnings and precautions:
  - Diarrhea: Most patients experience diarrhea during treatment. Counsel to stop laxatives prior to initiating therapy. If diarrhea occurs, patients should start antidiarrheal treatment, increase oral fluids, and notify their healthcare provider. Interrupt, reduce dose, or discontinue trofinetide if severe diarrhea occurs or if dehydration is suspected.
  - Weight loss: may occur in patients treated with trofinetide. Monitor weight and interrupt, reduce dose, or discontinue therapy if significant weight loss occurs.
- Adverse effects
  - Most common in clinical trials: diarrhea and vomiting.

Increlex (mecasermin)

- Contraindications:
  - Hypersensitivity to mecasermin
  - Intravenous (IV) administration
  - Closed epiphyses
  - Malignant neoplasia (current or history of)
- Warnings and precautions:
  - Risk of hypoglycemia: due to insulin-like effects.
  - Hypersensitivity and allergic reactions, including anaphylaxis: Parents and patients should be informed that such reactions are possible and that if a systemic allergic reaction occurs, treatment should be interrupted and prompt medical attention should be taken.
  - Intracranial hypertension: funduscopic examination is recommended at the initiation and periodically during therapy.
  - Lymphoid tissue hypertrophy
  - Slipped capital femoral epiphysis (SCFE): characterized by limp or hip/knee pain.
  - Progression of scoliosis
  - Risk of malignant neoplasms: Several cases of malignant neoplasia have been observed in pediatric patients treated with mecasermin. Therapy should be discontinued if evidence of malignant neoplasia develops, and appropriate expert medical care sought.
  - Risk of serious adverse reactions (including death) in infants due to benzyl alcohol preserved solution: use in infants is not recommended.
- Adverse effects
  - Most common in clinical trials: hypoglycemia, local and systemic hypersensitivity, and tonsillar hypertrophy.

Dosing and Administration

Table 3. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Daybue (trofinetide)	Solution	Oral	Twice daily in the morning and evening	Dosing is based on patient weight. May be administered with or without food. May be administered orally or via gastrostomy

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				(G) tube through a G-port.
Increlex (mecasermin)	Injection	SC	Twice daily	Administer shortly before or after a meal or snack due to insulin-like hypoglycemic effect. Pre-prandial glucose monitoring is recommended at treatment initiation and until a well-tolerated dose is established. Injection sites should be rotated to a different site (upper arm, thigh, buttock, or abdomen) with each injection to help prevent lipohypertrophy.

See the current prescribing information for full details.

Conclusion

- IGF-1 is a hormone that manages the effects of GH. Together, they promote the normal linear growth of bones and tissues. GHI occurs when the body is unable to adequately use GH, generally caused by loss-of-function mutations.
- Mecasermin is an injectable recombinant IGF-1, that is FDA-approved for the long-term treatment of growth failure in pediatric patients with severe primary IGF-1 deficiency (defined as both height and serum IGF-1 concentration below –3 SD despite normal or elevated GH levels), or patients with GH gene deletion who developed neutralizing antibodies to GH after a trial of GH therapy. Eligible children must have an open epiphysis.
- In a pooled analysis of 5 clinical trials, mecasermin showed a statistically significant acceleration of linear growth as characterized by height velocity compared to baseline from year 1 through year 6. These results were also consistent in subsequent studies that demonstrated increased in mean first-year height velocities in patients with severe primary IGF-1 deficiency treated with 80 and 120 ug/kg twice daily mecasermin).
  - The safety and effectiveness have not been established in children less than 2 years of age.
  - Use in infants is not recommended due to risk of serious adverse reactions (including death) due to benzyl alcohol preservative content.
- The 2016 guidelines from the Pediatric Endocrine Society recommend starting directly on IGF-1 therapy to increase height in patients with severe primary IGF-1 deficiency and in patients with hormone signaling defects known to be unresponsive to GH treatment.
- Contraindications to the use of mecasermin include hypersensitivity to the drug, IV administration, individuals with closed epiphyses, or with current or history of cancer.
- IGF-1 is associated with insulin-like hypoglycemic effects, so it is recommended to be administered after a carbohydrate containing meal or snack.
- Long-term studies have demonstrated that recombinant IGF-1 (mecasermin) has proven efficacy in stimulating height velocity for a very small patient population that is affected by GHI characterized by a lack of normal growth due to mutations in GH receptor and IGF-1 and continues to be an important treatment option for these patients.
- Rett syndrome is a rare developmental disorder, and the second leading cause of intellectual disability in girls. Treatment is mostly supportive care across a wide range of body systems. In the LAVENDER trial, trofinetide demonstrated a statistically significant improvement from baseline in Rett Syndrome behaviors as assessed by caregiver questionnaire (RSBQ) and CGI-I scales; offering patients and families a potential option to treat a debilitating

range of symptoms. Trofinetide is administered orally twice daily, and most patients will experience diarrhea during treatment.

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