North Dakota Medicaid
Drug Utilization Review Board Meeting
June 4, 2025
Conference Room 210/212

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Meeting Notice

North Dakota Medicaid Drug Use Review Board

Wednesday, June 4th, 2025
1:00 p.m. to 4:00 p.m. CT

In - Person Information

Conference Room 210/212, 2nd Floor, Judicial Wing, State Capitol
600 E. Boulevard Ave., Bismarck, ND 58505

Virtual Information

Join virtually: Click here to join the meeting
Join by phone: 701-328-0950, Conference ID: 239 115 078 594

Agenda

- Call to Order
- Roll Call
- Review and Approval of Minutes
- Reports from Department
    - Administrative Report: Legislative Update, Member Updates
    - Financial Report: Top Drugs
    - Retrospective DUR Report
    - Clinical Report
        - Prior Authorization Update
        - Criteria updates: Amyloidosis, Chronic Kidney Disease, Hemophilia
- Special Orders: Presiding Officer and Vice-Presiding Officer Elections
- New business
    - Second Review of Diabetes Mellitus
    - First Review of Non-Opioid Analgesia
    - Review of retrospective DUR criteria recommendations
    - Provider suggestions for clinical practice education or RDUR ICER criteria
- Announcements: Next Meeting (September 3, 2025)
- Adjourn

Individuals with disabilities who need accommodations, including appropriate auxiliary aids to participate, can contact Ashley Gerving at 701-328-2354, toll-free 800-755-2604, 711 (TTY) or gervingashley@nd.gov.

Date Posted: May 22nd, 2025

Meeting Minutes

North Dakota Medicaid Drug Use Review (DUR) Board
Meeting Date: March 5th, 2025
Time and Location: 1:00 pm CST in Bismarck, North Dakota

Call to Order:
A regular quarterly meeting of the North Dakota Medicaid Drug Use Review (DUR) Board meeting was convened at 1:06 pm CST with K. Martian presiding as Presiding Officer. DUR Board Coordinator, J. McKee recording minutes.

Roll Call:
Board Members Voting:
Present: Stephanie Antony, Gabriela Balf, Amanda Dahl, Kurt Datz, Andrea Honeyman, Laura Kroetsch, Kevin Martian, Kristen Peterson, Amy Werremeyer, Jessica Ziegler, Matthew Zimny
Absent: Tanya Schmidt
Quorum Present: Yes

Board Members Non-Voting: Kathleen Traylor
Absent:

Medicaid Pharmacy Department:
Present: Jeff Hostetter, Brendan Joyce, Alexi Murphy, Katie Steig
Absent: LeNeika Roehrich
Approval of Meeting Minutes:
Motion: Moved by K. Datz to approve the minutes of the December 4th, 2024, meeting, motion was seconded by K. Martian. **Motion carried.**
The minutes of the December 4th, 2024, meeting were approved as distributed.

Reports:
Financial Report: Budget provided by B. Joyce
B. Joyce shared with the Board trends of reimbursement amount vs net spend for pharmacy drug claims. This information can be found in the handout.

Financial Report: Top Drugs provided by B. Joyce
B. Joyce presented the quarterly review of the top 25 drugs based on total number and cost of claims and the top 15 therapeutic classes based on number and cost of claims. This report can be found in the handout.

Retrospective Drug Utilization Review (RDUR) Report by J. McKee
J. McKee reviewed the quarterly RDUR criteria that were selected for review of each month and information from a targeted mailing. This material can be found in the handout.

Clinical Report and Annual PDL Review: Prior Authorization and Criteria Updates by J. McKee
J. McKee presented prior authorization and criteria updates with emphasis on the following sections in the PDL: Amyloidosis, GLP-1 Receptor Agonist Combinations, Metabolic Dysfunction-Associated Steatohepatitis, Parkinson's Disease. Testimony was provided by Shawn Hanse from Novo Nordisk on Ozempic, Tara McKinely from Madrigal Pharmaceuticals on Rezdiffra, and Christine Dube from Astrazeneca on Airsupra.

Unfinished business: provided by J. McKee

J. McKee provided updates on alternative RDUR communication tools. The presented material can be found in the handout.

New business:
First Reviews presented by J. McKee
J. McKee presented an overview of diabetes mellitus. The presented material can be found in the handout.
Motion: Moved by K. Martian to draft prior authorization for diabetes mellitus, motion was seconded by A. Werremeyer. **Motion carried.**

Second Reviews presented by J. McKee
J. McKee presented group prior authorization criteria for Migraine Prophylaxis and Treatment. Testimony was provided by Jasmine Inman from Teva on Ajovy.
Motion: Moved by K. Datz to place Migraine Prophylaxis and Treatment on prior authorization, motion was seconded by K. Martian. **Motion carried.**

J. McKee presented group prior authorization criteria for Nonsteroidal Anti-Inflammatory Drugs.
Motion: Moved by A. Werremeyer to place Nonsteroidal Anti-Inflammatory Drugs on prior authorization, motion was seconded by A. Dahl. **Motion carried.**

J. McKee presented group prior authorization criteria for Primary Biliary Cholangitis.
Motion: Moved by K. Martian to place Primary Biliary Cholangitis on prior authorization, motion was seconded by K. Datz. **Motion carried.**

Retrospective Drug Utilization Review (RDUR) Criteria Recommendations:
RDUR criteria recommendations were reviewed. The presented material can be found in the handout.
Motion: Moved by K. Martian to approve the RDUR criteria, motion was seconded by K. Datz. **Motion carried.**

Announcements:
Next meeting is June 4th, 2025.

Adjournment:
Meeting adjourned by K. Martian at 1:54 pm CST.

Date of Minutes Approval:
Minutes submitted by: Julie McKee, Acentra Health

Administrative Report

New Members

Dr. Matthew Zimney, MD – Welcome!

Expired Terms

Dr. Tanya Schmidt, PharmD - has served on the DUR Board since April 1, 2012

Legislative Report

SB2076 Summary of Changes

Previous:

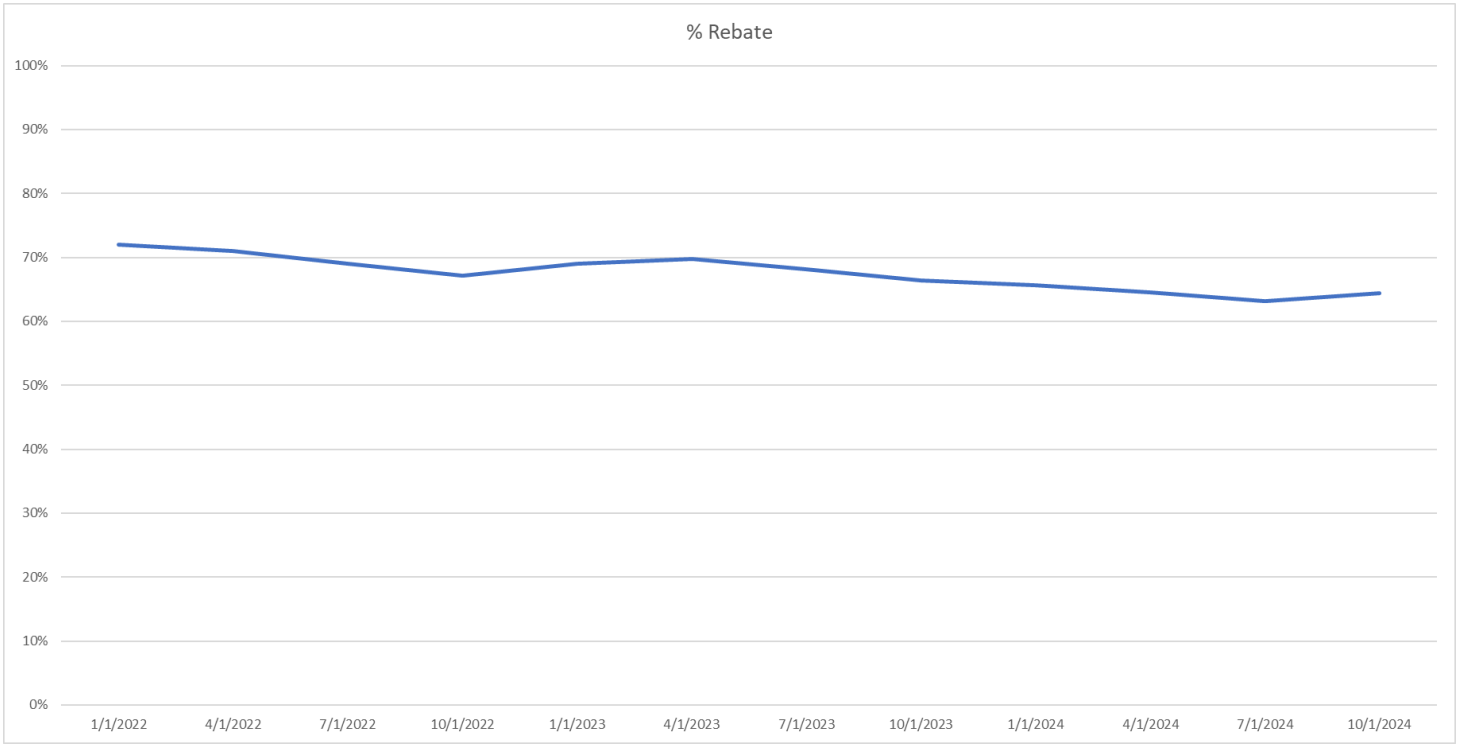
- Required prior authorization for members less than 18 years old that are on 5 or more psychotropic drugs for prescribers to have a peer-to-peer consult with a board-certified child and adolescent psychiatrist. Following the consultation, the department approves prior authorization.
- Department may not prior authorize substantially all drugs in the following restricted classes: antipsychotics, antidepressants, anticonvulsants, antiretrovirals for human immunodeficiency virus, antineoplastics, immunosuppressants for organ transplant.

Now:

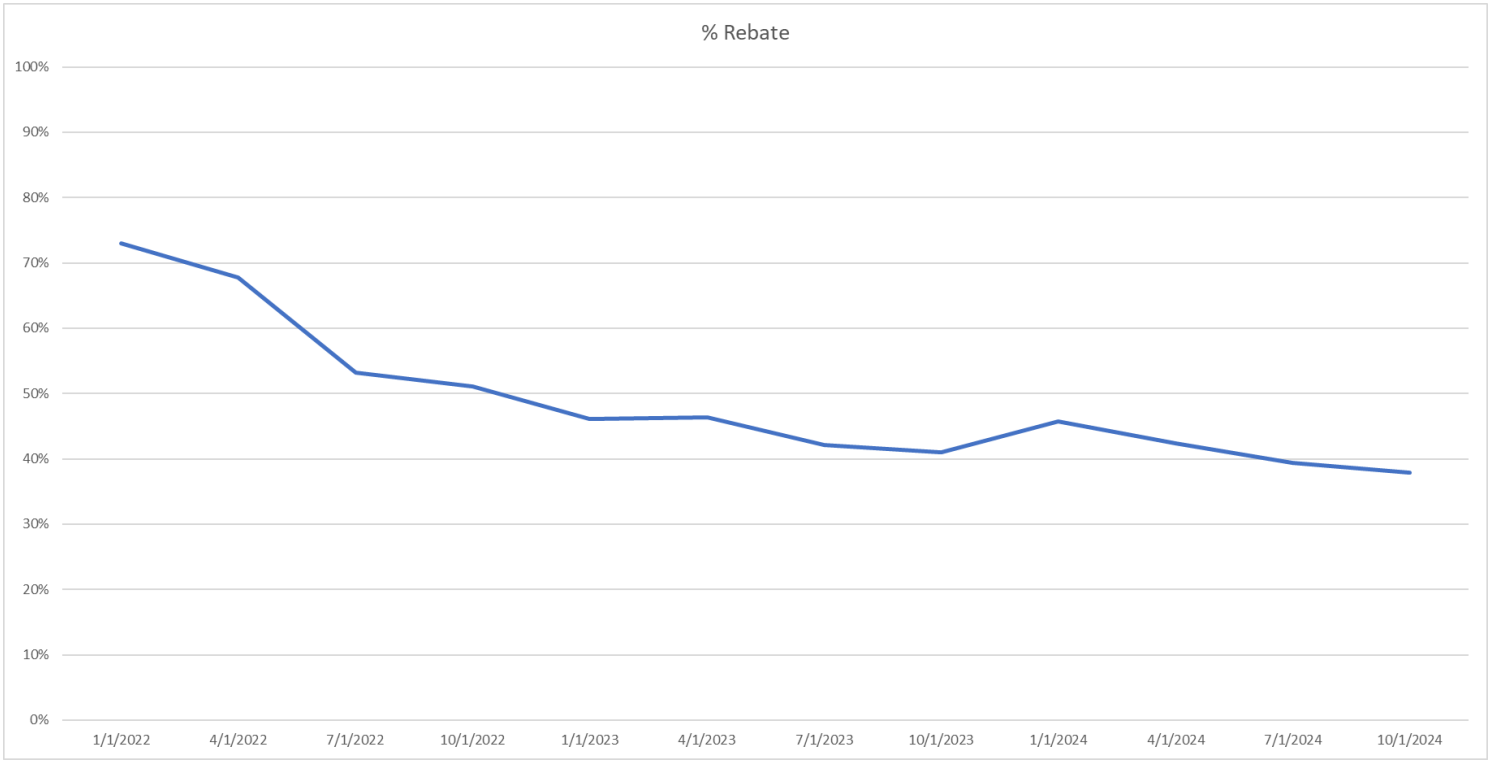
- Department will send letters to prescribers of members who are less than 22 years old that are on 5 or more psychotropic drugs to certify that the medication is medically necessary. If the prescriber does not certify, the department may deny payment until certification.
- Department may prior authorize drugs in the restricted classes if the department will not be able to access offers due to the restriction.

Financial Report

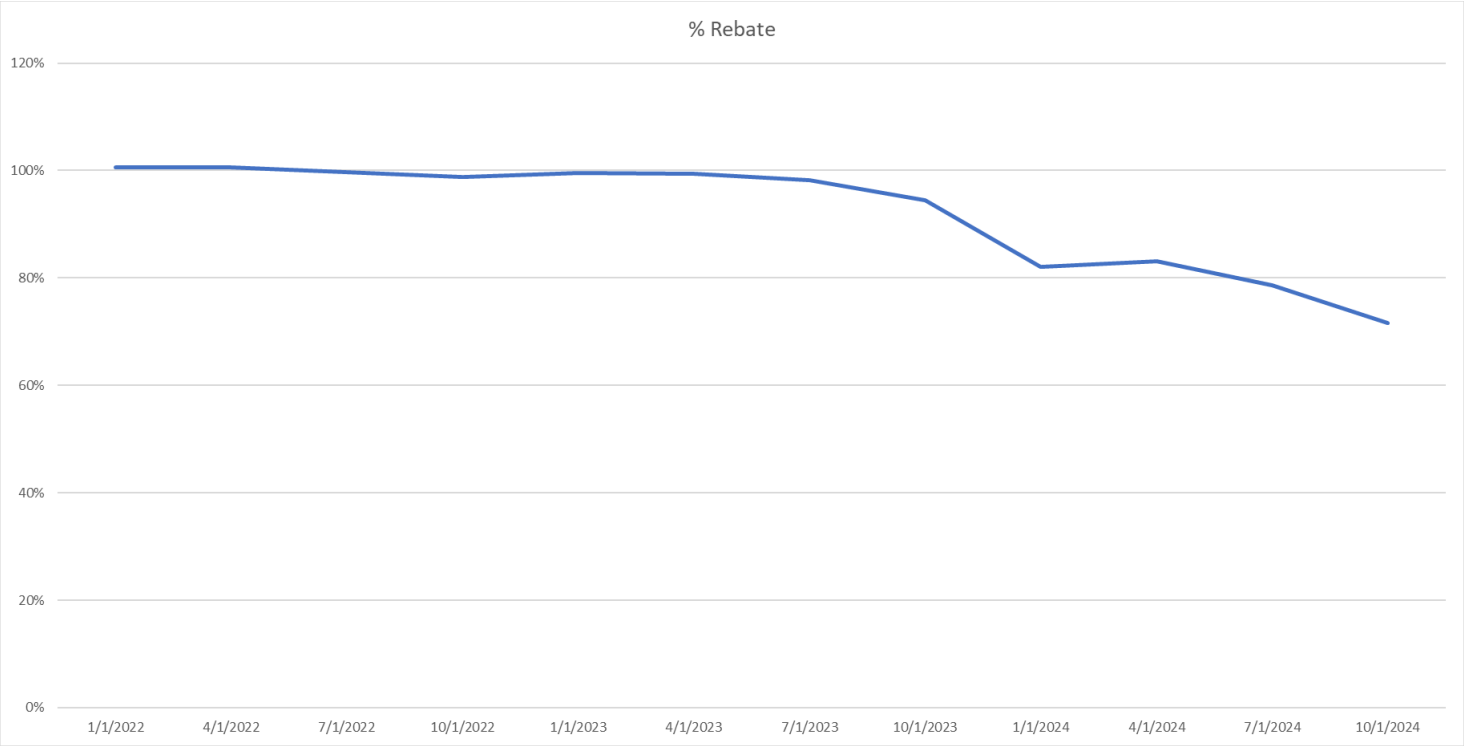
% Rebate is decreasing



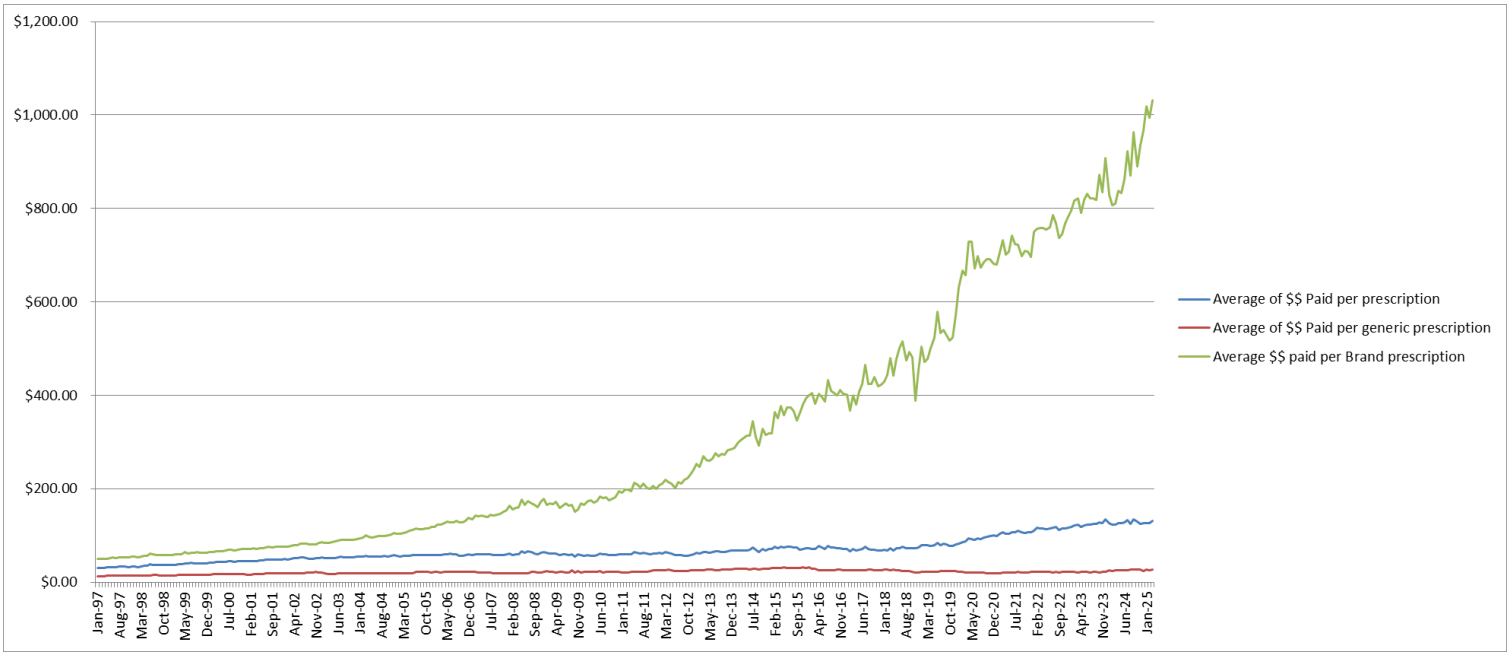
Drug classes dominated by generics driving rebate % decrease: Anticonvulsants, Cholesterol, Hypertension



AMP Cap price decreases and switches to generic preferences are a recent contributor particularly in the ADHD Stimulants, COPD, Insulins, and Steroid/LABA combinations classes.



Branded drugs now costing on average more than $1000 per prescription

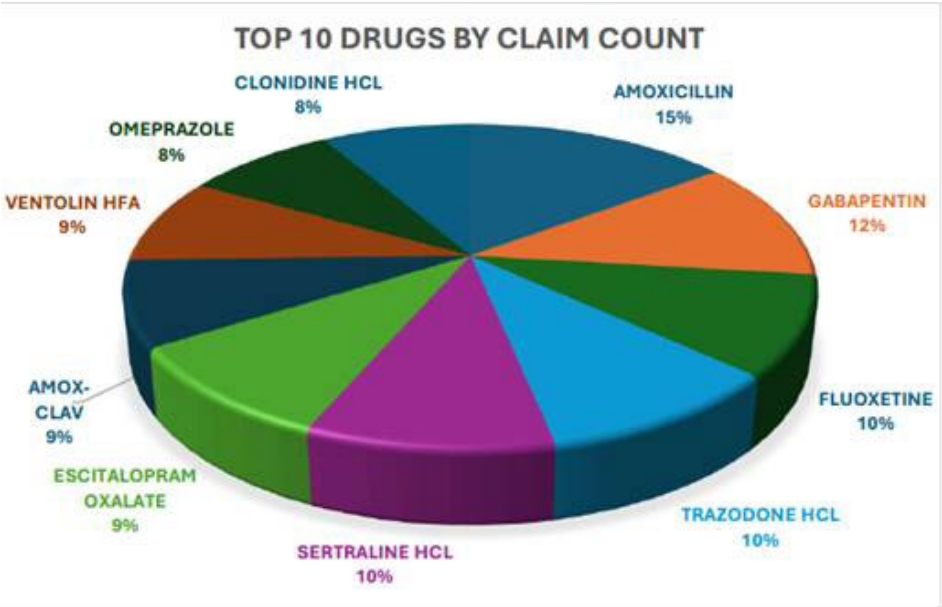


On the horizon:

- Linagliptin products will be sole preferred (e.g., Trajenta)
    - Sitagliptin products (e.g., Januvia) will require prior authorization on 7/1/25
- Dulera will be sole preferred
    - Advair Diskus and Advair HFA will require prior authorization on 10/1/25

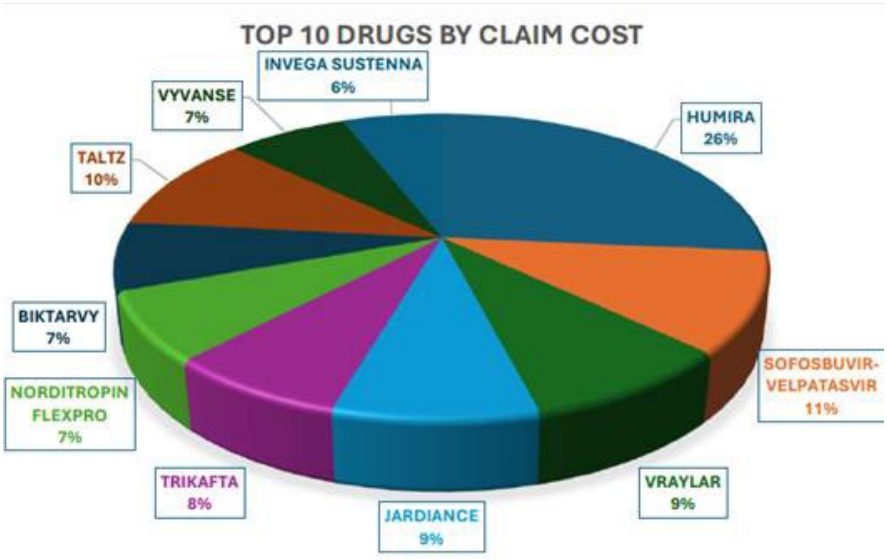
Top 25 Drugs Based on Number of Claims from 1/1/2025 to 3/31/2025

#	Drug Name	Claims	Claims Cost	Patients	Cost/Claim	% Claims	Dif.
1	AMOXICILLIN	5,532	$87,859.33	5,151	$15.88	2.10%	↑1
2	GABAPENTIN	4,479	$64,377.67	1,861	$14.37	1.70%	↓1
3	FLUOXETINE HCL	3,709	$48,851.10	1,999	$13.17	1.41%	↑3
4	TRAZODONE HCL	3,685	$49,160.42	1,947	$13.34	1.40%	↓1
5	SERTRALINE HCL	3,635	$48,701.14	2,026	$13.40	1.38%	↓2
6	ESCITALOPRAM OXALATE	3,551	$47,248.60	1,974	$13.31	1.35%	↓2
7	AMOXICILLIN-CLAVULANATE POTASS	3,185	$56,759.20	2,988	$17.82	1.21%	↑6
8	VENTOLIN HFA	3,183	$204,529.06	3,143	$64.26	1.21%	↑1
9	OMEPRAZOLE	3,145	$41,836.28	1,887	$13.30	1.19%	↓2
10	CLONIDINE HCL	3,136	$38,549.24	1,538	$12.29	1.19%	NC
11	PREDNISONE	3,030	$35,804.87	2,425	$11.82	1.15%	↑3
12	LEVOTHYROXINE SODIUM	2,988	$42,960.97	1,580	$14.38	1.13%	↓4
13	HYDROXYZINE HCL	2,813	$38,081.84	1,729	$13.54	1.07%	↑3
14	BUPROPION XL	2,791	$46,624.08	1,503	$16.71	1.06%	↓2
15	ATORVASTATIN CALCIUM	2,791	$43,575.16	1,619	$15.61	1.06%	↓4
16	DEXTROAMPHETAMINE-AMPHET ER	2,685	$80,872.69	1,106	$30.12	1.02%	↑1
17	LISINOPRIL	2,676	$35,060.12	1,619	$13.10	1.01%	↓2
18	ONDANSETRON ODT	2,639	$37,714.34	2,109	$14.29	1.00%	↑10
19	VYVANSE	2,605	$747,501.09	1,212	$286.95	0.99%	↑3
20	METHYLPHENIDATE ER	2,584	$72,297.58	1,079	$27.98	0.98%	↓2
21	ARIPIPRAZOLE	2,393	$37,968.24	1,153	$15.87	0.91%	↓2
22	LAMOTRIGINE	2,386	$33,211.52	994	$13.92	0.90%	↑1
23	PANTOPRAZOLE SODIUM	2,350	$32,311.45	1,341	$13.75	0.89%	↓3
24	HYDROCODONE-ACETAMINOPHEN	2,311	$34,381.11	1,482	$14.88	0.88%	↓3
25	DULOXETINE HCL	2,257	$37,268.00	1,185	$16.51	0.86%	↓1
Total Claims							**263, 703**



Top 25 Drugs Based on Total Claims Cost from 1/1/25 – 3/31/25

#	Drug Name	Claims	Claims Cost	Patients	Cost/Patient	% Cost	Dif.
1	HUMIRA	316	$2,775,642.35	128	$18,513.85	7.32%	NC
2	SOFOSBUVIR-VELPATASVIR	49	$1,115,439.45	49	$22,764.07	2.94%	NC
3	TALTZ	130	$1,079,290.08	59	$71,097.34	2.85%	NC
4	VRAYLAR	875	$938,432.87	347	$ 2,704.42	2.48%	↑2
5	JARDIANCE	1,177	$900,360.82	631	$1,426.88	2.38%	NC
6	TRIKAFTA	35	$796,751.15	14	$56,910.80	2.10%	↑3
7	DUPIXENT	206	$785,688.90	90	$17,319.68	2.07%	NC
8	NORDITROPIN FLEXPRO	117	$769,216.75	44	$17,482.20	2.03%	↑4
9	BIKTARVY	353	$756,722.07	154	$4,913.78	2.00%	↑1
10	VYVANSE	2,605	$747,501.09	1,212	$ 616.75	1.97%	↑1
11	INVEGA SUSTENNA	221	$623,742.07	86	$7,252.81	1.65%	NC
12	VICTOZA	793	$474,407.71	553	$1,785.34	1.25%	↓6
13	ELIQUIS	734	$450,768.72	356	$1,266.20	1.19%	↑1
14	SUBLOCADE	178	$370,786.60	78	$4,753.67	0.98%	↑1
15	COSENTYX	36	$356,217.91	15	$72,283.97	0.94%	↓5
16	INGREZZA	42	$336,111.86	18	$18,672.88	0.89%	↑1
17	STELARA	12	$297,522.21	9	$33,058.02	0.79%	↓1
18	VERZENIO	19	$277,585.95	7	$39,655.14	0.73%	↑6
19	XIFAXAN	98	$270,525.15	52	$5,202.41	0.71%	↑3
20	DULERA	784	$245,466.89	472	$520.06	0.65%	NC
21	LISPRO	1156	$ 242,774.38	743	$537.48	0.64%	↑15
22	ABILIFY MAINTENA	91	$ 237,419.19	36	$6,594.98	0.63%	↓1
23	FARXIGA	357	$221,670.04	186	$1,191.77	0.58%	NC
24	SKYRIZI PEN	10	$206,528.24	7	$29,504.03	0.54%	↑26
25	VENTOLIN HFA	3,183	$204,529.06	3,143	$65.07	0.54%	↑1
Total Cost						**$37,895,615.57**	

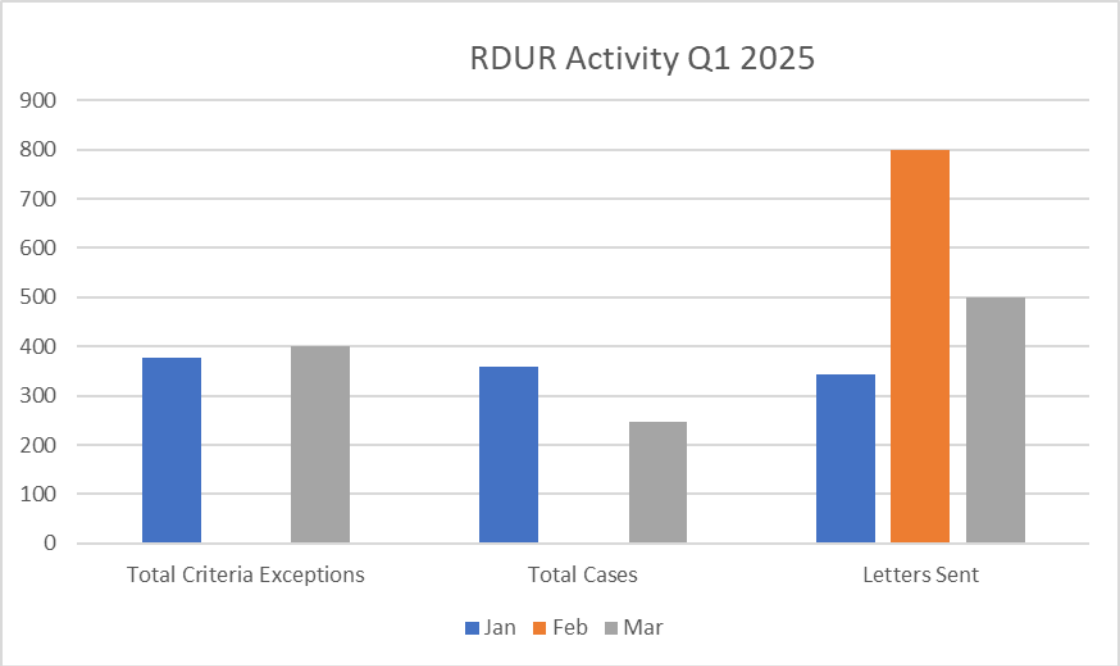


Top 15 Therapeutic Classes Based on Number of Claims from 1/1/25 – 3/31/25

#	Therapeutic Class Description	Claims	Claims Cost	Patients	Cost/Claim	% Claims	Dif.
1	ANTIDEPRESSANTS	26,651	585,037.61	11,036	21.95	10.11%	NC
2	ANTIPSYCHOTIC AGENTS	10,288	2,908,012.35	4,051	282.66	3.90%	NC
3	PENICILLIN ANTIBIOTICS	8,996	149,177.40	7,943	16.58	3.41%	↑3
4	AMPHETAMINES	7,476	960,498.93	2,976	128.48	2.84%	↓1
5	RESPIRATORY AND CNS STIMULANTS	7,289	425,894.57	2,765	58.43	2.76%	↓1
6	GABA-MEDIATED ANTICONVULSANTS	6,968	137,047.78	2,797	19.67	2.64%	↓1
7	BETA-ADRENERGIC AGONISTS	6,886	816,938.73	4,792	118.64	2.61%	NC
8	OPIOID AGONISTS (28:08)	6,008	106,877.56	3,113	17.79	2.28%	↑1
9	CENTRAL ALPHA-AGONISTS	5,938	83,044.96	2,605	13.99	2.25%	↑1
10	ADRENALS	5,919	212,706.65	4,326	35.94	2.24%	↑2
11	PROTON-PUMP INHIBITORS	5,835	102,346.14	3,364	17.54	2.21%	↓3
12	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	5,672	76,946.64	3,848	13.57	2.15%	↓1
13	ANTICONVULSANTS, MISCELLANEOUS	5,410	367,124.20	2,195	67.86	2.05%	↑1
14	HMG-COA REDUCTASE INHIBITORS	5,026	75,998.72	2,942	15.12	1.91%	↓1
15	BETA-ADRENERGIC BLOCKING AGENTS	4,960	81,948.07	2,816	16.52	1.88%	NC

Top 15 Therapeutic Classes Based on Claims Cost from 1/1/25 – 3/31/25

#	Therapeutic Class Description	Total Claims	Total Claims Cost	Total Patients	Cost Per Patient	% Cost	Dif.
1	TNF INHIBITORS	399	3,250,471.12	156	20,836.35	8.58%	NC
2	ANTIPSYCHOTIC AGENTS	10,288	2,908,012.35	4,051	717.85	7.67%	NC
3	INTERLEUKIN AGENTS	181	1,744,815.68	75	23,264.21	4.60%	NC
4	ANTINEOPLASTIC AGENTS	579	1,654,842.23	242	6,838.19	4.37%	↑3
5	ANTIRETROVIRALS	823	1,319,725.69	303	4,355.53	3.48%	↓1
6	HCV ANTIVIRALS	52	1,162,260.63	51	22,789.42	3.07%	↑2
7	SGLT2 INHIB	1,589	1,153,830.85	842	1,370.35	3.04%	↓2
8	AMPHETAMINES	7,476	960,498.93	2,976	322.75	2.53%	↓1
9	CFTR CORRECTORS	37	843,254.03	15	56,216.94	2.23%	↑2
10	PITUITARY	372	821,384.74	154	5,333.67	2.17%	↑6
11	BETA AGONISTS	6,886	816,938.73	4,792	170.48	2.16%	↓1
12	SKIN AGENTS	219	786,111.21	101	7,783.28	2.07%	NC
13	INCRETIN MIMETICS	1,200	767,560.71	600	1,279.27	2.03%	↓6
14	INSULINS	3,157	623,960.02	1,294	482.19	1.65%	↓1
15	ANTIDEPRESSANTS	26,651	585,037.61	11,036	53.01	1.54%	↓1



January Cases by Type of Criteria		
Criteria Description	**# of Cases**	**% of Cases**
Underuse Precaution	96	58.53%
Drug-Drug/Diagnosis	35	21.34%
Therapeutic Appropriateness	16	9.76%
Drug-Drug Interaction	14	8.54%
Drug-Disease Precaution	2	1.22%
Overuse Precaution	1	0.61%

March Cases by Type of Criteria		
Criteria Description	**# of Cases**	**% of Cases**
Underuse Precaution	122	49.39%
Overuse Precaution	37	14.98%
Drug-Disease Precaution	36	14.57%
Therapeutic Appropriateness	23	9.31%
Drug-Drug/Diagnosis	14	5.67%
High Dose Alert	10	4.05%
Drug-Drug Interaction	5	2.02%

February Special Mailing
800 Letters Sent

Dear Prescriber,

In accordance with the SUPPORT ACT under Section 5042 (effective October 1, 2021), all Medicaid providers authorized to prescribe controlled substances are required to assess the prescription drug history from a qualified prescription drug monitoring program (PDMP) before prescribing controlled substances to Medicaid members. Exclusions to this requirement include prescriptions written for the following members:

- Receiving hospice, palliative care, or cancer treatment
- Resident of a long-term care facility or facility with a single pharmacy contract[1,2]

A recent review of claims data indicated that you have written a prescription for a controlled substance from October 1, 2023 until September 30, 2024 for a Medicaid member. If there appears to be an error in the information provided, please note the discrepancy.

The PDMP should be checked prior to prescribing controlled substances for Medicaid members (except excluded member categories). State Medicaid programs are required to report provider PDMP use percentages to CMS annually. **Please respond to the attached questionnaire regarding your use of the PDMP for the period of October 1, 2023 through September 30, 2024 and fax it to 866-798-4904.**

Thank you for your professional consideration.

Sincerely,

Brendan K. Joyce, PharmD

Administrator, Pharmacy Services

References:

1. *Library of Congress. H.R.6 – SUPPORT for Patients and Communities Act (2017-2018). [Internet}. Available from: https://www.congress.gov/bill/115th-congress/house-bill/6/text*
2. *Department of Health and Human Services. Frequently Asked Questions: SUPPORT for Patients and Communities Act, Section 5042 – Medicaid PARTNERSHIP Act [Internet]. Baltimore (MD): Centers for Medicare & Medicare Services. Available from: https://www.hhs.gov/guidance/sites/default/files/hhs-guidance-documents/faq051519_199.pdf*

Clinical Report

Prior Authorization Updates

Drug	PA Status	Class
Cortrophin	PA	>3000 criteria
diclofenac powder pack (generic Cambia)	PA	Migraine
Gomekli	PA	>3000 criteria
Hemiclor	PA	Antihypertensive
Inzirqo	PA	Diuretics
Onapgo	PA	Parkinson's Disease
Otulfi	PA	Cytokine Modulators
Qfitlia	PA	Hemophilia
Raldesy	PA	Non-Solid Dosage Forms
Symbravo	PA	Migraine treatment
Tezruly	PA	Benign Prostatic Hyperplasia
Vanrafia	PA	Chronic Kidney Disease
Xdemvy	PA	Ophthalmic Anti-infectives
Zunveyl	PA	Alzheimer's Disease

Criteria Updates

Summary of Changes

Amyloidosis

Amvuttra added indication for ATTR-CM

We have non-preferred Amvuttra for ATTR-CM, and added language allowing coverage if member meets criteria for both indications

Polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN)

TTR-specific small interfering RNA (siRNA)

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
ONPATTRO (patisiran) – *Medical Billing*	

Transthyretin-directed small interfering RNA (siRNA)

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
AMVUTTRA (vutrisiran) – *Medical Billing*	

Antisense Oligonucleotide (ASO)

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
WAINUA (eplontersen)	

Prior Authorization Criteria

Initial Criteria – Approval Duration: 6 months

- The member must meet FDA-approved label for use (e.g., use outside of studied population will be considered investigational)
- The requested medication must be prescribed by, or in consult with, a neurologist, geneticist, or specialist in the treatment of amyloidosis.
- The diagnosis must be confirmed by both of the following:
  - Genetic testing confirming a pathogenic TTR mutation (e.g., V30M)
  - Amyloid deposits via tissue biopsy
- One of the following must be provided:
  - Baseline polyneuropathy disability (PND) score ≤ IIIb
  - Baseline Coutinho staging system stage 1 or 2
  - Baseline Neuropathy Impairment Score [NIS] of 5–130
  - Karnofsky Performance Status score of ≥60%
- The member has not had a liver transplant.
- The member has clinical signs and symptoms of the disease (e.g., peripheral neuropathy, numbness, altered pain and temperature sensation, decreased pinprick sensation)
- The member is not receiving any other TTR reducing agent (i.e., acoramidis, tafamidis)

Renewal Criteria – Approval Duration: 12 months

- The member has received a therapeutic response as evidenced by stabilization or improvement (e.g., improved neurologic impairment, motor function, quality of life, slowing of disease progression, etc.) from baseline in one of the following:
  - PND score ≤ IIIb
  - Coutinho staging system stage 1 or 2
  - Baseline Neuropathy Impairment Score [NIS] of 5–130
  - Karnofsky Performance Status score of ≥60%

Cardiomyopathy of transthyretin-mediated amyloidosis (ATTR-CM)

Transthyretin-directed small interfering RNA (siRNA)

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
	AMVUTTRA (vutrisiran) – *Medical Billing*

TTR Stabilizers

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
ATTRUBY (acoramidis)	
VYNDAQEL (tafamidis)	
VYNDAMAX (tafamidis)	

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months

- The member must meet FDA-approved label for use (e.g., use outside of studied population will be considered investigational)
- The requested medication must be prescribed by, or in consult with, a cardiologist, geneticist, or specialist in the treatment of amyloidosis.
- Confirmation of the diagnosis by both of the following must be provided:
  - presence of grade 2 or 3 positive bone tracer cardiac scintigraphy
  - absence of monoclonal protein confirmed by serum protein immunofixation, urine protein immunofixation, or serum free light chain ratio analysis
- The member must have heart failure class I or II with at least 1 prior hospitalization for heart failure or with symptoms of volume overload or elevated intracardiac pressures (e.g., elevated jugular venous pressure, shortness of breath or signs of pulmonary congestion on x-ray or auscultation, peripheral edema) despite 6-months of adherent use of a diuretic.
- The member has an end-diastolic interventricular septal wall thickness of at least 12 mm.
- For Attruby only: The member must not have any of the following:
  - ALT or AST > 2x ULN or Total Bilirubin >3x ULN
  - NT-proBNP level > 8500 pg/mL
- The member must not have any of the following:
  - eGFR < 25 mL/min/1.73m^2
  - NYHA class IV symptoms or severe aortic stenosis
  - Previous heart transplant or implanted cardiac mechanical assist device
  - Previous liver transplant
- Baseline 6MWT > 100 meters must be submitted.
- The member is not receiving any other TTR reducing agent (i.e., patisiran, elplontersen)

For Amvuttra Only:

- The member must have failed a 90-day trial of each Attruby and Vyndaqel/Vyndamax, as evidenced by paid claims or pharmacy printouts
- Coverage will be allowed without trial of preferred medications if the member also meets the criteria for hATTR-PN

Renewal Criteria – Approval Duration: 12 months

- For Attruby only: The member has received a therapeutic response as evidenced by stabilization or improvement from baseline in both of the following:
  - 6MWT
  - NT-proBNP level
- For Vyndaqel/Vyndamax and Amvuttra: The member has received a therapeutic response as evidenced by stabilization or improvement from baseline in both of the following:

- 6MWT
- NYHA class

References:

1. Ando Y, Coelho T, Berk JL, Cruz MW, Ericzon BG, Ikeda S, Lewis WD, Obici L, Planté-Bordeneuve V, Rapezzi C, Said G, Salvi F. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013 Feb 20;8:31. doi: 10.1186/1750-1172-8-31. PMID: 23425518; PMCID: PMC3584981.

Chronic Kidney Disease

Vanrafia was added to the section

Fabhalta and Filspari criteria were split to differentiate the cause of proteinuria from Complement 3 Glomerulopathy (C3G) or IGA Nephropathy (IgAN).

Therapeutic Duplication

- Medication classes not payable together:
  - Filspari, ACE Inhibitors, ARBs, and Renin Inhibitors are not allowed with each other.

Dual endothelin angiotensin receptor antagonist

CLINICAL PA REQUIRED
FILSPARI (sparsentan)

Endothelin receptor antagonist

CLINICAL PA REQUIRED
VANRAFIA (atrasentan)

Factor B Inhibitors

CLINICAL PA REQUIRED
FABHALTA (iptacopan)

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months

Fabhalta Only

- The member must have eGFR ≥ 30.
- If member is on renal dialysis, Medicare eligibility must be ruled out *(6-month approval may be allowed to determine eligibility)*.
- The member must be experiencing proteinuria > 1 gram/day or UPCR ≥ 1.0 g/g despite 3-month trials with good compliance of the following at the target or maximally tolerated dose, as evidenced by paid claims or pharmacy printouts:
  - ACE inhibitor or an ARB
  - systemic corticosteroid
  - SGLT-2 inhibitor (IgAN diagnosis only)
  - mycophenolate mofetil/sodium (C3G diagnosis only)

Filspari Only

- The member must have eGFR ≥ 30.
- If member is on renal dialysis, Medicare eligibility must be ruled out *(6-month approval may be allowed to determine eligibility)*.
- The member must be experiencing proteinuria > 1 gram/day or UPCR ≥ 1.5 g/g despite 3-month trials with good compliance of the following at the target or maximally tolerated dose, as evidenced by paid claims or pharmacy printouts:
  - ACE inhibitor or an ARB
  - A SGLT-2 inhibitor
  - systemic corticosteroid

Vanrafia Only

- The member must have eGFR ≥ 30.
- If member is on renal dialysis, Medicare eligibility must be ruled out *(6-month approval may be allowed to determine eligibility)*.
- The member must be experiencing proteinuria > 1 gram/day or UPCR ≥ 1.5 g/g despite 3-month trials with good compliance of the following at the target or maximally tolerated dose, as evidenced by paid claims or pharmacy printouts:
  - ACE inhibitor or an ARB
  - A SGLT-2 inhibitor

Renewal Criteria – Approval Duration: 12 months

- If member is on renal dialysis, Medicare eligibility must be ruled out *(6-month approval may be allowed to determine eligibility)*.
- The member must have experienced meaningful clinical benefit since starting treatment with the requested medication, as evidenced by the following scores and symptoms:
- *Fabhalta, Filspari, Tarpeyo and Vanrafia Only*: proteinuria <0.5 gram/day or UPCR < 1.5 g/g or reduction of 30% from baseline
- *Kerendia Only*: The member has experienced a stabilization in eGFR or one of the following:
  - albuminuria <1 gram/day or reduction of 30% from baseline
  - UACR < 1.5 g/g or reduction of 30% from baseline

Hemophilia

Procoagulants Alhemo, Hympavzi, and Qfitlia were added to the section. These medications work to lower the amount of anticoagulants (such as antithrombin) to balance the clotting cascade from a different direction than from factor replacement.

Hemophilia A already has a subcutaneous prophylaxis option with a long half-life that is well-established as effective, so Hemlibra is preferred for these members.
Hemophilia B does not have any other SQ options for prophylaxis, so the member can use Alhemo or Hympavzi, depending on their inhibitor status, reserving Qfitlia for those who have failed previous trials.

Hemophilia A

Recombinant humanized bispecific monoclonal antibody

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
HEMLIBRA (emicizumab-kxwh)	

Procoagulant (TFPI inhibitors/Antithrombin inhibitors)

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)

	ALHEMO (concizumab-mtci)
	HYMPAVZI (marstacimab-hncq)
	QFITLIA (fitusiran)

Hemophilia B

Procoagulant (TFPI inhibitors/Antithrombin inhibitors)

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
ALHEMO (concizumab-mtci)	QFITLIA (fitusiran)
HYMPAVZI (marstacimab-hncq)	

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months

- The date of the member's last appointment with a Hemophilia Treatment Center must be within the past year.
- The contact information for Hemophilia Treatment Center must be provided.

Non-Preferred Agents Criteria:

- Clinical justification must be provided explaining why the member is unable to use a preferred agent (subject to clinical review).
- The member may qualify for non-preferred product if they are stable on current therapy (have had a paid claim for requested therapy in the past 45 days)
- *Alhemo only*:
  - The member must have one of the following:
    - A diagnosis of Hemophilia A with inhibitors AND has failed a 6-month trial with Hemlibra
    - A diagnosis of Hemophilia B with inhibitors
- *Hympavzi only*:
  - The member must have one of the following:
    - A diagnosis of Hemophilia A without inhibitors AND has failed a 6-month trial with Hemlibra
    - A diagnosis of Hemophilia B without inhibitors
- *Qfitlia only:*
  - The member must have one of the following:
    - A diagnosis of Hemophilia A with or without inhibitors AND has failed a 6-month trial with Hemlibra
    - A diagnosis of Hemophilia B with or without inhibitors AND has failed a 6-month trial with Hympavzi OR Alhemo, depending on inhibitor status

New Business:

Second Review

Diabetes

References:

1. American Diabetes Association Diabetes Care 2020 Jan; 43(Supplement 1): S98-S110. https://doi.org/10.2337/dc20-S009

Covered options in combination with Insulin therapy:

- GLP-1 agonists, DPP-4 inhibitors, SGLT-2 inhibitors, TZDs, and metformin
  - GLP-1 Agonist and SGLT-2 inhibitors are recommended first line treatments for every pathway indicated in the guidelines (ASCVD, HF, CKD, hypoglycemia risk, and to minimize weight gain)
  - TZDs increase insulin sensitivity and hypoglycemia risk should be monitored.
  - Metformin is recommended throughout treatment escalation.

Therapeutic Duplication

- One Strength of one medication is allowed at a time.
- Medication classes not payable together:
  - DPP-4 Inhibitors and GLP-1 Agonists
    - GLP-1 and DPP-4 Inhibitors should not be used concurrently due to similar mechanisms of action.
  - Sulfonylureas and Insulins
    - When initiating injectable therapy, sulfonylureas and DPP-4 inhibitors are typically discontinued.
  - Humulin R U-500 is not allowed with any other insulin (basal or prandial)
    - Humulin R U-500 is indicated for monotherapy. It acts differently than regular insulin (U-100). It provides both basal and prandial coverage. Injections can be increased to 3 times per day for prandial coverage.

Underutilization

- Toujeo, Tresiba, and Metformin 1000 mg must be used adherently and will reject on point of sale for late fill.

Biologics

CLINICAL PA REQUIRED
TZIELD (teplizumab-mzwv) – *Medical Billing*

High-Cost Drug:

This 14-day treatment course costs $193,900.

- In study TN-10; 72 people were enrolled – 44 in active treatment group and 32 in placebo group. By month 36, 63.7% (28) in the active treatment group and 71.9% (23) in the placebo group had experienced Stage 3 Type 1 Diabetes onset.

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months

- The requested medication must be prescribed by, or in consult with, an endocrinologist.
- The member has a family history of Type 1 Diabetes

- The member has at least two of the following pancreatic islet cell autoantibodies:
  - Glutamic acid decarboxylase 65 (GAD) autoantibodies
  - Insulin autoantibody (IAA)
  - Insulinoma-associated antigen 2 autoantibody (IA-2A)
  - Zinc transporter 8 autoantibody (ZnT8A)
  - Islet cell autoantibody (ICA)
- The member has no symptoms of Type 1 Diabetes (e.g., polyuria, polydipsia, weight loss, fatigue, DKA)
- The member has abnormal blood sugar levels determined by an oral glucose tolerance test.

DPP-4 Inhibitors

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
JANUMET (sitagliptin/metformin)	alogliptan/pioglitazone
JANUMET XR (sitagliptin/metformin)	alogliptin
JANUVIA (sitagliptin)	alogliptin/metformin
JENTADUETO (linagliptin/metformin)	KAZANO (alogliptin/metformin)
JENTADUETO XR (linagliptin/metformin)	NESINA (alogliptin)
TRADJENTA (linagliptin)	ONGLYZA (saxagliptin)
	OSENI (alogliptin/pioglitazone)
	saxagliptin
	saxagliptin/metformin
	sitagliptin/metformin
	ZITUVIMET XR (sitagliptin/metformin)
	ZITUVIO (sitagliptin)

++Clinically Non-Preferred: Alogliptin and saxagliptan have a potentially higher risk for heart failure.

Electronic Age Verification

- The member must be 18 years or older for Januvia, Janumet, or Janumet XR

Electronic Concurrent Medications Required

- A total of 28-day supply of metformin must be paid within 100 days prior to the DPP-4 Inhibitor's date of service. Members with GI intolerances to high dose IR metformin must trial at minimum a dose of 500 mg ER, as evidenced by paid claims or pharmacy printouts.
  - Metformin is recommended to be continued with therapy with DPP-4 Inhibitors**.** If metformin is not tolerated, SGLT2 inhibitor and GLP-1 Agonists are recommended as part of the glucose-lowering regimen independent of A1C or TIR and are first line alternatives.
  - Metformin is more effective than DPP-4 inhibitors and lowering A1c and weight when used as monotherapy.

* GI intolerances (typically will not be considered to bypass trial requirements):
  - If on high dose IR metformin, member must trial at minimum a dose of 500 mg ER, as evidenced by paid claims or pharmacy printouts.
  - The member experiencing GI side effects should be counseled: reduction in meal size, eating slower, decreased intake of greasy, high-fat or spicy food, refrain from laying down after eating.

References:

1. American Diabetes Association Diabetes Care 2020 Jan; 43(Supplement 1): S98-S110. https://doi.org/10.2337/dc20-S009

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months

- The member has been unable to achieve goal A1C (≤ 7%) or TIR (>70%) despite two 90-day trials of triple combination therapy, as evidenced by paid claims or pharmacy printouts.
- Zituvio and sitagliptin/metformin only: See *Preferred Dosage Form* Criteria

DPP-4 Inhibitors / SGLT2 Inhibitors Combination

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
TRIJARDY XR (empagliflozin/linagliptan/metformin)	GLYXAMBI (empagliflozin/linagliptin)
	STEGLUJAN (ertugliflozin/sitagliptin)
	++QTERN (dapagliflozin/saxagliptin)

++Clinically Non-Preferred: Saxagliptan has a potentially higher risk for heart failure.

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months

- See Preferred Dosage Form Criteria
- Clinical justification must be provided explaining why the member cannot use individual preferred products separately or preferred agent.

GLP-1 Agonists^

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (STEP 1 – PA REQUIRED)	NON-PREFERRED AGENTS (STEP 2 – PA REQUIRED)
liraglutide - *generic allowed due to shortage but brand preferred*	OZEMPIC (semaglutide)	TRULICITY (dulaglutide)
VICTOZA (liraglutide) - *Brand Preferred*	RYBELSUS (semaglutide)	

++Clinically Non-Preferred: Byetta is less effective than other available agents.
^ See GIP/GLP-1 Agonists section for Mounjaro (tirzepatide) criteria

Clinical information: dose comparison recommendations for switching between GLP-1 agonists

- For GI side effects (start titration at lowest available dose)
- For any other reason, may consider starting at equivalent dose to minimize disruption to glycemic control
  - Victoza 1.2 mg = Trulicity 0.75 mg = Ozempic 0.25 mg
  - Victoza 1.8 mg = Trulicity 1.5 mg = Ozempic 0.5 mg = Rybelsus 7 mg or 14 mg = Mounjaro 2.5 mg
  - Trulicity 3 mg = Ozempic 0.5 mg or 1 mg
  - Trulicity 4.5 mg = Ozempic 1 mg
  - Mounjaro 5 mg = Ozempic 2 mg

References:

1. Almandoz JP, Lingvay I, Morales J, Campos C. Switching Between Glucagon-Like Peptide-1 Receptor Agonists: Rationale and Practical Guidance. Clin Diabetes. 2020 Oct;38(4):390-402. Doi: 10.2337/cd19-0100. PMID: 33132510; PMCID: PMC7566932.

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months

- Step 1: Ozempic and Rybelsus:
  - One of the following apply (A or B):

        - The member has been unable to achieve goal A1C (≤ 7%) or TIR (>70%) despite a 90-day trial of triple combination therapy with liraglutide, metformin, SGLT-2 inhibitor or insulin, as evidenced by paid claims or pharmacy printouts.
            - If triple therapy cannot be met with liraglutide, clinical justification must be provided (subject to clinical review*), and triple therapy must be met with SGLT-2 inhibitor + DPP4 inhibitor + metformin
            - If triple therapy cannot be met with SGLT-2 inhibitor + DPP4 inhibitor + metformin, clinical justification must be provided (subject to clinical review*)
        - The request is for Ozempic, as evidenced by paid claims or pharmacy printouts, and is eligible for approval for semaglutide based on the MASH criteria or tirzepatide based on the Sleep Apnea criteria.
- Step 2:
    - The member has been unable to achieve goal A1C (≤ 7%) or TIR (>70%) despite two 90-day trials of triple combination therapy (one trial with liraglutide and one with Ozempic, subject to clinical review*) along with metformin, SGLT-2 inhibitor or insulin, as evidenced by paid claims or pharmacy printouts.
        - If triple therapy cannot be met with liraglutide or Ozempic, clinical justification must be provided (subject to clinical review*), and triple therapy must be met with SGLT-2 inhibitor + DPP4 inhibitor + metformin.
        - If triple therapy cannot be met with SGLT-2 inhibitor + DPP4 inhibitor + metformin, clinical justification must be provided (subject to clinical review*)
    - One of the following have been met:
        - The requested medication must be prescribed by, or in consult with, an endocrinologist or diabetes specialist.
        - The member has received diabetes education from a diabetic specialist, diabetic educator, or pharmacist (may be accomplished through the MTM program).

*GI intolerances (typically will not be considered to bypass trial requirements):

- If on high dose IR metformin, the member must trial at minimum a dose of 500 mg ER.
- If on liraglutide or Ozempic, the member should be evaluated on potential for GI side effects; GI effects are common across all GLP-1 agonist agents and transient in nature, typically lessening with ongoing treatment.
- If the member is experiencing GI side effects, mitigation efforts should be trialed for at least two months: reduction in meal size, eating slower, decreased intake of greasy, high-fat or spicy food, refrain from laying down after eating.

Note: If the member qualifies for semaglutide, the most cost effective semaglutide product will be authorized.

GIP/GLP-1 Agonists

CLINICAL PA REQUIRED
MOUNJARO (tirzepatide)

Prior Authorization Criteria

<u>Initial Criteria – Approval Duration:</u> 12 months

- One of the following is met (A or B):
    - The member meets both of the following (1 and 2):
        - The member has been unable to achieve goal A1C (≤ 7%) or TIR (>70%) despite two 90-day trials of triple combination therapy (one trial with liraglutide and one with Ozempic, subject to clinical review*) along with metformin, SGLT-2 inhibitor or insulin, as evidenced by paid claims or pharmacy printouts.
            - If triple therapy cannot be met with liraglutide or Ozempic, clinical justification must be provided (subject to clinical review*), and triple therapy must be met with SGLT-2 inhibitor + DPP4 inhibitor + metformin.
            - If triple therapy cannot be met with SGLT-2 inhibitor + DPP4 inhibitor + metformin, clinical justification must be provided (subject to clinical review*)

- One of the following have been met (a or b):
  a. The requested medication must be prescribed by, or in consult with, an endocrinologist or diabetes specialist.
  b. The member has received diabetes education from a diabetic specialist, diabetic educator, or pharmacist (may be accomplished through the MTM program).
- The request is for Mounjaro and the member is otherwise eligible for approval for tirzepatide based on the Sleep Apnea criteria.

*GI intolerances (typically will not be considered to bypass trial requirements):

- If on high dose IR metformin, member must trial at minimum a dose of 500 mg ER.
- If on liraglutide or Ozempic, the member should be evaluated on potential for GI side effects, with GI effects being common across all GLP-1 agonist agents and transient in nature, typically lessoning with ongoing treatment.
- If the member is experiencing GI side effects, mitigation efforts should be trialed for at least two months: reduction in meal size, eating slower, decreased intake of greasy, high-fat or spicy food, refrain from laying down after eating.

Note: If the member qualifies for tirzepatide, the most cost effective tirzepatide product will be authorized.

Gastroparesis

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
metoclopramide tablet	GIMOTI (metoclopramide nasal spray)

Prior Authorization Criteria

Initial Criteria – Approval Duration: 3 months

- Clinical justification must be provided explaining why the member is unable to use an oral dosage formulation (including solution formulations), subject to clinical review.

Glucose Rescue Medications

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
BAQSIMI (glucagon) SPRAY – Labeler 00548	BAQSIMI (glucagon) SPRAY – Labeler 00002
GVOKE (glucagon) INJECTION	glucagon kit
ZEGALOGUE (dasiglucagon) AUTOINJECTOR	

Electronic Duration Verification

- 4 doses are covered every 60 days without an override.

If one of the following criteria are met (A or B), please request an override by calling provider relations at 1-800-755-2604 or emailing medicaidpharmacy@nd.gov:

A. The previous dose has expired.
B. The dose was used by member for a hypoglycemic episode. (In this case, it is recommended to follow up with prescriber to discuss frequency of use and potential regimen review/adjustments)

Insulin/GLP-1 Agonist Combination

CLINICAL PA REQUIRED
SOLIQUA (insulin glargine/lixisenatide)
XULTOPHY (insulin degludec/liraglutide)

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months

- Clinical justification must be provided explaining why the member is unable to use the preferred products (subject to clinical review).

Insulin

Rapid Acting Insulin

Insulin Lispro

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
HUMALOG U-100 (insulin lispro) CARTRIDGE	insulin lispro vials – See Biosimilar Agents
insulin lispro U-100 pen, jr pen	

Insulin Aspart

PREFERRED AGENTS (ELECTRONIC STEP REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
FIASP (insulin aspart)	insulin aspart
	NOVOLOG (insulin aspart)
	RELION NOVOLOG (insulin aspart)

Insulin Glulisine

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
	APIDRA (insulin glulisine)

Insulin Regular, Human

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
	++AFREZZA (insulin regular, human)
	++HUMULIN R (insulin regular, human) VIAL
	++NOVOLIN R (insulin regular, human)
	++ RELION NOVOLIN R (insulin regular, human)

++Clinically Non-Preferred: ACOG (American College of Obstetricians and Gynecologists) guidelines prefer insulin analogues (insulin aspart and lispro) over regular insulin due to better compliance, better glycemic control, and overall fewer hypoglycemic episodes.

Electronic Step Therapy Required

- Fiasp
  - PA Not Required Criteria: A 3-month supply of insulin lispro has been paid within 180 days prior to Fiasp's date of service.
  - PA Required Criteria: The member must have failed a 3-month trial from insulin lispro, as evidenced by paid claims or pharmacy printouts.
- Insulin Vials
  - PA Not Required Criteria: A 28-day supply of Omnipod has been paid within 90 days prior to insulin lispro vial's date of service.
  - PA Required Criteria: The member has an insulin pump.

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months

- Apidra: The member must have failed a 3-month trial of each of the following agents, as evidenced by paid claims or pharmacy printouts:
  - insulin lispro
  - Fiasp
- Humalog U-200: Request must not be for use in an insulin pump: HUMALOG® (insulin lispro) 200 Units/mL: Do Not Use in a Pump (lillymedical.com)
  - Doses ≤ 200 units/day: Clinical justification must be provided why member cannot tolerate the volume of insulin required to use Humalog U-100 or tolerate two injections per dose.
  - Doses > 200 units/day: Clinical justification must be provided why member is not a candidate for Humulin R U-500.
- Regular Insulin (Humulin R / Novolin R / Afrezza): The member must have failed a 3-month trial of each of the following agents, as evidenced by paid claims or pharmacy printouts:
  - insulin lispro
  - Fiasp
- Non-Preferred Agents: See *Preferred Dosage Form* Criteria

Intermediate Acting Insulin

PREFERRED AGENTS (NO PA REQUIRED)	PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
HUMULIN R U-500 (insulin regular, human)	++ NOVOLIN N (insulin NPH human isophane)	++ HUMULIN N (insulin NPH human isophane)
	++ RELION NOVOLIN N (insulin NPH human isophane)	

++ Clinically non-preferred: Lantus have been demonstrated to reduce the risk of symptomatic and nocturnal hypoglycemia compared with NPH insulin.

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months (6 months or until due date, if known, for gestational diabetes)

- One of the following must be met:
  - The member must be pregnant or breastfeeding.
  - The member must be tube feedings.
  - The member must be post-solid organ transplant.
    - For kidney transplant – Medicare eligibility must be ruled out *(6-month approval may be allowed to determine eligibility)*
  - Clinical justification explaining why the member is unable to use Lantus (subject to clinical review)

Non-Preferred Agent Criteria

- See *Preferred Dosage Form* Criteria

Long-Acting Insulin

Insulin Glargine

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
LANTUS U-100 (insulin glargine) – *Brand Required*	insulin glargine U-100 (generic Toujeo)
TOUJEO U-300 (insulin glargine) *No PA required for doses 100 unit/day to 200 unit/day – *Brand Required*	insulin glargine (Lantus) – See Biosimilar Agents

Insulin Degludec

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
TRESIBA (insulin degludec) FLEXTOUCH U-200 *No PA required for doses 100 unit/day to 200 unit/day *- Brand Required*	insulin degludec U-100 and U-200
	TRESIBA (insulin degludec) U-100

Quantity Override Request

- Toujeo Solostar 300 unit/mL, Toujeo Max Solostar 300 unit/mL and Tresiba 200 unit/mL:
  - Doses > 200 units/day:
    - Clinical justification must be provided explaining why the member is not a candidate for U-500R + Toujeo and Tresiba are not intended as replacements for U-500R insulin
  - Doses >100 units/day to ≤ 200 units/day: No prior authorization required.
    - Please call for an override by calling provider relations at 1-800-755-2604 if the day supply is less than 30 days and dose is between 100 units/day and 200 units/day (e.g., short-cycle filling).
  - Doses ≤ 100 units/day:
    - Must meet Prior Authorization Criteria below

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months
- The requested medication must be prescribed by, or in consult with, an endocrinologist or diabetes specialist.
- The member has had a 90-day trial of Lantus with good compliance, as evidenced by paid claims or pharmacy printouts.
- One of the following must be met, as evidenced by provided clinical notes or labs:
  - The member experiences recurrent episodes of hypoglycemia despite adjustments to current regimen (prandial insulin, interacting drugs, meal, and exercise timing).
  - The member must be experiencing inconsistent blood sugars.

Renewal Criteria – Approval Duration: 12 months
- The member must have experienced at least one of the following, as evidenced by provided clinical notes or labs:
  - Reduction in frequency and/or severity of hypoglycemia
  - Improved glycemic control (evidenced by A1c or TIR)

Mixed Insulin

Insulin NPL/Insulin Lispro

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
HUMALOG MIX 50/50 (insulin NPL/insulin lispro) VIAL	HUMALOG MIX 50/50 (insulin NPL/insulin lispro) KWIKPEN
insulin lispro mix 75/25 kwikpen	HUMALOG MIX 75/25 (insulin NPL/insulin lispro)

Insulin Aspart Protamine/Insulin Aspart

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
insulin aspart protamine/insulin aspart 70/30	NOVOLOG MIX 70/30 (insulin aspart protamine/insulin aspart) – *Brand Required*
	RELION NOVOLOG MIX 70/30 (insulin aspart protamine/insulin aspart)

Insulin NPH Human/Regular Insulin Human

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
HUMULIN MIX 70/30 (insulin NPH human/regular insulin human)	NOVOLIN MIX 70-30 (insulin NPH human/regular insulin human)
	RELION NOVOLIN MIX 70-30 (insulin NPH human/regular insulin human)

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months (6 months or until due date, if known, for gestational diabetes)

- Humulin 70/30 and Novolin 70/30 only:
  - One of the following must be met:
    - Member must be pregnant or breastfeeding.
    - Member must be on tube feedings.
    - Member must be post-solid organ transplant.
      - For kidney transplant – Medicare eligibility must be ruled out *(6-month approval may be allowed to determine eligibility)*

Non-Preferred Agent Criteria

- See *Preferred Dosage Form* Criteria
- Clinical justification must be provided explaining why the member is unable to use the preferred products or a long acting plus short acting regimen (subject to clinical review).

SGLT2 Inhibitors

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
FARXIGA (dapagliflozin) – *Brand Required*	dapagliflozin
JARDIANCE (empagliflozin)	dapagliflozin/metformin XR 5mg-1000mg, 10mg-1000mg
SYNJARDY (empagliflozin/metformin)	INVOKANA (canagliflozin)
XIGDUO XR (dapagliflozin/metformin) 5 MG-500 MG, 5 MG-1000 MG, 10 MG-500 MG, 10 MG-1000 MG – *Brand Required*	INVOKAMET (canagliflozin/metformin)
	INVOKAMET XR (canagliflozin/metformin)
	STEGLATRO (ertugliflozin)
	SEGLUROMET (ertugliflozin/metformin)
	SYNJARDY XR (empagliflozin/metformin)
	XIGDUO XR (dapagliflozin/metformin) 2.5 MG – 1000 MG

++ Canagliflozin has shown an increase in the risk of lower limb amputations and fractures in studies.
++ Dapagliflozin did not reduce atherosclerotic cardiovascular morbidity or mortality in a primary analysis, however it decreased cardiovascular in the sub analysis of prior myocardial infarction.
++ Ertugliflozin was not superior to placebo in reducing the primary composite cardiovascular endpoint.

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months

- The member must have failed a 30-day trial of each preferred SGLT2 inhibitor of a unique active ingredient, as evidenced by paid claims or pharmacy printouts.
- Clinical justification must be provided explaining why the member is unable to use the preferred agents and other classes of medication (subject to clinical review).

References:

1. DeSantis A. Sodium-glucose cotransporter 2 inhibitors for the treatment of hyperglycemia in type 2 diabetes mellitus. In: *UpToDate*, Post TW (Ed), UpToDate, Waltham, MA, 2023

Sulfonylureas

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
glimepiride 1 mg, 2 mg, and 4 mg	glimepiride 3 mg
glipizide IR 5 mg, 10 mg	glipizide 2.5 mg
glipizide ER	++glyburide
glipizide/metformin	++glyburide/metformin
glipizide ER	++glyburide, micronized

++Clinically Non-preferred: Glyburide is not recommended due to hypoglycemia.

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months

- The member must have failed a 30-day trial of glipizide and glimepiride, as evidenced by paid claims or pharmacy printouts.
- See *Preferred Dosage Form* Criteria

First Review of Non-Opioid Analgesics

Nonopioid Analgesic Therapies[1]		
Medication	**Type of Pain**	**Important Info**
Acetaminophen	Acute pain (typically as part of a multimodal regimen)	• Max 4 g/day • Avoid in patients with hepatic impairment
Gabapentinoids	Neuropathic pain	• Use reduced dose in kidney impairment and older adults • Can cause respiratory depression when administered with opioids • Dose-dependent ataxia and somnolence (avoid in patients > 75 years of age) • Elevated abuse potential
NSAIDs	Acute pain (typically as part of a multimodal regimen)	• Risk of CV thrombotic events (higher with COX-2-selective) • Avoid use in patients with kidney dysfunction, CV disease, or peptic ulcer disease
Lidocaine	Localized pain	• May be less effective or convenient for some types of pain
Skeletal muscle relaxants	Muscle spasm contributing to pain	• Elevated abuse potential • Can cause sedation and dizziness • Use in caution with opioids

Treatment options for Moderate and Severe acute pain:

- Gabapentinoids
- Opioids on an as needed basis for both moderate and severe pain. Can be used scheduled for severe pain.

- Both NCT05558410 and NCT05553366 assessed Journavx vs placebo vs hydrocodone/APAP 5/325mg, along with ibuprofen 400mg prn, to treatment postsurgical pain after abdominoplasty and bunionectomy.
    - Journavx showed a faster onset to pain relief if the abdominoplasty trial compared to hydrocodone/APAP.
    - Journavx had a slower onset to pain relief in the bunionectomy trial
    - Both trials showed similar efficacy between Journavx and hydrocodone/APAP 5/325mg in reduction of mean pain relief scale.

A NEW NONOPIOID ANALGESIC OPTION FOR ACUTE PAIN

Journavx is a sodium calcium channel blocker for the treatment of moderate to severe acute pain in adults.[2]

Mechanism of action: selective blocker of the Na(v)1.8 voltage-gated sodium channel which inhibits transmission of pain signals to the spinal cord and brain. [2]

Journavx (suzetrigine) [2]	
Indication	Moderate to severe acute pain
Market Landscape	
Clinical Studies[3]	• NCT05558410 – studied 1,118 participants aged 18-69. The median time to meaningful pain relief (2-point reduction in NPRS) was 119 minutes. • NCT05553366 – studied 1,073 participants aged 18-75. The median time to meaningful pain relief (2-point reduction in NPRS) was 240 minutes.
Dosing	100mg once on an empty stomach, then 50mg every 12 hours
Important Considerations	• Duration beyond 14 days has not been studied and is only indicated for treatment of acute pain • Should not be used with strong CYP3A inhibitors • Half-life 23.6 hours (metabolite half-life 33 hours) • Avoid use in severe hepatic impairment • Avoid use in eGFR < 15 ml/min • Additional nonhormonal contraception should be used during and 28 days after discontinuation in patients taking progestins other than levonorgestrel and norethindrone
Cost	$465 (30 count bottle) or $18.60/unit[4]

FDA Approval

Journavx (suzetrigine): May 30, 2024; 505(b) New Drug Application (NDA) pathway Type 1 – New Molecular Entity.[5]

Current Utilization

Quarter 2 2024 thru Quarter 1 2025

Medication	Rx Count	Claims Cost
Journavx	1	$370.24

References:

1. *Schwenk, ES, et al. Nonopioid pharmacotherapy for acute pain in adults. UpToDate. Feb 24, 2025. Nonopioid pharmacotherapy for acute pain in adults - UpToDate*
2. *Journavx (suzetrigine). Red Book. IBM Micromedex Solutions. Tuven Health Analytics, Inc. Ann Arbor, MI. March 4, 2025. https://www.Micromedexsolutions.com*
3. *Journavx (suzetrigine). [prescribing information]. Vertex Pharmaceuticals, Inc. US Food and Drug Administration. Boston, MA. Jan 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219209Orig1s000lbl.pdf*
4. *Journavx. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. April 15, 2025. https://www.micromedexsolutions.com*
5. *U.S. Food and Drug Administration, Center for Drug Evaluation and Research. Journavx NDA 219209 approval letter, May 30, 2024. www.accessdata.fda.gov/drugsatfda_docs/appletter/2025/219209Orig1s000ltr.pdf*

NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
2nd QUARTER 2025

Criteria Recommendations ***Approved*** ***Rejected***

1. Repotrectinib / Overuse _____ _____

Alert Message: Augtyro (repotrectinib) may be over-utilized. The recommended dosage of repotrectinib for adult and pediatric patients 12 years of age and older is 160 mg taken orally once daily with or without food for 14 days, then increase to 160 mg twice daily and continue until disease progression or unacceptable toxicity.

Drugs/Diseases

Util A	Util B	Util C
Repotrectinib		

Max Dose: 320 mg/day

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Augtyro Prescribing Information, June 2024, Bristol-Myers Squibb.

2. Repotrectinib / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Augtyro (repotrectinib) have not been established in pediatric patients younger than 12 years of age with solid tumors who have an NTRK gene fusion.

Drugs/Diseases

Util A	Util B	Util C
Repotrectinib		

Age Range: 0 – 11 yoa

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Augtyro Prescribing Information, June 2024, Bristol-Myers Squibb.

3. Repotrectinib / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Augtyro (repotrectinib) in pediatric patients with ROS1-positive NSCLC have not been established.

Drugs/Diseases

Util A	Util B	Util C (Include)
Repotrectinib		Neoplasm of Lungs

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Augtyro Prescribing Information, June 2024, Bristol-Myers Squibb.

4. Repotrectinib / Hepatotoxicity _____ _____

Alert Message: Augtyro (repotrectinib) can cause hepatotoxicity. Among the 426 patients treated with repotrectinib in clinical trials, increased alanine transaminase (ALT) occurred in 38%, and increased aspartate aminotransferase (AST) occurred in 41%. The median time to onset of increased ALT or AST was 15 days (range: 1 day to 1.9 years). Monitor liver function tests, including ALT, AST, and bilirubin, every 2 weeks during the first month of treatment, then monthly thereafter and as clinically indicated. Withhold and then resume at the same or reduced dose upon improvement or permanently discontinue repotrectinib based on the severity.

Drugs/Diseases

Util A	Util B	Util C
Repotrectinib	Abnormal Liver Enzyme Test	

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Augtyro Prescribing Information, June 2024, Bristol-Myers Squibb.

5. Repotrectinib / Interstitial Lung Disease _____ _____

Alert Message: Augtyro (repotrectinib) can cause interstitial lung disease (ILD)/pneumonitis. Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis. Immediately withhold repotrectinib in patients with suspected ILD/pneumonitis and permanently discontinue repotrectinib if ILD/pneumonitis is confirmed.

Drugs/Diseases

Util A	Util B	Util C
Repotrectinib	Interstitial Lung Disease	

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Augtyro Prescribing Information, June 2024, Bristol-Myers Squibb.

6. Repotrectinib / Skeletal Fractures _____ _____

Alert Message: Augtyro (repotrectinib) can cause skeletal fractures. Promptly evaluate patients with signs or symptoms (e.g., pain, changes in mobility, deformity) of fractures. There are no data on the effects of repotrectinib on the healing of known fractures and the risk of future fractures.

Drugs/Diseases

Util A	Util B	Util C
Repotrectinib	Bone Fractures	

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Augtyro Prescribing Information, June 2024, Bristol-Myers Squibb.

7. Repotrectinib / P-gp Inhibitors _____ _____

Alert Message: The concomitant use of Augtyro (repotrectinib), a P-gp substrate, with P-gp inhibitors should be avoided. Concomitant use of repotrectinib with a P-gp inhibitor may increase repotrectinib exposure, which may increase the incidence and severity of repotrectinib adverse reactions.

Drugs/Diseases

Util A	Util B		Util C
Repotrectinib	Abrocitinib	Lapatinib	
	Amiodarone	Quinidine	
	Cyclosporine	Ranolazine	

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Augtyro Prescribing Information, June 2024, Bristol-Myers Squibb.

8. Repotrectinib / Strong & Moderate CYP3A4 Inhibitors _____ _____

Alert Message: The concomitant use of Augtyro (repotrectinib) with strong or moderate CYP3A inhibitors should be avoided. Concurrent use of repotrectinib with a strong or moderate CYP3A inhibitor may increase repotrectinib exposure, which may increase the incidence and severity of adverse reactions of repotrectinib. Discontinue CYP3A inhibitors for 3 to 5 elimination half-lives of the CYP3A inhibitor prior to initiating repotrectinib.

Drugs/Diseases

Util A	Util B		Util C
Repotrectinib	Atazanavir	Idelalisib	
	Aprepitant	Itraconazole	
	Clarithromycin	Ketoconazole	
	Cobicistat	Nefazodone	
	Crizotinib	Nelfinavir	
	Diltiazem	Posaconazole	
	Dronedarone	Ritonavir	
	Erythromycin	Tipranavir	
	Fluconazole	Verapamil	
	Fluvoxamine	Voriconazole	
	Fosamprenavir		

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Augtyro Prescribing Information, June 2024, Bristol-Myers Squibb.

9. Repotrectinib / Strong or Moderate CYP3A4 Inducers _____ _____

Alert Message: The concomitant use of Augtyro (repotrectinib) with strong or moderate CYP3A inducers should be avoided. Concomitant use of repotrectinib with a strong or moderate CYP3A inducer may decrease repotrectinib plasma concentrations, which may decrease the efficacy of repotrectinib.

Drugs/Diseases

Util A	Util B		Util C
Repotrectinib	Apalutamide	Phenytoin	
	Bosentan	Primidone	
	Carbamazepine	Rifabutin	
	Efavirenz	Rifampin	
	Etravirine	Rifapentine	
	Phenobarbital		

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Augtyro Prescribing Information, June 2024, Bristol-Myers Squibb.

Criteria Recommendations ***Approved*** ***Rejected***

10. Repotrectinib / Certain 3A4 Substrates w/ NTI _____ _____
Alert Message: The concurrent use of Augtyro (repotrectinib) with a CYP3A4 substrate with a narrow therapeutic index should be avoided unless the use is otherwise recommended in the Prescribing Information for CYP3A substrates. Repotrectinib is a CYP3A4 inducer. Concomitant use of repotrectinib with a sensitive CYP3A4 substrate decreases the concentration of the CYP3A4 substrate, which can reduce the efficacy of the substrate. If concomitant use is unavoidable, increase the CYP3A4 substrate dosage in accordance with approved product labeling.

Drugs/Diseases

Util A	Util B	Util C
Repotrectinib	Sirolimus	
	Tacrolimus	
	Warfarin	

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Augtyro Prescribing Information, June 2024, Bristol-Myers Squibb.

11. Repotrectinib / Hormonal Contraceptives _____ _____
Alert Message: Augtyro (repotrectinib) is a CYP3A4 inducer, which can decrease progestin or estrogen exposure to an extent that could reduce the effectiveness of hormonal contraceptives. Avoid concomitant use of repotrectinib with hormonal contraceptives. Advise females of reproductive potential to use an effective nonhormonal contraceptive.

Drugs/Diseases

Util A	Util B	Util C
Repotrectinib	Progestin Estrogen Contraceptives	

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Augtyro Prescribing Information, June 2024, Bristol-Myers Squibb.

12. Repotrectinib / Pregnancy / Pregnancy Negating _____ _____
Alert Message: Based on literature reports in humans with congenital mutations leading to

changes in tropomyosin receptor tyrosine kinase (TRK) signaling, findings from animal studies, and its mechanism of action, Augtyro (repotrectinib) can cause fetal harm when administered to a pregnant patient. Oral administration of repotrectinib to pregnant rats during the period of organogenesis resulted in fetal malformations at doses approximately 0.3 times the recommended 160 mg twice daily dose based on body surface area (BSA).

Drugs/Diseases

Util A	Util B	Util C (Negate)
Repotrectinib	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Augtyro Prescribing Information, June 2024, Bristol-Myers Squibb.

13. Repotrectinib / Lactation _____ _____

Alert Message: There are no data on the presence of Augtyro (repotrectinib) in human milk or its effects on either the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed children from repotrectinib, advise a lactating woman to discontinue breastfeeding during treatment with repotrectinib and for 10 days after the last dose.

Drugs/Diseases

Util A	Util B	Util C
Repotrectinib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Augtyro Prescribing Information, June 2024, Bristol-Myers Squibb.

14. Repotrectinib / Therapeutic Appropriateness _____ _____

Alert Message: Advise females of reproductive potential to use effective non-hormonal contraception during treatment with Augtyro (repotrectinib) and for 2 months following the last dose, since repotrectinib can render some hormonal contraceptives ineffective. Repotrectinib can cause embryo-fetal harm when administered to a pregnant woman.

Drugs/Diseases

Util A	Util B	Util C
Repotrectinib		

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Augtyro Prescribing Information, June 2024, Bristol-Myers Squibb.

15. Repotrectinib / Therapeutic Appropriateness _____ _____

Alert Message: Based on genotoxicity findings, advise male patients with female partners of childbearing potential to use effective contraception during treatment with repotrectinib and for 4 months following the last dose.

Drugs/Diseases

Util A	Util B	Util C
Repotrectinib		

Gender: Male

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Augtyro Prescribing Information, June 2024, Bristol-Myers Squibb.

16. Repotrectinib / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Augtyro (repotrectinib). Nonadherence to the prescribed dosing regimen may result in subtherapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs.

Drugs/Diseases

Util A	Util B	Util C
Repotrectinib		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Ruddy K, Mayer E, Partridge A. Patient Adherence and Persistence With Oral Anticancer Treatment. CA Cancer J Clin 2009;59:56-66.
Barillet M, Prevost V, Joly F, Clarisse B. Oral Antineoplastic Agents: How do We Care About Adherence?. Br J Clin Pharmacol. 2015;80(6):1289–1302. doi:10.1111/bcp.12734
Greer JA, Amoyal N, Nisotel L, et al. Systemic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist. 2016;21:354-376.

17. Upadacitinib LQ / Therapeutic Appropriateness – Atopic Dermatitis _____ _____

Alert Message: The safety and effectiveness of Rinvoq LQ (upadacitinib oral solution) in pediatric patients with atopic dermatitis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, ulcerative colitis, or Crohn's disease have not been established.

Drugs/Diseases

Util A	Util B	Util C (Include)
Upadacitinib LQ		Atopic Dermatitis Ankylosing Spondylitis Non-Radiographic Axial Spondyloarthritis, Ulcerative Colitis, Crohn's Disease

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Rinvoq/Rinvoq LQ Prescribing Information, April 2024, AbbVie Inc.

18. Upadacitinib LQ / Psoriatic Arthritis and pJIA _____ _____

Alert Message: Rinvoq LQ (upadacitinib oral solution) may be overutilized. The recommended dosage of upadacitinib oral solution for the treatment of psoriatic arthritis or polyarticular juvenile idiopathic arthritis in pediatric patients is weight-based. For pediatric patients weighing 30 kg or more the recommended dose is 6 mg twice daily. Pediatric patients weighing 20 kg to less than 30 kg should receive 4 mg twice daily and patients weighing 10 kg to less than 20 kg should receive 3 mg twice daily.

Drugs/Diseases

Util A	Util B	Util C (Include)
Upadacitinib LQ		Psoriatic Arthritis Polyarticular Juvenile Idiopathic Arthritis

Age Range: 2 – 17 yoa
Max Dose: 12 mg/day

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Rinvoq/Rinvoq LQ Prescribing Information, April 2024, AbbVie Inc.

Criteria Recommendations ***Approved*** ***Rejected***

19. Ketorolac / Probenecid _____ _____

Alert Message: The concomitant use of ketorolac tromethamine and probenecid is contraindicated. In drug interaction studies, concomitant administration of ketorolac and probenecid resulted in decreased clearance and volume of distribution of ketorolac and significant increases in ketorolac plasma levels (total AUC increased approximately threefold from 5.4 mcg/h/mL to 17.8 mcg/h/mL), and terminal half-life increased approximately twofold from 6.6 hours to 15.1 hours.

Drugs/Diseases

Util A	Util B	Util C
Ketorolac	Probenecid	

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Ketorolac Tromethamine Prescribing Information, August 2024, Chartwell RX, LLC.

20. Sitagliptin/metformin XR / Overuse _____ _____

Alert Message: Zituvimet XR (sitagliptin/metformin extended-release) may be over-utilized. The manufacturer's recommended maximum dose is 100 mg sitagliptin/2000 mg metformin daily.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Sitagliptin/Metformin XR		CKD Stage 4
		CKD Stage 5
		ESRD
		Hemodialysis

Max Dose: 100 mg/2000mg day

References:
Merative Micromedex DRUGDEX (electronic version). Merative, Ann Arbor, Michigan, USA. 2024.
UpToDate Inc. (2024). Sitagliptin and Metformin: Drug Information. Lexi-Drugs, UpToDate Lexidrug. Retrieved August 14, 2024.
Zituvimet XR Prescribing Information, July 2024, Zydus Pharmaceuticals, Inc.

21. Sitagliptin/metformin XR / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Zituvimet XR (sitagliptin/metformin extended-release)

have not been established in pediatric patients.

Drugs/Diseases

Util A	Util B	Util C
Sitagliptin/Metformin XR		

Age Range: 0 – 17 yoa

References:
Merative Micromedex DRUGDEX (electronic version). Merative, Ann Arbor, Michigan, USA. 2024.
UpToDate Inc. (2024). Sitagliptin and Metformin: Drug Information. Lexi-Drugs, UpToDate Lexidrug. Retrieved August 14, 2024.
Zituvimet XR Prescribing Information, July 2024, Zydus Pharmaceuticals, Inc.

22. Sitagliptin/metformin XR / Severe Renal Impairment _____ _____

Alert Message: Zituvimet XR (sitagliptin/metformin extended-release) use is contraindicated in patients with severe renal impairment (eGFR below 30 mL/min/1.73m2). In clinical studies, a 4-fold increase in the plasma AUC of sitagliptin was observed in patients with severe renal impairment including patients with end-stage renal disease (ESRD) on hemodialysis, compared to normal healthy control subjects.

Drugs/Diseases

Util A	Util B	Util C
Sitagliptin/Metformin XR	CKD Stage 4	
	CKD Stage 5	
	ESRD	
	Hemodialysis	

References:

Merative Micromedex DRUGDEX (electronic version). Merative, Ann Arbor, Michigan, USA. 2024.
Zituvimet XR Prescribing Information, July 2024, Zydus Pharmaceuticals, Inc.

23. Sitagliptin/metformin XR / Moderate Renal Impairment _____ _____

Alert Message: Zituvimet XR (sitagliptin/metformin extended-release) use is not recommended in patients with an eGFR between 30 and less than 45 mL/min/1.73 m2 because these patients require a lower dosage of sitagliptin than what is available in the fixed combination sitagliptin/metformin product.

Drugs/Diseases

Util A	Util B	Util C
Sitagliptin/Metformin XR	CKD Stage 3b	

References:

Merative Micromedex DRUGDEX (electronic version). Merative, Ann Arbor, Michigan, USA. 2024.
UpToDate Inc. (2024). Sitagliptin and Metformin: Drug Information. Lexi-Drugs, UpToDate Lexidrug. Retrieved August 14, 2024.
Zituvimet XR Prescribing Information, July 2024, Zydus Pharmaceuticals, Inc.

24. Sitagliptin/metformin XR / Type 1 Diabetes _____ _____

Alert Message: Zituvimet XR (sitagliptin/metformin extended-release) should not be used in patients with type 1 diabetes mellitus.

Drugs/Diseases

Util A	Util B	Util C
Sitagliptin/Metformin XR	Type 1 Diabetes	

References:

Merative Micromedex DRUGDEX (electronic version). Merative, Ann Arbor, Michigan, USA. 2024.
UpToDate Inc. (2024). Sitagliptin and Metformin: Drug Information. Lexi-Drugs, UpToDate Lexidrug. Retrieved August 14, 2024.
Zituvimet XR Prescribing Information, July 2024, Zydus Pharmaceuticals, Inc.

25. Sitagliptin/metformin XR / Insulin & Insulin Secretagogues _____ _____

Alert Message: The concurrent use of Zituvimet XR (sitagliptin/metformin extended-release) with insulin and insulin secretagogues can increase the risk of hypoglycemia. A lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with sitagliptin/metformin.

Drugs/Diseases

Util A	Util B	Util C
Sitagliptin/Metformin XR	Insulin	
	Insulin Secretagogues	

References:

Merative Micromedex DRUGDEX (electronic version). Merative, Ann Arbor, Michigan, USA. 2024.
UpToDate Inc. (2024). Sitagliptin and Metformin: Drug Information. Lexi-Drugs, UpToDate Lexidrug. Retrieved August 14, 2024.
Zituvimet XR Prescribing Information, July 2024, Zydus Pharmaceuticals, Inc.

26. Sitagliptin/metformin XR / Pregnancy / Pregnancy Negating _____ _____

Alert Message: The limited available data with Zituvimet XR (sitagliptin/metformin extended-release) in pregnant women are not sufficient to inform a drug associated risk for major birth defects and miscarriage. Published studies with methodologies use during pregnancy have not reported a clear association with metformin and major birth defect or miscarriage risk. During pregnancy, consider appropriate alternative therapies. Sitagliptin/metformin should be used during pregnancy only if clearly needed.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Sitagliptin/Metformin XR	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:

Merative Micromedex DRUGDEX (electronic version). Merative, Ann Arbor, Michigan, USA. 2024.
UpToDate Inc. (2024). Sitagliptin and Metformin: Drug Information. Lexi-Drugs, UpToDate Lexidrug. Retrieved August 14, 2024.
Zituvimet XR Prescribing Information, July 2024, Zydus Pharmaceuticals, Inc.
American Diabetes Association (ADA). 15. Management of Diabetes in Pregnancy. Standards of Care in Diabetes-2024. Diabetes Care 2024;47(Suppl. 1):S282-S294.

27. Sitagliptin/metformin XR / Lactation _____ _____

Alert Message: There is no information regarding the presence of Zituvimet XR (sitagliptin/metformin extended-release) in human milk, the effects on the breastfed infant, or milk production. Sitagliptin is present in rat milk and, therefore, possibly in human milk. Limited published studies report that metformin is present in human milk. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for sitagliptin/metformin and any potential adverse effects on the breastfed infant from sitagliptin/metformin or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Sitagliptin/Metformin XR	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:

Merative Micromedex DRUGDEX (electronic version). Merative, Ann Arbor, Michigan, USA. 2024.
UpToDate Inc. (2024). Sitagliptin and Metformin: Drug Information. Lexi-Drugs, UpToDate Lexidrug. Retrieved August 14, 2024.
Zituvimet XR Prescribing Information, July 2024, Zydus Pharmaceuticals, Inc.

28. Sitagliptin/metformin XR / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Zituvimet XR (sitagliptin/metformin extended-release). Nonadherence to the prescribed dosing regimen may result in subtherapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs.

Drugs/Diseases

Util A	Util B	Util C
Sitagliptin/Metformin XR		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.

Ho PM, Rumsfeld JS, Masoudi FA, et al., Effect of Medication Nonadherence in Diabetes Mellitus. Cardiology Review, April 2007, Vol. 24 No. 4. p.18-22.

Currie CJ, Peyrot M, Morgan CL, et al. The Impact of Treatment Noncompliance on Mortality in People With Type 2 Diabetes. Diabetes Care 35:1279-1284, June 2012.

Butler RJ, Davis TK, Johnson WL, et al. Effects of Nonadherence with Prescription Drugs Among Older Adults. Am J Manag Care. 2011 Feb; 17(2):153-60.

29. Ropinirole IR / Overuse – Parkinson's Disease _____ _____

Alert Message: Ropinirole may be over-utilized. The maximum recommended dose of ropinirole for the treatment of Parkinson's disease is 24 mg per day (8 mg 3 times a day).

Drugs/Diseases

Util A	Util B	Util C (Include)
Ropinirole IR		Parkinson's Disease

Max Dose: 24 mg/day

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.

Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.

Ropinirole Hydrochloride Tablet Prescribing Information, Dec. 2024, Alembic Pharmaceuticals.

30. Ropinirole IR / Severe Renal Impairment _____ _____

Alert Message: Ropinirole may be over-utilized. The maximum recommended dose of ropinirole for the treatment of Parkinson's disease in patients with end-stage renal disease on dialysis is 18 mg per day.

Drugs/Diseases

Util A	Util B	Util C (Include)
Ropinirole IR		Dialysis

Max Dose: 18 mg/day

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.

Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.

Ropinirole Hydrochloride Tablet Prescribing Information, Dec. 2024, Alembic Pharmaceuticals.

31. Ropinirole IR / Overuse – Restless Legs Syndrome _____ _____
Alert Message: Ropinirole may be over-utilized. The maximum recommended dose of ropinirole for the treatment of Restless Legs Syndrome is 4 mg once daily.

Drugs/Diseases

Util A	Util B	Util C (Include)
Ropinirole IR		Restless Legs Syndrome

Max Dose: 4 mg/day

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Ropinirole Hydrochloride Tablet Prescribing Information, Dec. 2024, Alembic Pharmaceuticals.

32. Ropinirole IR / Severe Renal Impairment in Restless Legs Syndrome _____ _____
Alert Message: Ropinirole may be over-utilized. The maximum recommended dose of ropinirole for the treatment of Restless Legs Syndrome in patients with end-stage renal disease on dialysis is 3 mg per day.

Drugs/Diseases

Util A	Util B	Util C (Include)
Ropinirole IR	Dialysis	Restless Legs Syndrome

Max Dose: 3 mg/day

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Ropinirole Hydrochloride Tablet Prescribing Information, Dec. 2024, Alembic Pharmaceuticals.

33. Ropinirole / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of ropinirole in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C
Ropinirole IR		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Ropinirole Hydrochloride Tablet Prescribing Information, Sept. 2024, Alembic Pharmaceuticals.

34. Ropinirole IR / Levodopa / Dyskinesia _____ _____

Alert Message: Ropinirole tablets may cause or exacerbate pre-existing dyskinesia in patients treated with L-dopa for Parkinson's disease. Decreasing the dose of dopaminergic medications may ameliorate this adverse reaction.

Util A	Util B	Util C (Include)
Ropinirole IR	Levodopa	Dyskinesia

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Ropinirole Hydrochloride Tablet Prescribing Information, Sept. 2024, Alembic Pharmaceuticals.

35. Ropinirole IR / Impulse Control _____ _____

Alert Message: Reports suggest that patients can experience intense urges to gamble, increased sexual urges, intense urges to spend money, binge or compulsive eating, and/or other intense urges, and the inability to control these urges while taking medications that increase central dopaminergic tones, including ropinirole tablets. Because patients may not recognize these behaviors as abnormal, it is important for prescribers to specifically ask patients or their caregivers about the development of new or increased gambling urges, sexual urges, uncontrolled spending, binge or compulsive eating, or other urges while being treated with ropinirole tablets for Parkinson's disease and RLS. Physicians should consider dose reduction or stopping the medication if a patient develops such urges while taking ropinirole tablets.

Drugs/Diseases

Util A	Util B	Util C
Ropinirole IR	Pathological Gambling	
	Other Impulse Disorders	
	Binge Eating Disorder	

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Ropinirole Hydrochloride Tablet Prescribing Information, Dec. 2024, Alembic Pharmaceuticals.

36. Ropinirole IR / Hallucinations & Psychotic-Like Behavior _____ _____

Alert Message: Postmarketing reports indicate that patients with Parkinson's disease or RLS may experience new or worsening mental status and behavioral changes, which may be severe, including psychotic-like behavior during treatment with ropinirole tablets or after starting or increasing the dose of ropinirole tablets. This abnormal thinking and behavior can consist of one or more of a variety of manifestations including paranoid ideation, delusions, hallucinations, confusion, psychotic-like behavior, mania, disorientation, aggressive behavior, agitation, and delirium. Patients with a major psychotic disorder should ordinarily not be treated with ropinirole tablets because of the risk of exacerbating psychosis.

Drugs/Diseases

Util A	Util B	Util C
Ropinirole IR	Paranoid ideation	
	Delusions	
	Hallucinations	
	Confusion	
	Psychotic-like behavior	
	Mania	
	Schizophrenia	
	Disorientation	
	Aggressive behavior	
	Agitation	
	Delirium	

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Ropinirole Hydrochloride Tablet Prescribing Information, Dec. 2024, Alembic Pharmaceuticals.

Criteria Recommendations ***Approved*** ***Rejected***

37. Ropinirole IR / Dopamine Antagonists _____ _____

Alert Message: Ropinirole is a dopamine agonist, and concurrent use with dopamine antagonists such as neuroleptics (e.g., phenothiazines, butyrophenones, thioxanthene) or metoclopramide may reduce the efficacy of ropinirole.

Drugs/Diseases

Util A	Util B		Util C
Ropinirole IR	Chlorpromazine	Aripiprazole	
	Fluphenazine	Asenapine	
	Haloperidol	Iloperidone	
	Loxapine	Lumateperone	
	Molindone	Lurasidone	
	Perphenazine	Olanzapine	
	Pimozide	Paliperidone	
	Prochlorperazine	Risperidone	
	Thioridazine	Ziprasidone	
	Thiothixene		
	Trifluoperazine		
	Metoclopramide		

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Ropinirole Hydrochloride Tablet Prescribing Information, Dec. 2024, Alembic Pharmaceuticals.

38. Ropinirole IR / Higher Dose Estrogen _____ _____

Alert Message: Concomitant use of ropinirole and higher doses of estrogens may increase the exposure of ropinirole. A dose adjustment of ropinirole may be needed when estrogen therapy is initiated or discontinued.

Drugs/Diseases

Util A	Util B	Util C
Ropinirole IR	Conjugated Estrogen	
	Esterified Estrogen	
	Estradiol	
	Ethinyl Estradiol	

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Ropinirole Hydrochloride Tablet Prescribing Information, Dec. 2024, Alembic Pharmaceuticals.

39. Ropinirole IR / CYP1A2 Inhibitors _____ _____

Alert Message: Ropinirole is a CYP1A2 substrate, and concurrent use with a CYP1A2 inhibitor may result in increased ropinirole concentrations. Therefore, if therapy with a drug known to be a potent inhibitor of CYP1A2 is initiated or discontinued during treatment with ropinirole, adjustment of ropinirole dose may be required.

Drugs/Diseases

Util A	Util B	Util C
Ropinirole IR	Ciprofloxacin	
	Fluvoxamine	
	Viloxazine	

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Ropinirole Hydrochloride Tablet Prescribing Information, Dec. 2024, Alembic Pharmaceuticals.

40. Ropinirole IR / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no adequate data on the developmental risk associated with the use of ropinirole in pregnant women. In animal studies, ropinirole had adverse effects on development when administered to pregnant rats at doses similar to (neurobehavioral impairment) or greater than (teratogenicity and embryolethality at > 36 times) the MRHD for Parkinson's disease. Ropinirole should be used in pregnancy only if the potential benefit to the mother outweighs the potential risk to the fetus.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Ropinirole IR	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.

41. Ropinirole IR / Lactation _____ _____

Alert Message: There are no data on the presence of ropinirole in human milk, the effects of ropinirole on the breastfed infant, or the effects of ropinirole on milk production. However, inhibition of lactation is expected because ropinirole inhibits the secretion of prolactin in humans. Ropinirole or metabolites, or both, are present in rat milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ropinirole and any potential adverse effects on the breastfed infant from ropinirole or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Ropinirole IR	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.

42. Ropinirole IR / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing ropinirole. Nonadherence to the prescribed dosing regimen may result in subtherapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs.

Drugs/Diseases

Util A	Util B	Util C
Ropinirole IR		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Richy FF, Guilhem P, Moran, et al., Compliance with Pharmacotherapy and Direct Healthcare Costs with Parkinson's Disease: A Retrospective Claims Database Analysis. Appl Health Econ Health Policy. 2013 Aug;11(4):395-406.

Daley DJ, Myint PK, Gray RJ, Deane KH. Interventions for Improving Medication Adherence in Patients with Idiopathic Parkinson's Disease. Cochrane Database Systematic Rev 2014. DOI:10.1002/14651858.CD011191

43. Sodium Oxybate ER Suspension / Overuse (Adults) _____ _____

Alert Message: Lumryz (sodium oxybate extended-release oral suspension) may be overutilized. The recommended dosage range for the treatment of cataplexy or excessive daytime sleepiness in patients 7 years of age and older with narcolepsy is 6 g to 9 g once per night orally. Doses higher than 9 g per night have not been studied and should not ordinarily be administered.

Drugs/Diseases
Util A Util B Util C
Sodium Oxybate ER Susp

Max Dose: 9 g/day
Age Range: 18 – 999 yoa

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Lumryz Prescribing Information, Oct. 2024, Avadel CNS Pharmaceuticals, LLC.

44. Sodium Oxybate ER Suspension / Overuse (Pediatric) _____ _____

Alert Message: Lumryz (sodium oxybate extended-release oral suspension) may be overutilized. The recommended starting dosage of sodium oxybate ER in pediatric patients 7 years and older weighing at least 45 kg is 4.5 g once per night administered orally. Increase the dosage by 1.5 g per night at weekly intervals to the maximum recommended dosage of 9 g once nightly. Because the recommended starting dosage in pediatric patients 7 years and older weighing less than 45 kg cannot be achieved with the available strengths of sodium oxybate ER, use another sodium oxybate product to initiate treatment. The maximum recommended dosage for patients 7 years and older weighing 20 kg to < 30 kg is 6 g once per night, and the maximum recommended dosage for patients 7 years and older weighing 30 kg to < 45 kg is 7.5 g once per night orally. There is insufficient information to provide specific dosing recommendations for patients 7 years and older who weigh less than 20 kg.

Drugs/Diseases
Util A Util B Util C
Sodium Oxybate ER Susp

Max Dose: 9 g/day
Age Range: 7 - 17 yoa

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Lumryz Prescribing Information, Oct. 2024, Avadel CNS Pharmaceuticals, LLC

45. Sodium Oxybate ER Suspension / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Lumryz (sodium oxybate extended-release oral suspension) have not been established in pediatric patients younger than 7.

Drugs/Diseases
Util A Util B Util C
Sodium Oxybate ER Susp

Age Range: 0 – 6 yoa

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Lumryz Prescribing Information, Oct. 2024, Avadel CNS Pharmaceuticals, LLC.

46. Sodium Oxybate ER Suspension / Box Warning _____ _____

Alert Message: Lumryz (sodium oxybate extended-release oral suspension) is the sodium salt of gamma-hydroxybutyrate (GHB). Abuse or misuse of illicit GHB, either alone or in combination with other CNS depressants, is associated with CNS adverse reactions, including seizure, respiratory depression, decreases in the level of consciousness, coma, and death. Because illicit use and abuse of GHB have been reported, physicians should carefully evaluate patients for a history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse of GHB.

Drugs/Diseases

Util A	Util B	Util C
Sodium Oxybate ER Susp	History of Drug Abuse	

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Lumryz Prescribing Information, Oct. 2024, Avadel CNS Pharmaceuticals, LLC.

47. Sodium Oxybate ER Suspension / Contraindication _____ _____

Alert Message: Lumryz (sodium oxybate extended-release oral suspension) is contraindicated for use in patients with succinic semialdehyde dehydrogenase deficiency.

Drugs/Diseases

Util A	Util B	Util C (Include)
Sodium Oxybate ER Susp		Succinic Semialdehyde Dehydrogenase Deficiency

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Lumryz Prescribing Information, Oct. 2024, Avadel CNS Pharmaceuticals, LLC.

48. Sodium Oxybate ER Suspension / Sedative Hypnotics (Box Warning) _____ _____

7lert Message: Lumryz (sodium oxybate extended-release oral suspension) is contraindicated in combination with alcohol and sedative-hypnotics. Sodium oxybate is a central nervous system (CNS) depressant. Clinically significant respiratory depression and obtundation have occurred in patients taking the immediate-release sodium oxybate. The concurrent use of sodium oxybate ER with other CNS depressants may increase the risk of respiratory depression, hypotension, profound sedation, syncope, and death.

Drugs/Diseases

Util A	Util B		Util C
Sodium Oxybate ER Susp	Estazolam	Suvorexant	
	Eszopiclone	Tasimelteon	
	Flurazepam	Temazepam	
	Lemborexant	Triazolam	
	Quazepam	Zaleplon	
	Phenobarbital	Zolpidem	
	Ramelteon		

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Lumryz Prescribing Information, Oct. 2024, Avadel CNS Pharmaceuticals, LLC.

49. Sodium Oxybate ER Suspension / Divalproex Sodium _____ _____

Alert Message: The concurrent use of Lumryz (sodium oxybate extended-release oral suspension) with divalproex sodium may result in an increased risk of CNS depression. In a drug interaction study, co-administration of a single dose of sodium oxybate XR (6 g) with divalproex sodium ER at steady state resulted in an approximate 18% increase in AUC (90% CI ratio range of 112%-123%), which is not expected to be clinically meaningful, while Cmax was comparable. A single dose of sodium oxybate XR (6 g) did not appear to affect the pharmacokinetics of divalproex sodium. However, a pharmacodynamic interaction between sodium oxybate XR and divalproex sodium, a sedative antiepileptic drug, cannot be ruled out.

Drugs/Diseases

Util A	Util B	Util C
Sodium Oxybate ER Susp	Divalproex Sodium	

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Lumryz Prescribing Information, Oct. 2024, Avadel CNS Pharmaceuticals, LLC.

50. Sodium Oxybate ER Suspension / CNS Depressants _____ _____

Alert Message: The concurrent use of Lumryz (sodium oxybate extended-release oral suspension) with other CNS depressants may increase the risk of respiratory depression, hypotension, profound sedation, syncope, and death. The sodium oxybate product is a central nervous system depressant. If the use of CNS depressants in combination with sodium oxybate is required, dose reduction or discontinuation of one or more CNS depressants (including sodium oxybate ER) should be considered.

Drugs/Diseases

Util A	Util B	Util C
Sodium Oxybate ER Susp	CNS Depressants	

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Lumryz Prescribing Information, Oct. 2024, Avadel CNS Pharmaceuticals, LLC.

51. Sodium Oxybate ER Suspension / Depression & Suicide _____ _____

Alert Message: Depression and suicidal ideation and behavior can occur in patients treated with Lumryz (sodium oxybate extended-release oral suspension). The emergence of depression in patients treated with sodium oxybate requires careful and immediate evaluation. Patients with a previous history of a depressive illness and/or suicide attempt should be monitored carefully for the emergence of depressive symptoms while taking sodium oxybate.

Drugs/Diseases

Util A	Util B	Util C
Sodium Oxybate ER Susp	Depression	
	Suicidal Ideation	

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Lumryz Prescribing Information, Oct. 2024, Avadel CNS Pharmaceuticals, LLC.

52. Sodium Oxybate ER Suspension / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no adequate data on the developmental risks associated with the use of Lumryz (sodium oxybate extended-release oral suspension) during human pregnancy. Animal studies produced no clear evidence of developmental toxicity; however, increased stillbirths and decreased postnatal viability and growth were seen at clinically relevant doses.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Sodium Oxybate ER Susp	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Lumryz Prescribing Information, Oct. 2024, Avadel CNS Pharmaceuticals, LLC.

53. Sodium Oxybate ER Suspension / Lactation _____ _____

Alert Message: The active moiety of Lumryz (sodium oxybate extended-release oral suspension) is oxybate or gamma-hydroxybutyrate (GHB). GHB is excreted in human milk after oral administration of sodium oxybate. There is insufficient information on the risk to a breastfed infant, and there is insufficient information on milk production in nursing mothers. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for sodium oxybate and any potential adverse effects on the breastfed infant from sodium oxybate or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Sodium Oxybate ER Susp	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2024 Elsevier/Gold Standard.
Facts & Comparisons, 2024 Updates, Wolters Kluwer Health.
Lumryz Prescribing Information, Oct. 2024, Avadel CNS Pharmaceuticals, LLC.

54. Cabotegravir/Rilpivirine / Contraindication _____ _____

Alert Message: The concurrent use of Cabenuva (cabotegravir/rilpivirine) is contraindicated with certain strong inducers of CYP3A4 or uridine diphosphate (UDP)-glucuronosyltransferase (UGT1A1/1A9). Coadministration of cabotegravir/rilpivirine with these agents may result in increased cabotegravir/rilpivirine clearance and loss of virologic response and development resistance.

Drugs/Diseases

Util A	Util B		Util C
Cabotegravir/Rilpivirine	Carbamazepine	Rifabutin	
	Dexamethasone	Rifampin	
	Oxcarbazepine	Rifapentine	
	Phenobarbital		
	Phenytoin		

References:
Cabenuva Prescribing Information, Sept. 2024, ViiV Healthcare.
Clinical Pharmacology, 2025 Elsevier/Gold Standard.

55. Cabotegravir/Rilpivirine / Therapeutic Appropriateness _____ _____
Alert Message: Cabenuva (cabotegravir/rilpivirine) is a complete regimen for the treatment of HIV-1 infection, and coadministration with other antiretroviral medications is not recommended.

Drugs/Diseases

Util A	Util B	Util C
Cabotegravir/Rilpivirine	All Other Antiretrovirals	

References:
Cabenuva Prescribing Information, Sept. 2024, ViiV Healthcare.
Clinical Pharmacology, 2025 Elsevier/Gold Standard.

56. Cabotegravir/Rilpivirine / Therapeutic Appropriateness _____ _____
Alert Message: The safety, efficacy, and pharmacokinetics of Cabenuva (cabotegravir/rilpivirine) have not been established in pediatric patients younger than 12 years of age or weighing less than 35 kg.

Drugs/Diseases

Util A	Util B	Util C
Cabotegravir/Rilpivirine		

Age Range: 0 – 11 yoa

References:
Cabenuva Prescribing Information, Sept. 2024, ViiV Healthcare.
Clinical Pharmacology, 2025 Elsevier/Gold Standard.

57. Cabotegravir/Rilpivirine / Non-adherence _____ _____
Alert Message: Based on the refill history, your patient may be under-utilizing Cabenuva (cabotegravir/rilpivirine). Nonadherence to antiretroviral therapy may result in insufficient plasma levels and partial suppression of viral load leading to the development of resistance, HIV progression, and increased mortality.

Drugs/Diseases

Util A	Util B	Util C
Cabotegravir/Rilpivirine		

References:
Cabenuva Prescribing Information, Sept. 2024, ViiV Healthcare.
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. Available at https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/tables-adult-adolescent-arv.pdf Accessed January 09, 2025.
Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/pediatric-arv/guidelines-pediatric-arv.pdf Accessed Jan. 9, 2025.
Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission. Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States. Department of Health and Human Services. Available at https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/perinatal-hiv/guidelines-perinatal.pdf Accessed Jan. 09, 2025.

58. Xanomeline/Trospium / Overuse _____ _____
Alert Message: Cobenfy (xanomeline/trospium) may be over-utilized. The maximum recommended dose of xanomeline/trospium is 125 mg/30 mg twice daily.

Drugs/Diseases
Util A Util B Util C
Xanomeline/Trospium

Max Dose: 250 mg/60 mg per day
Age Range: 18 – 64 yoa

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Cobenfy Prescribing Information, September 2024, Bristol Myers-Squibb.

59. Xanomeline/Trospium / Overuse _____ _____
Alert Message: Cobenfy (xanomeline/trospium) may be over-utilized. The maximum recommended dose of xanomeline/trospium in geriatric patients is one 100 mg/20 mg capsule twice daily.

Drugs/Diseases
Util A Util B Util C
Xanomeline/Trospium

Max Dose: 200 mg/40 mg per day
Age Range: ≥ 65 yoa

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Cobenfy Prescribing Information, September 2024, Bristol Myers-Squibb.

60. Xanomeline/Trospium / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of Cobenfy (xanomeline/trospium) in pediatric patients have not been established.

Drugs/Diseases
Util A Util B Util C
Xanomeline/Trospium

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Cobenfy Prescribing Information, September 2024, Bristol Myers-Squibb.

61. Xanomeline/Trospium / Urinary Retention _____ _____

Alert Message: Cobenfy (xanomeline/trospium) use is contraindicated in patients with pre-existing urinary retention. Xanomeline/trospium can cause urinary retention. Monitor xanomeline/trospium recipients for symptoms of urinary retention, including urinary hesitancy, weak stream, incomplete bladder emptying, and dysuria. In patients with symptoms, consider reducing the dose of the medication, discontinuing treatment, or referring patients for urologic evaluation as clinically indicated.

Drugs/Diseases

Util A	Util B	Util C (Include)
Xanomeline/Trospium		Urinary Retention

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Cobenfy Prescribing Information, September 2024, Bristol Myers-Squibb.

62. Xanomeline/Trospium / Hepatic Impairment _____ _____

Alert Message: Cobenfy (xanomeline/trospium) use is contraindicated in patients with moderate to severe hepatic impairment (Child-Pugh Class B & C) and not recommended in patients with mild hepatic impairment. Patients with hepatic impairment have higher systemic exposures of xanomeline, a component of the combination product, compared to patients with normal hepatic function, which may result in an increased incidence of xanomeline-related adverse reactions.

Drugs/Diseases

Util A	Util B	Util C
Xanomeline/Trospium	Hepatic Impairment	

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Cobenfy Prescribing Information, September 2024, Bristol Myers-Squibb.

63. Xanomeline/Trospium / Gastric Retention _____ _____

Alert Message: Cobenfy (xanomeline/trospium) use is contraindicated in patients with gastric retention. The trospium component of the combination product is an antimuscarinic agent and may decrease gastrointestinal motility.

Drugs/Diseases

Util A	Util B	Util C
Xanomeline/Trospium	Gastroparesis Pyloric Stenosis	

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Cobenfy Prescribing Information, September 2024, Bristol Myers-Squibb.

64. Xanomeline/Trospium / Narrow Angle Glaucoma _____ _____

Alert Message: Cobenfy (xanomeline/trospium) use is contraindicated in patients with untreated narrow-angle glaucoma. Pupillary dilation may occur due to the anticholinergic effects of xanomeline/trospium and may trigger an acute angle closure attack in patients with anatomically narrow angles. In patients known to have anatomically narrow angles, xanomeline/trospium should only be used if the potential benefits outweigh the risks and with careful monitoring.

Drugs/Diseases

Util A	Util B	Util C
Xanomeline/Trospium	Narrow Angle Glaucoma	

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Cobenfy Prescribing Information, September 2024, Bristol Myers-Squibb.

65. Xanomeline/Trospium / GI Obstruction _____ _____

Alert Message: Cobenfy (xanomeline/trospium) should be administered with caution in patients with gastrointestinal obstructive disorders because of the risk of gastric retention. The trospium component of the combination product is an antimuscarinic agent and can decrease gastrointestinal motility. Xanomeline/trospium use is contraindicated in patients with gastric retention.

Drugs/Diseases

Util A	Util B	Util C
Xanomeline/Trospium	GI Obstruction	
	Ulcerative Colitis	
	Intestinal Atony	
	Myasthenia gravis	

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Cobenfy Prescribing Information, September 2024, Bristol Myers-Squibb.

66. Xanomeline/Trospium / Moderate to Severe Renal Impairment _____ _____

Alert Message: The use of Cobenfy (xanomeline/trospium) is not recommended in patients with moderate to severe renal impairment. The trospium component of the combination product is an anticholinergic agent and is substantially excreted by the kidney. Systemic exposure to trospium is higher in patients with moderate and severe renal impairment, and anticholinergic adverse reactions are expected to be greater in this patient population.

Drugs/Diseases

Util A	Util B	Util C (Include)
Xanomeline/Trospium		CKD Stage 3
		CKD Stage 4
		CKD Stage 5
		ERD

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Cobenfy Prescribing Information, September 2024, Bristol Myers-Squibb.

67. Xanomeline/Trospium / Strong CYP2D6 Inhibitors _____ _____

Alert Message: The xanomeline component of the combination product Cobenfy (xanomeline/trospium) is a CYP2D6 substrate. Concomitant use of xanomeline/trospium with strong CYP2D6 inhibitors may increase xanomeline plasma concentrations, increasing the frequency and/or severity of xanomeline-related adverse reactions. Monitor patients for increased frequency and/or severity of xanomeline-related adverse reactions.

Drugs/Diseases

Util A	Util B		Util C
Xanomeline/Trospium	Bupropion	Quinidine	
	Fluoxetine	Terbinafine	
	Paroxetine		

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Cobenfy Prescribing Information, September 2024, Bristol Myers-Squibb.

68. Xanomeline/Trospium / Drugs Eliminated by Tubular Secretion _____ _____

Alert Message: Concomitant use of Cobenfy (xanomeline/trospium) with drugs that are eliminated by active tubular secretion may increase plasma concentrations of trospium, a component of the combination product, and/or the concomitantly used drug due to competition for this elimination pathway. Concurrent use may increase the frequency and/or severity of adverse reactions from xanomeline/trospium and/or the concurrent drug eliminated by active tubular secretion. Monitor patients for increased frequency and/or severity of adverse reactions.

Drugs/Diseases

Util A	Util B			Util C
Xanomeline/Trospium	Adefovir	Entecavir	Quinidine	
	Amiloride	Memantine	Ranitidine	
	Cimetidine	Midodrine	Tenofovir	
	Dofetilide	Procainamide	Trimethoprim	

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Cobenfy Prescribing Information, September 2024, Bristol Myers-Squibb.

69. Xanomeline/Trospium / Sensitive CYP3A4 Substrates _____ _____

Alert Message: The xanomeline component of the combination product Cobenfy (xanomeline/trospium) is a CYP3A4 inhibitor. Concomitant use of xanomeline/trospium with sensitive CYP3A4 substrates may result in increased plasma concentrations of the sensitive 3A4 substrate and frequency and/or severity of adverse reactions related to the sensitive 3A4 substrate. Monitor patients for increased frequency and/or severity of adverse reactions related to the sensitive 3A4 substrate.

Drugs/Diseases

Util A	Util B					Util C
Xanomeline/Trospium	Avanafil	Eletriptan	Lurasidone	Simvastatin	Vardenafil	
	Budesonide	Eplerenone	Maraviroc	Sirolimus		
	Buspirone	Everolimus	Midazolam	Tacrolimus		
	Conivaptan	Felodipine	Naloxegol	Ticagrelor		
	Darifenacin	Ibrutinib	Nisoldipine	Tipranavir		
	Darunavir	Lomitapide	Quetiapine	Tolvaptan		
	Dronedarone	Lovastatin	Sildenafil	Triazolam		

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Cobenfy Prescribing Information, September 2024, Bristol Myers-Squibb.

70. Xanomeline/Trospium / P-gp Substrates w/ NTI _____ _____

Alert Message: Concomitant use of Cobenfy (xanomeline/trospium) with drugs that are substrates of P-gp transport may increase plasma concentrations of the P-gp substrates, increasing the risk of P-gp substrate-related adverse reactions. The xanomeline component of the combination product transiently inhibits P-gp transport locally in the gut. Monitor patients for increased frequency and/or severity of adverse reactions related to oral drugs that are narrow therapeutic index substrates of P-gp transport.

Drugs/Diseases

Util A	Util B		Util C
Xanomeline/Trospium	Cyclosporine	Sirolimus	
	Digoxin	Tacrolimus	
	Everolimus		

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Cobenfy Prescribing Information, September 2024, Bristol Myers-Squibb.

71. Xanomeline/Trospium / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no available data on Cobenfy (xanomeline/trospium) use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. In animal reproduction studies, oral administration of xanomeline alone or in combination with trospium chloride during the period of organogenesis or pregnancy and lactation caused maternal toxicities of adverse clinical signs, decreased body weight, weight gain and food consumption, and/or maternal death. At these maternally toxic doses, embryofetal and developmental toxicities included decreased fetal and neonatal weight, stillborn pups, and/or neonatal deaths.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Xanomeline/Trospium	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Cobenfy Prescribing Information, September 2024, Bristol Myers-Squibb.

72. Xanomeline/Trospium / Lactation _____ _____

Alert Message: There are no data on the presence of either component of Cobenfy (xanomeline/trospium) in human milk, the effects on the breastfed infant, or the effects on milk production. Xanomeline and trospium are present in animal milk. When a drug is present in animal milk, it is likely that the drug will be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for xanomeline/trospium and any potential adverse effects on the breastfed infant from xanomeline/trospium or from the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Xanomeline/Trospium	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.

Cobenfy Prescribing Information, September 2024, Bristol Myers-Squibb.

Criteria Recommendations ***Approved*** ***Rejected***

73. Xanomeline/Trospium / Non-adherence _____ _____
Alert Message: Based on refill history, your patient may be under-utilizing Cobenfy (xanomeline/trospium). Nonadherence to the prescribed dosing regimen may result in
subtherapeutic effects, which may lead to decreased patient outcomes and additional
healthcare costs.

Drugs/Diseases
Util A Util B Util C
Xanomeline/Trospium

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Higashi k, Medic G, Littlewood K, et al., Medication Adherence in Schizophrenia: Factors Influencing Adherence and Consequences of Nonadherence, A Systemic Literature Review. Ther Adv Psychopharmacol. 2013 2(4):200-218.

Stephenson JJ, Tuncelli O, Gu T, et al. Adherence to Oral Second-Generation Antipsychotic Medications in Patients with Schizophrenia and Bipolar Disorder: Physicians' Perceptions of Adherence vs. Pharmacy Claims. Int J Clin Pract, June 2012, 66, 6, 565-573.

Acsher-Svanum H, Zhu B, Faries DE, et al., The Cost of Relapse and the Predictors of Relapse in the Treatment of Schizophrenia. BMC Psychiatry 2010, 10:2.

74. Suzetrigine / Overuse _____ _____
Alert Message: Journavx (suzetrigine) may be over-utilized. The recommended maximum dose of suzetrigine is 50 mg orally every 12 hours. The use of suzetrigine for the treatment of moderate to severe acute pain has not been studied beyond 14 days.

Drugs/Diseases
Util A Util B Util C (Negating)
Suzetrigine Strong & Moderate CYP3A Inhibitors
Moderate and Severe Hepatic Impairment

Max Dose: 100 mg/day

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Journavx Prescribing Information, Jan. 2025, Vertex Pharmaceuticals Incorporated.

75. Suzetrigine / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of Journavx (suzetrigine) has not been established in pediatric patients.

Drugs/Diseases
Util A Util B Util C
Suzetrigine

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.

Journavx Prescribing Information, Jan. 2025, Vertex Pharmaceuticals Incorporated.

76. Suzetrigine / Strong CYP3A Inhibitors _____ _____

Alert Message: The concomitant use of Journavx (suzetrigine) with a strong CYP3A inhibitor is contraindicated. Suzetrigine and its active metabolite (M6-SUZ) are CYP3A substrates, and use with a strong CYP3A inhibitor will increase exposure to and adverse effects of suzetrigine. In clinical studies, concurrent use of suzetrigine with a strong CYP3A inhibitor increased the AUC of suzetrigine and M6-SUZ by 4.79-fold and 4.42-fold, respectively.

Drugs/Diseases

Util A	Util B		Util C
Suzetrigine	Clarithromycin	Nelfinavir	
	Cobicistat	Posaconazole	
	Itraconazole	Ritonavir	
	Ketoconazole	Voriconazole	
	Nefazodone		

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Journavx Prescribing Information, Jan. 2025, Vertex Pharmaceuticals Incorporated.

77. Suzetrigine / Moderate CYP3A Inhibitors _____ _____

Alert Message: Exercise caution when Journavx (suzetrigine) is co-administered with a moderate CYP3A inhibitor. Suzetrigine and its active metabolite (M6-SUZ) are CYP3A substrates, and use with a moderate CYP3A inhibitor can increase exposure to and adverse effects of suzetrigine. Dosage adjustment of suzetrigine is recommended during concurrent use with a moderate CYP3A inhibitor. Dose 1 is 100 mg, then starting 12 hours after the initial dose, take 50 mg every 12 hours for Doses 2, 3, and 4. For Dose 5 (starting 12 hours after Dose 4) and subsequent doses, take 50 mg every 24 hours.

Drugs/Diseases

Util A	Util B			Util C
Suzetrigine	Aprepitant	Diltiazem	Imatinib	
	Cimetidine	Dronedarone	Verapamil	
	Ciprofloxacin	Erythromycin		
	Crizotinib	Fluconazole		
	Cyclosporine	Fluvoxamine		

Max Dose: 50 mg every day starting after dose 4

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Journavx Prescribing Information, Jan. 2025, Vertex Pharmaceuticals Incorporated.

78. Suzetrigine / Severe Hepatic Impairment _____ _____

Alert Message: The use of Journavx (suzetrigine) should be avoided in patients with severe hepatic impairment (Child-Pugh Class C). Suzetrigine has not been studied in this patient population. In pharmacokinetic studies, patients with moderate hepatic impairment (Child-Pugh Class B) receiving suzetrigine had higher systemic exposure to suzetrigine and its active metabolite, M6-SUX, at steady state than those with normal hepatic function. No significant

differences in pharmacokinetics were seen in patients with mild hepatic impairment.

Drugs/Diseases

Util A	Util B	Util C
Suzetrigine	Cirrhosis	
	Hepatic Failure	

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Journavx Prescribing Information, Jan. 2025, Vertex Pharmaceuticals Incorporated.

79. Suzetrigine / Strong or Moderate CYP3A Inducers _____ _____

Alert Message: The concurrent use of Journavx (suzetrigine) with strong and moderate CYP3A inducers should be avoided. Suzetrigine and its active metabolite (M6-SUZ) are CYP3A substrates, and concurrent use with strong or moderate CYP3A inducers can decrease exposure to suzetrigine and M6-UZ, which may reduce suzetrigine efficacy.

Drugs/Diseases

Util A	Util B		Util C
Suzetrigine	Apalutamide	Phenytoin	
	Bosentan	Primidone	
	Carbamazepine	Rifabutin	
	Efavirenz	Rifampin	
	Etravirine	Rifapentine	
	Phenobarbital		

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Journavx Prescribing Information, Jan. 2025, Vertex Pharmaceuticals Incorporated.

80. Suzetrigine / Moderate Hepatic Impairment _____ _____

Alert Message: Caution should be exercised when Journavx (suzetrigine) is administered in patients with moderate hepatic impairment (Child-Pugh Class B). In pharmacokinetic studies, patients with moderate hepatic impairment receiving suzetrigine had higher systemic exposure to suzetrigine and its active metabolite, M6-SUX, at steady state than those with normal hepatic function. Dosage adjustment of suzetrigine is recommended in patients with moderate hepatic impairment. Dose 1 is 100 mg, then starting 12 hours after the initial dose, take 50 mg every 12 hours for Doses 2, 3, and 4. For Dose 5 (starting 12 hours after Dose 4) and subsequent doses, take 50 mg every 24 hours. No significant differences in pharmacokinetics were seen in patients with mild hepatic impairment.

Drugs/Diseases

Util A	Util B	Util C
Suzetrigine	Moderate Hepatic Impairment	

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Journavx Prescribing Information, Jan. 2025, Vertex Pharmaceuticals Incorporated.

81. Suzetrigine / Sensitive CYP3A Substrates _____ _____

Alert Message: If Journavx (suzetrigine) is used concomitantly with sensitive CYP3A substrates or CYP3A substrates where minimal concentration changes may lead to loss of efficacy, refer to the prescribing information for the CYP3A substrates for dosing adjustment instructions. Suzetrigine is an inducer of CYP3A. Concomitant use with suzetrigine may reduce the exposure of sensitive CYP3A substrates, which may decrease the efficacy of these substrates. Discontinuation of suzetrigine may increase the exposure of sensitive CYP3A substrates. Dosage modification of the concomitant CYP3A substrates may be required when initiating or discontinuing suzetrigine.

Drugs/Diseases

Util A	Util B					Util C
Suzetrigine	Avanafil	Eletriptan	Lurasidone	Simvastatin	Vardenafil	
	Budesonide	Eplerenone	Maraviroc	Sirolimus		
	Buspirone	Everolimus	Midazolam	Tacrolimus		

Conivaptan	Felodipine	Naloxegol	Ticagrelor
Darifenacin	Ibrutinib	Nisoldipine	Tipranavir
Darunavir	Lomitapide	Quetiapine	Tolvaptan
Dronedarone	Lovastatin	Sildenafil	Triazolam

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Journavx Prescribing Information, Jan. 2025, Vertex Pharmaceuticals Incorporated.

82. Suzetrigine / Hormonal Contraceptives _____ _____

Alert Message: Journavx (suzetrigine) treated patients using hormonal contraceptives containing progestins other than levonorgestrel and norethindrone should use additional nonhormonal contraceptives or alternative contraceptives during treatment with suzetrigine and for 28 days after discontinuation of suzetrigine. Suzetrigine is an inducer of CYP3A, and use with hormonal contraceptives that are CYP3A substrates may result in decreased efficacy of the contraceptive agent.

Drugs/Diseases

Util A	Util B		Util C
Suzetrigine	Desogestrel/Ethinyl Estradiol	Norgestrel	
	Dienogest/Estradiol Valerate	Norgestrel/Ethinyl Estradiol	
	Drospirenone/Ethinyl Estradiol	Segesterone/Ethinyl Estradiol	
	Etonogestrel/Ethinyl Estradiol		

References:

Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Journavx Prescribing Information, Jan. 2025, Vertex Pharmaceuticals Incorporated.

83. Suzetrigine / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no available data with Journavx (suzetrigine) during pregnancy to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. In animal studies, administration of suzetrigine to rats at exposures 2.2 times or more than the maximum recommended human dose (MRHD) during early embryonic development or throughout organogenesis resulted in adverse effects on implantation and maintenance of pregnancy. The clinical relevance of these findings to humans is unclear.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Suzetrigine	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Journavx Prescribing Information, Jan. 2025, Vertex Pharmaceuticals Incorporated.

84. Suzetrigine / Lactation _____ _____

Alert Message: There are no data on the presence of Journavx (suzetrigine) or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production. Suzetrigine is present in animal milk. When a drug is present in animal milk, the drug will likely be present in human milk. Development and health benefits of breastfeeding should be considered, along with the mother's clinical need for suzetrigine and any potential adverse effects on the breastfed child from suzetrigine or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Suzetrigine	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Journavx Prescribing Information, Jan. 2025, Vertex Pharmaceuticals Incorporated.

Criteria Recommendations ***Approved*** ***Rejected***

85. Esketamine / Overuse _____ _____
Alert Message: The recommended maximum maintenance dosage of Spravato (esketamine) for the treatment of depressive symptoms in adults with major depressive disorder with acute suicidal ideation or behavior is 84 mg twice weekly. Evidence of therapeutic benefit should be evaluated at the end of the induction phase to determine the need for continued treatment.

Util A	Util B	Util C (Include)
Esketamine		Attempted Suicide
		Suicide Ideation

Max Dose: 84 mg twice a week

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Spravato Prescribing Information, Jan. 2025, Janssen Pharmaceuticals, Inc.

Board Suggestions for clinical practice education or RDUR ICER criteria

1. Is there anything in clinical practice that you've seen that you feel needs to be addressed?
    a. New best practices?
    b. Fraud, waste, or abuse?
2. Is there any new guideline information?
3. Requests for Utilization Review topics?