North Dakota Medicaid

Drug Use Review Board Meeting

June 3, 2026

HHS Hoteling Space, Room 308, State Capitol

NORTH Dakota | Health & Human Services
Be Legendary.

Meeting Notice

North Dakota Medicaid Drug Use Review Board

Wednesday, June 3, 2026
1 to 4 p.m. Central Time

In-Person Information

HHS Hoteling Space, Room 308, State Capitol
600 E. Boulevard Ave., Bismarck

Virtual Information

Join the virtual meeting
Join by phone: 701-328-0950, Conference ID 248 378 348 242 80

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

Agenda

1. Call to Order
2. Roll Call
3. Review and Approval of Minutes
4. Reports from Department
    - Administrative Report: Cost of Dispensing Survey, Website Overview
    - Financial Report: Top Drugs
    - Retrospective Drug Utilization Review (DUR) Report
    - Clinical Report:
        - Prior Authorization and Criteria Updates: Alzheimer's, Heart Failure, Imcivree, Mounjaro
5. Unfinished business
    - Aqvesme, Ozempic for Type 1 diabetes and chronic kidney disease, Leqembi renewal criteria, Sapropterin non-responsive after 1 month at 20 mg/kg
6. New business
    - Second Reviews of Acromegaly, Calcium Channel Blockers, Graft vs Host Disease, and Malaria
    - First Reviews of Familial Chylomicronemia Syndrome, Nausea and Vomiting, Thrombotic Microangiopathies (TMA)
    - Review of Retrospective DUR Criteria Recommendations
    - Provider suggestions for clinical practice education or Retrospective Drug Utilization Review (RDUR) Incremental Cost-Effectiveness Ratio (ICER) criteria
7. Announcements: Next Meeting (September 9, 2026)
8. Adjourn

Meeting Minutes

North Dakota Medicaid Drug Use Review (DUR) Board
Meeting Date: March 4, 2026
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 1:08 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, Paige Adkins, Kristen Peterson, Jessica Ziegler, Matthew Zimny
Absent: Amy Werremeyer
Quorum Present: Yes

Board Members Non-Voting:
Absent: Kathleen Traylor

Medicaid Pharmacy Department:
Present: Jeff Hostetter, Brendan Joyce, Alexi Murphy, LeNeika Roerich, Katie Steig
Absent:
Approval of Meeting Minutes:
Motion: Moved by K. Datz to approve the minutes of the December 3, 2025 meeting, motion was seconded by A. Honeyman. Motion carried.
The minutes of the December 3, 2025, meeting were approved as distributed.

Reports:
Administrative Report: A. Murphy
A.Murphy shared with the Board Core Measures, Cost of Dispensing Survey information, and did a Website Overview.

Financial Report: 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: 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: Anemia, Chronic Kidney Disease (IgA Nephropathy, C3 Glomerulopathy, Diabetic Kidney Disease), Cluster Headache, Heart Failure, Interstitial Lung Disease, Juvenile Idiopathic Arthritis, Myasthenia Gravis.

New business:

Second Reviews presented by J. McKee
J. McKee presented group prior authorization criteria for Alzheimer's Disease
Motion: Moved by M. Zimny to place Alzheimer's Disease on prior authorization, motion was seconded by K. Martian. Motion carried.

J. McKee presented group prior authorization criteria for PKU
Motion: Moved by K. Datz to place PKU on prior authorization, motion was seconded by M. Zimny. Motion carried.

J. McKee presented group prior authorization criteria for Non-Cystic Fibrosis Bronchiectasis
Motion: Moved by K. Martian to place Non-Cystic Fibrosis Bronchiectasis on prior authorization, motion was seconded by K. Datz. Motion carried.

First Reviews presented by J. McKee
J. McKee presented an overview of Acromegaly. The presented material can be found in the handout.
Motion: Moved by A. Dahl to draft prior authorization for Acromegaly, motion was seconded by M. Zimny. Motion carried.

First Reviews presented by J. McKee
J. McKee presented an overview of Calcium Channel Blockers. The presented material can be found in the handout.
Motion: Moved by K. Martian to draft prior authorization for Calcium Channel Blockers, motion was seconded by K. Datz. Motion carried.

First Reviews presented by J. McKee
J. McKee presented an overview of Graft vs Host Disease. The presented material can be found in the handout.
Motion: Moved by M. Zimny to draft prior authorization for Graft vs Host Disease, motion was seconded by K. Martian. Motion carried.

First Reviews presented by J. McKee
J. McKee presented an overview of Malara. The presented material can be found in the handout.
Motion: Moved by M. Zimny to draft prior authorization for Malaria, motion was seconded by K. Martian. 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 M. Zimny to approve the RDUR criteria, motion was seconded by K. Martian. Motion carried.

Announcements:
Next meeting is June 3, 2026.

Adjournment:
Meeting adjourned by K. Martian at 3:22 pm CST.

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

Administrative Report

Cost of Dispensing Survey Update

North Dakota Medicaid is conducting a pharmacy cost of dispensing survey. The survey results will be used to evaluate the professional dispensing fee in the North Dakota Medicaid pharmacy program. North Dakota Medicaid has engaged Myers and Stauffer LC, a national Certified Public Accounting firm with extensive experience in government healthcare and pharmacy reimbursement issues, to perform the pharmacy cost of dispensing study. The surveys were due March 31, 2026 and the deadline was extended to April 30, 2026.

Myers and Stauffer are now performing validations of surveys and preparing a report of their calculations of professional dispensing fee.

American with Disabilities Act Digital Accessibility Update

States must ensure websites, online services, and digital documents are accessible. You may see changes to state digital content.

ND HHS Non-Discrimination Policy

Discrimination means treating someone differently because of a particular characteristic such as race, color, sex, age, disability, or religion. North Dakota Department of Health and Human Services (HHS) makes available all services and assistance without regard to race, color, sex, age, disability, national origin, religion, or status with respect to marriage or public assistance.

For programs funded by the U.S. Department of Agriculture (USDA), HHS also makes services and assistance available without regard to political beliefs. These laws must be followed by persons who contract with or receive funds to provide services for HHS, including the state's eight regional Behavioral Health Clinics, the State Hospital, the Life Skills and Transition Center, and Human Service Zone offices.

The policies of HHS also require that:

- You be given the chance to apply for assistance or services, or both.
- The same eligibility standards apply to you as apply to others in similar situations.

In accordance with Federal law and North Dakota state law, HHS is prohibited from discriminating on the basis of race, color, sex, age, disability, national origin, religion, or status with respect to marriage or public assistance. In accordance with the USDA, HHS is also prohibited from discriminating against political beliefs or reprisal or retaliation for prior civil rights activity in any program or activity conducted or funded by the USDA.

Website Overview

Acentra's ND Medicaid Pharmacy Website

Acentra's DUR Board Website

NDC Drug Lookup Tool

Federal Policies and Medicaid Drug Pricing

Federal Policies:

Federal policies are creating pressure on drug pricing and focus on rare disease development.

- Affordable Care Act, 2010:
  - Changed rebate calculations and rebate amounts owed to federal government without state share (Unit Rebate Offset Amounts).
  - Line extension definitions formalized in 2020.
- American Rescue Plan Act, 2021:
  - Removed the Medicaid AMP rebate cap beginning in 2024 allowing unlimited inflationary rebates.
- Inflation Reduction Act, 2022:
  - Introduced Medicare drug price negotiations and the Maximum Fair Price (MFP) starting in 2026.
- Accelerating Rare Disease Cures (ARC) Program, 2022
  - Developed to speed and increase the development of rare disease drugs
- Most Favored Nation Executive Order, 2025
  - Linked drug prices to international reference pricing
- Section 232 Pharmaceutical Tariffs, 2026
  - Imposed tariffs on drugs
- Consolidated Appropriations Act, 2026 (PBM Reform)
  - Reduced spread pricing and rebate-driven revenue.

Manufacturers Response Effects on Medicaid:

Manufacturers are experiencing higher Medicare liability and shrinking margins and are changing their rebate strategies.

- Reduced Inflationary Rebates:
  - Wholesale cost of drugs decreases for existing drugs
  - New drugs launched at higher prices
  - Drug prices can increase by the rate of inflation without penalty
- Reduced Best Price Rebates:
  - Reduced commercial insurance rebates
  - Increased rare disease pipelines with little competition
- Decreased ability to manage high-cost drugs
  - Increased direct to consumer advertising
  - Increased shortages
  - Increased rare disease pipelines with little competition
- Reduced Medicaid supplemental rebates
  - Increased rare disease pipelines with little competition
  - Decreased rebates based on guaranteed net price

Commercial Insurances Response Effects on Medicaid:

Commercial Insurances are changing their revenue strategies away from dependence on rebates

- Shifted coverage liability to Medicaid
    - Increased premiums and deductibles
    - Narrowed formularies

Medicaid Rebate Calculations:

Brand Drugs (Except Pediatric Indications and Clotting Factors):
- Base (Statutory) Rebate: 23.1% Average Manufacturer Price (AMP)
- Best Price Rebate: If best price is > 23.1% of AMP, Base Rebate is AMP-Best Price
- Inflationary (Additional) Rebate: If a drugs AMP increases more quickly than inflation, the difference is rebated.
- Unit Rebate Offset Amount: If best price < 23.1%, the federal government gets part of the rebate equal to the difference between 15.1% and Best Price with no state share.

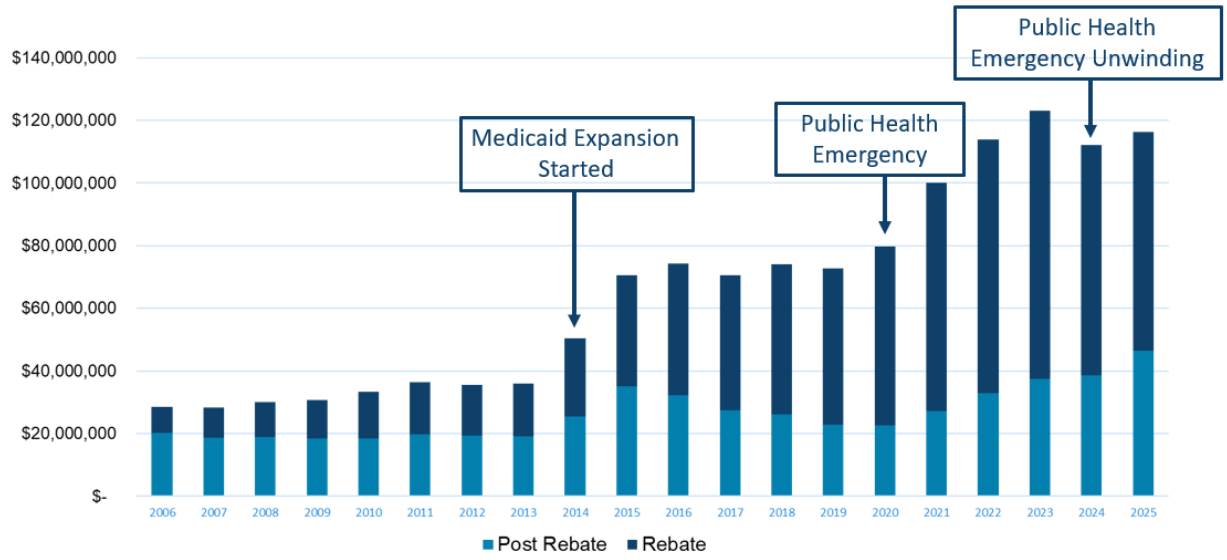
Generic Drugs:
- Base (Statutory) Rebate: 13% Average Manufacturer Price (AMP)
- Inflationary (Additional) Rebate: If a drugs AMP increases more quickly than inflation, the difference is rebated.
- Unit Rebate Offset Amount: Portion of rebate equal to 2% of AMP goes to federal government without state share.

Exclusive Pediatric Indications and Clotting Factors:
- Base (Statutory) Rebate: 17.1% Average Manufacturer Price (AMP)
- Best Price Rebate: If best price is > 17.1% of AMP, Base Rebate is AMP-Best Price
- Inflationary (Additional) Rebate: If a drugs AMP increases more quickly than inflation, the difference is rebated.
- Unit Rebate Offset Amount: If best price < 17.1%, the federal government gets the rebate difference between 15.1% and Best Price with no state share

Line Extensions:

- Additional Unit Rebate Offset Amount based on the difference in the inflationary rebate of the original drug and the standard brand drug rebate calculation.

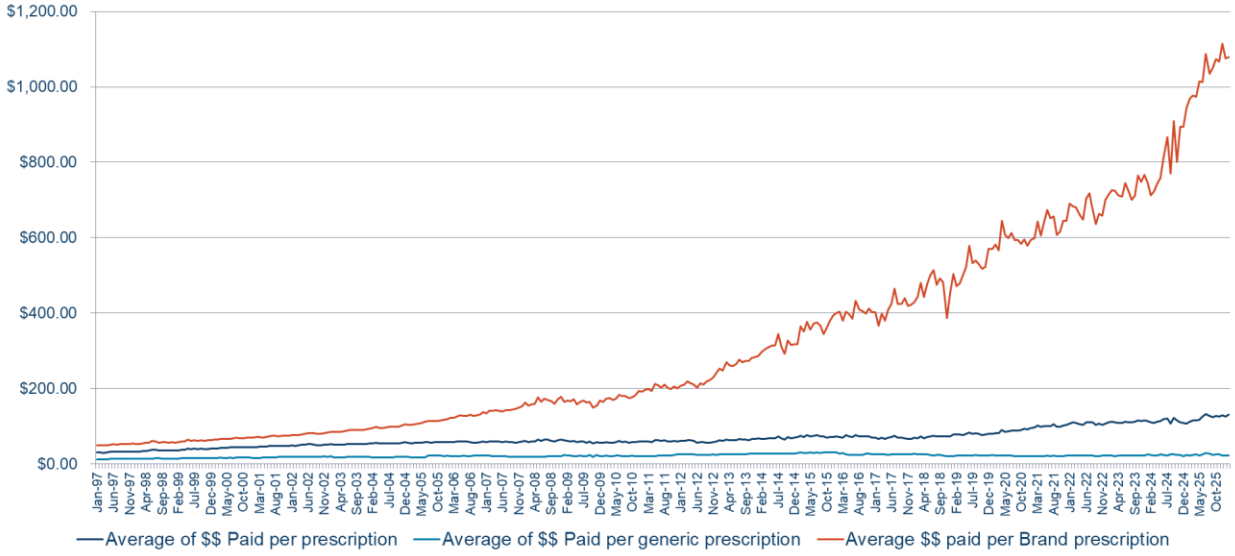
ND Medicaid Spending on Pharmacy



Detailed Description:
Bar graph showing Medicaid pharmacy spend, including post rebate spend and rebates, from 2006 to 2025. From 2006 to 2013, the bars are between $20 and $40 million. In 2014, Medicaid Expansion started and until 2020, bars are between $40 and $80 million. After the Public Health Emergency in 2020, bars increase from $80 million to over $120 million in 2023. After the Public Health Emergency unwinding, in 2024, the bars remain over $100 million.

Average Brand Name Cost

December 2015: $ 393.34 per brand prescription
December 2025: $1,115.28 per brand prescription



Detailed Description:
Line graph showing 3 lines from 1997 to 2025: average spend per prescription, average per generic prescription, and average per brand prescription. The average spend per prescription and average per generic prescription remain below $200. The average per brand increases from 2012 to 2024 from $200 to $800 and then increases sharply from $800 to over $1000 in 2025.

Top 10 Drugs - 2015

Drug Name	Use	Spend	Scripts
Abilify	Psychiatry	$4,399,281.06	6,711
Sovaldi	Hepatitis C	$3,000,307.70	104
Novolog	Diabetes	$2,426,104.64	5,443
Methylphenidate	ADHD	$2,211,005.75	17,713
Viekira Pak	Hepatitis C	$2,149,550.25	75
Harvoni	Hepatitis C	$2,032,005.70	63
Lantus	Diabetes	$1,869,289.95	4,735
Levemir	Diabetes	$1,670,580.34	3,654
Lyrica	Pain	$1,597,947.10	4,777
Vyvanse	ADHD	$1,368,432.16	7,174

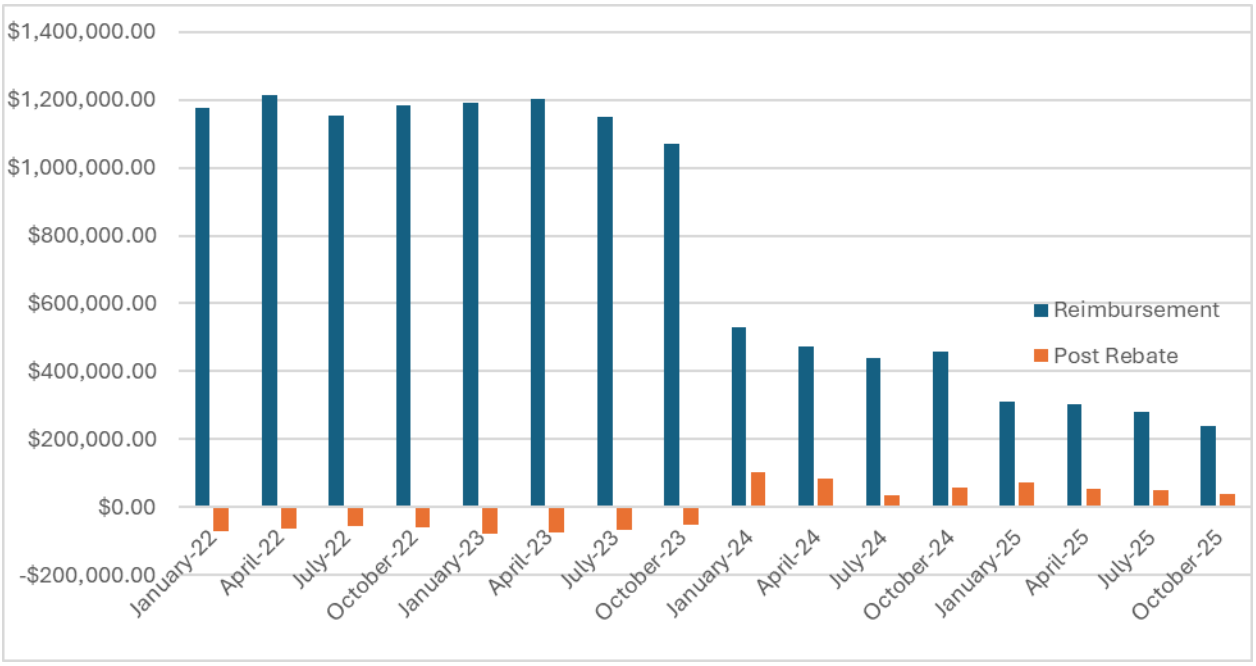
Top 10 Drugs - 2025

Drug Name	Use	Spend	Scripts
Humira	Monoclonal Antibody	$11,053,510.62	1,254
Epclusa	Hepatitis C	$4,506,732.82	199
Taltz	Monoclonal Antibody	$4,327,390.41	548
Jardiance	Diabetes	$4,092,442.64	5,817
Vyvanse	ADHD	$4,084,007.12	14,988
Vraylar	Psychiatry	$3,865,252.76	3,527
Invega	Psychiatry	$3,704,342.91	1,015
Dupixent	Monoclonal Antibody	$3,525,039.90	942
Trikafta	Cystic Fibrosis	$3,476,753.57	143
Norditropin	Growth Hormone	$3,147,395.19	442

2015
Average: $450/Rx
Total: $22,724,505 for 50,449 prescriptions

2025
Average: $1585/Rx
Total: $45,782,866 for 28,875 prescriptions

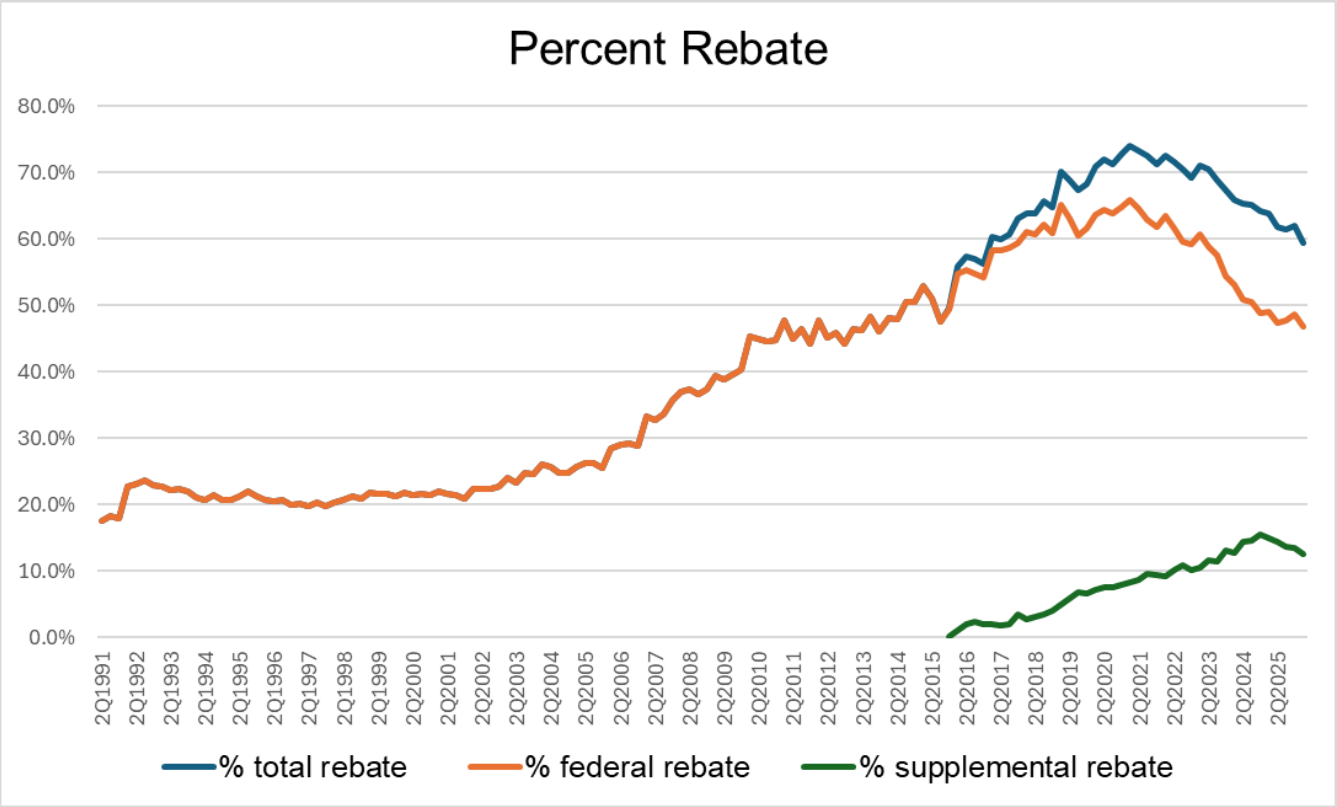
Effect of Price Decreases



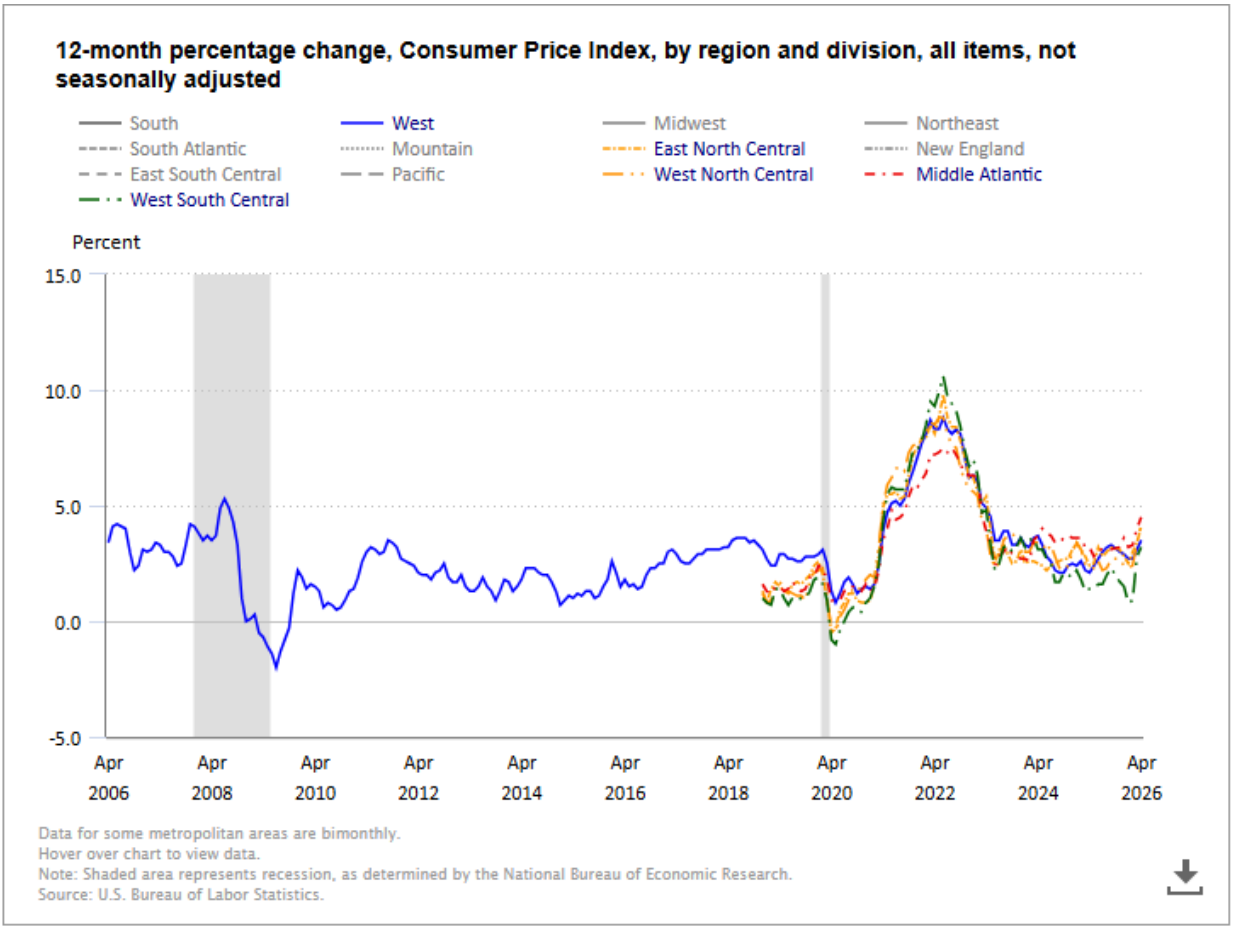
Detailed Description:
A bar chart showing reimbursement and post rebate spend from 1Q22 to 4Q25 with reimbursement dropping substantially in 1Q24 and again in 1Q25 with corresponding increases in post rebate spend.

Row Labels	Reimbursement	Post Rebate
1Q 2022	$1,176,269.18	-$69,065.59
2Q 2022	$1,212,885.87	-$64,476.21
3Q 2022	$1,152,072.41	-$57,467.34
4Q 2022	$1,184,909.85	-$60,109.45
1Q 2023	$1,190,538.19	-$77,588.74
2Q 2023	$1,200,837.44	-$74,703.84
3Q 2023	$1,148,800.91	-$65,432.02
4Q 2023	$1,071,819.30	-$51,473.83
1Q 2024	$531,224.63	$102,397.76
2Q 2024	$472,284.90	$83,499.58
3Q 2024	$439,281.66	$34,338.39
4Q 2024	$459,558.65	$58,935.99
1Q 2025	$309,457.63	$74,327.55
2Q 2025	$304,825.73	$53,761.25
3Q 2025	$281,165.61	$50,330.41
4Q 2025	$240,118.31	$40,038.59

Effect of Decreased Rebates



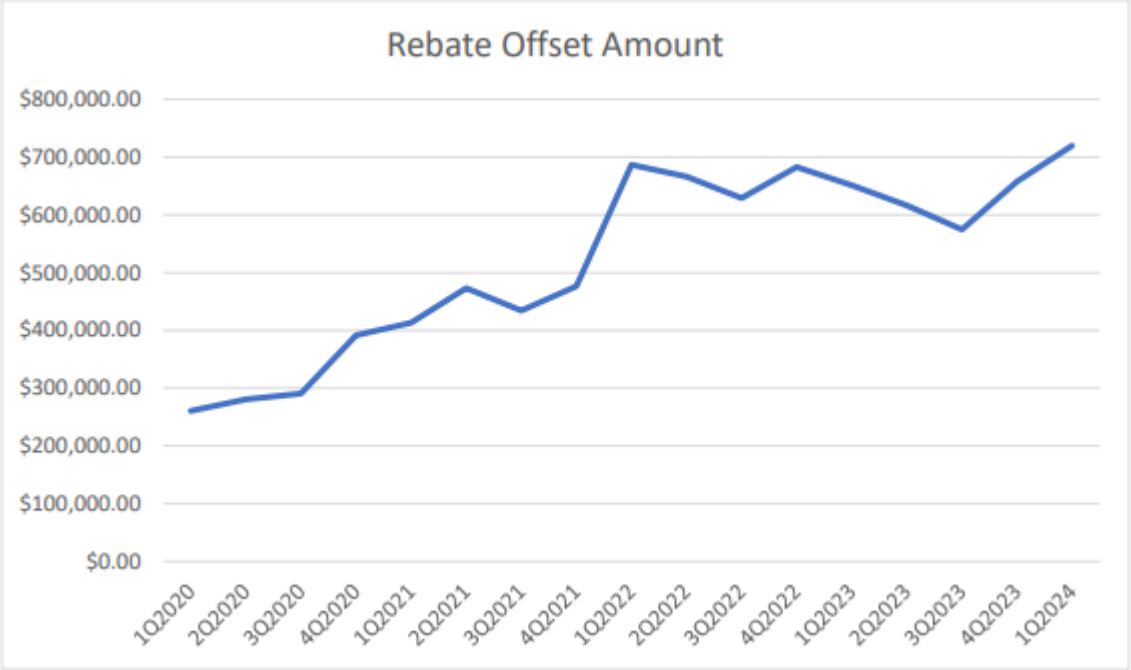
Detailed Description:
A line graph showing % total rebate, % federal rebate, and % supplemental rebate from 2Q1991 to 2Q2025. The % total and federal rebate lines overlap and are between 15% and 30% until 2007. The % total and federal rebate lines remain overlapped and increase to 50% in 2015 when supplemental rebates start. % total rebate continues to increase to 74% until 2021 when % total rebates and federal rebates start to decline. % Supplemental rebates start to decline in 2025.



Detailed Description:
Line graph showing inflation from April 2006 to April 2026. Generally the line stays between 0% and 5% except an increase to 10% in April 2022.

Effect of Rebate Offset Amount Calculations (Affordable Care Act, 2010)

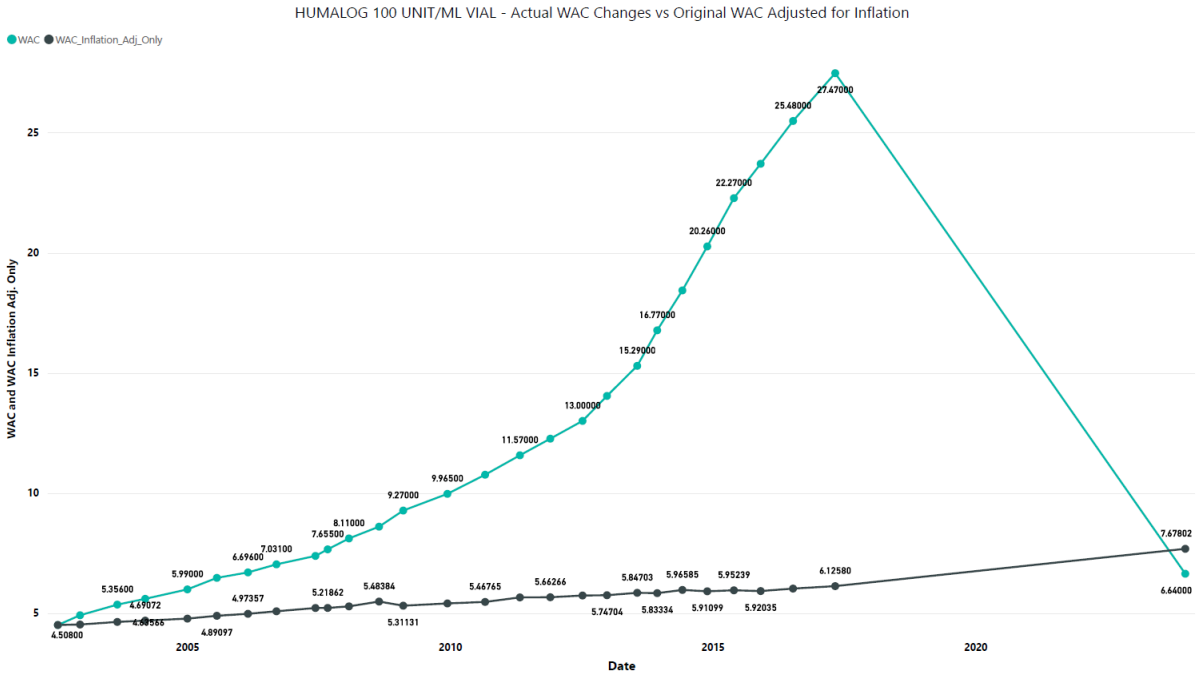
Line extension definitions formalized in 2020



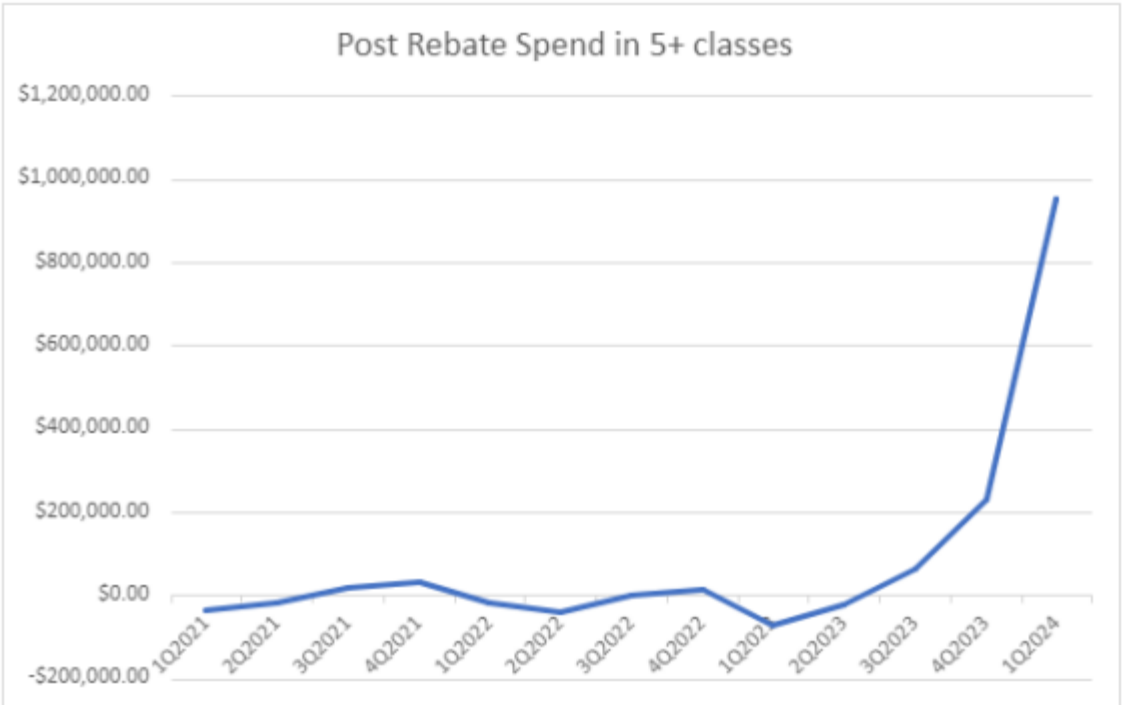
Detailed Description:
A line graph showing an increase in Rebate Offset Amount from $250,000 per quarter in 1Q20 to over $700,000 in 1Q24.

Effect of AMP Cap Removal
(American Rescue Plan Act, 2021)

Manufacturers dropped their price to below the level that triggers an inflationary rebate



Detailed Description:
A graph showing Humalog increasing price since launch and then sharply decreasing price to below the base price adjusted only by the factor of inflation.

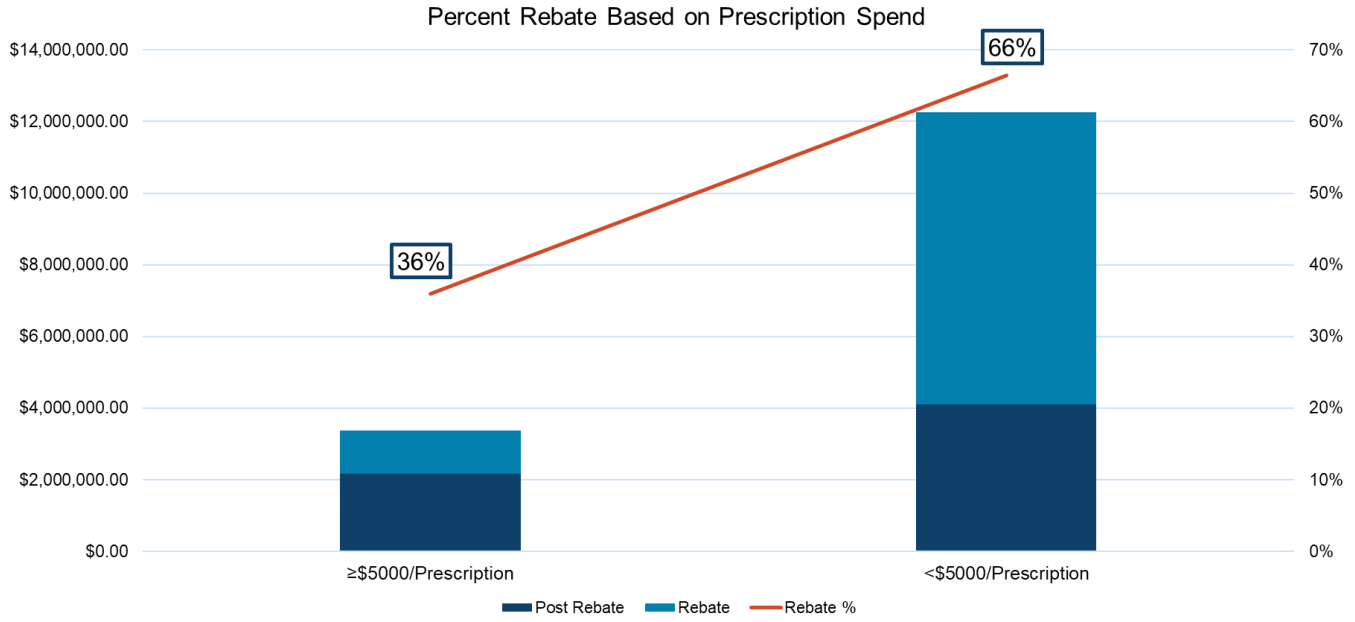


Detailed Description:
A line graph showing post rebate spend in 5 classes that was near or less than zero until sharply increasing to almost $1 million per quarter in 1Q24.

Effect of Increased Use of High-Cost Drugs (Accelerating Rare Disease Cures (ARC) Program, 2022)

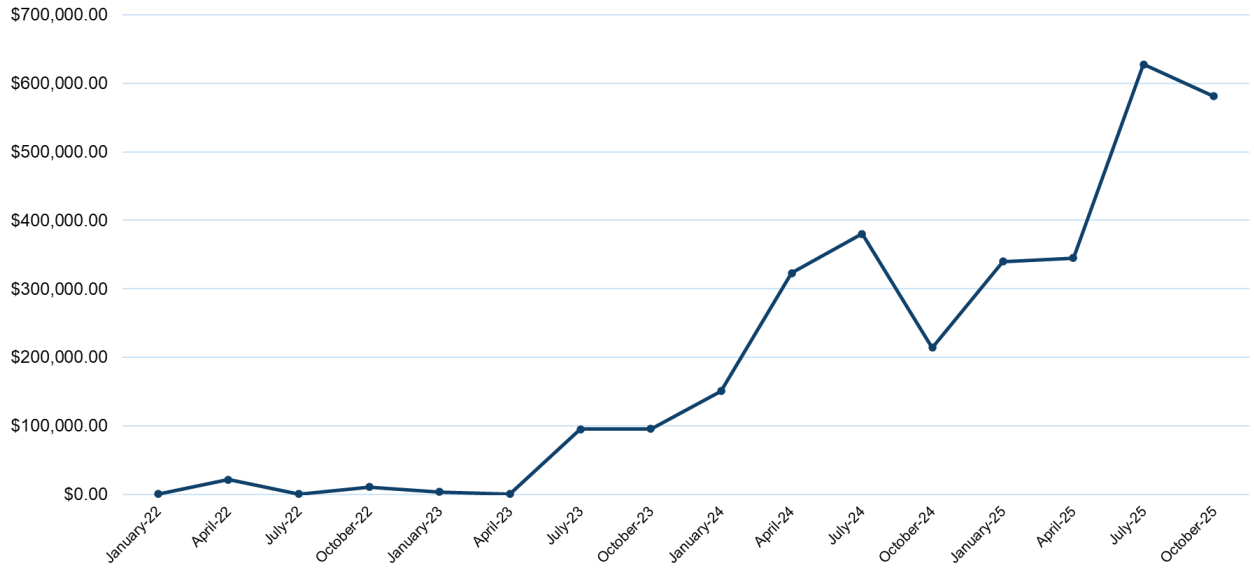
In 4Q25, only 4% (34 drugs) exceeded $5,000 per prescription and:

- accounted for 34% of net spend after rebates ($2.16 million)
- treated 85 people (0.1% of 80,006 eligible for traditional Medicaid)



Detailed Description:
A graph with the left axis showing dollars and the right axis showing percentage. There are two values on the x axis, $5000 per prescription and greater and less than $5000 per prescription. The $5000 per prescription and greater value shows post rebate spend at $2 million, total spend less than $4 million, and rebate percentage at 36%. The less than $5000 per prescription value shows post rebate spend at $4 million, total spend over $12 million and rebate % at 66%.

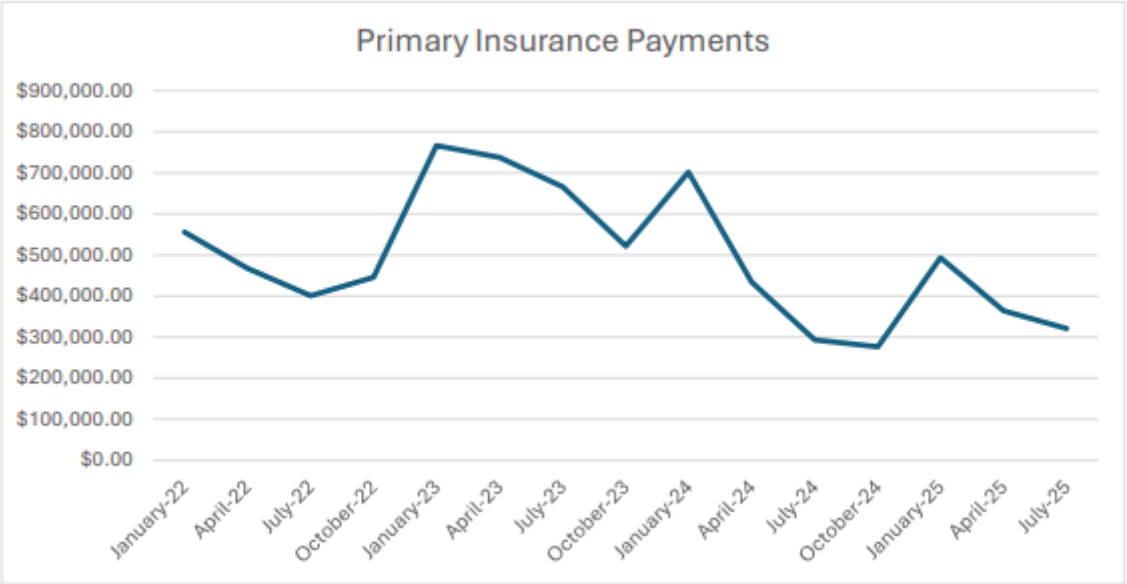
(Traditional Medicaid Per Quarter – 6 drugs)



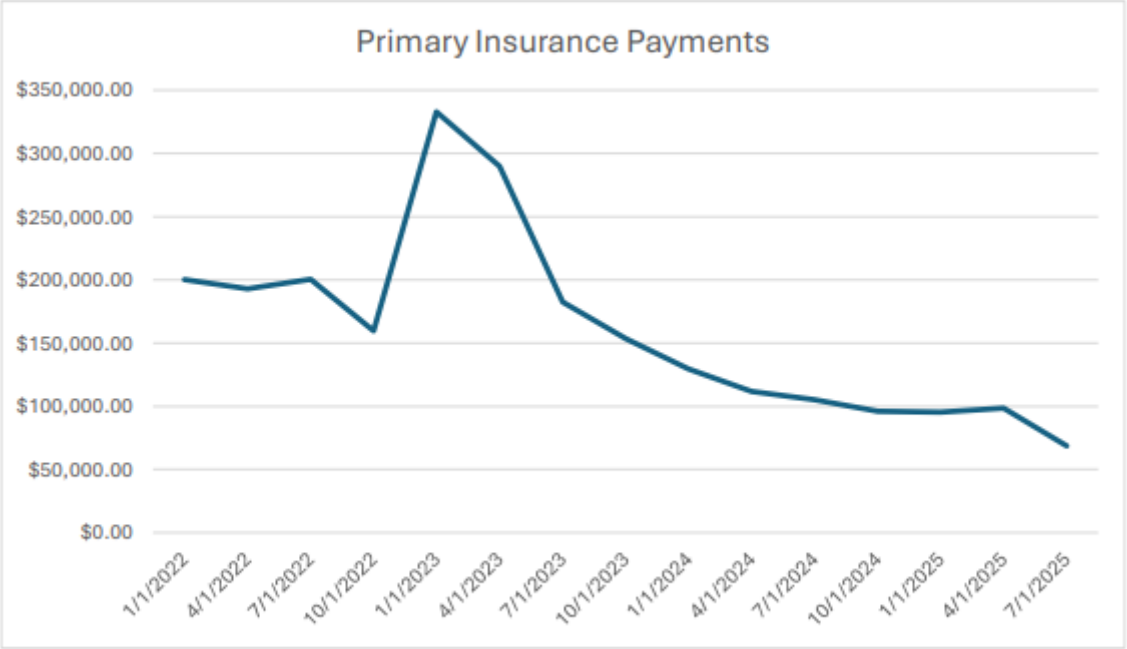
Detailed Description:
A line graph showing near zero spend until 2Q23 where it increases to around $600,000 per quarter in 4Q25.

Effect of Decreased Insurance Payments

Traditional Medicaid



Expansion Medicaid



Detailed Description:
Two graphs showing decreasing amounts of primary insurance payments in traditional and expansion Medicaid from 1Q22 to 3Q25. Traditional Medicaid starts at $555,000 and ends at $300,000. Expansion Medicaid starts at $200,000 and ends at $75,000.

Top 25 Drugs Based on Total Claims Cost from 1/1/26 – 3/31/26

Total Claims Cost - $17,146,380.21

#	Drug Name	Claims	Claims Cost	Patients	Cost/Patient	% Cost	Dif
1	HUMIRA	267	$2,342,597.65	112	$20,916.05	5.86%	NC
2	OZEMPIC	1712	$1,692,861.06	817	$2,072.05	4.23%	↑4
3	SOFOSBUVIR-VELPATASVIR	50	$1,168,621.96	50	$23,372.44	2.92%	↑5
4	VYVANSE	3542	$1,071,806.59	1420	$754.79	2.68%	↓2
5	DUPIXENT	264	$1,034,946.89	121	$8,553.28	2.59%	↑5
6	VRAYLAR	858	$1,024,205.28	350	$2,926.30	2.56%	↓1
7	TALTZ	125	$1,003,737.30	51	$19,681.12	2.51%	↓4
8	TRIKAFTA	32	$783,063.29	12	$65,255.27	1.96%	↓1
9	BIKTARVY	347	$732,911.86	168	$4,362.57	1.83%	↑2
10	NORDITROPIN	110	$728,487.94	46	$15,836.69	1.82%	NC
11	INVEGA SUSTENNA	195	$564,455.03	78	$7,236.60	1.41%	↑3
12	JARDIANCE	1213	$559,056.11	645	$866.75	1.40%	↓8
13	COSENTYX	49	$484,262.27	23	$21,054.88	1.21%	↓1
14	BIMZELX	27	$452,453.34	13	$34,804.10	1.13%	↓1
15	DULERA	1324	$446,222.65	937	$476.22	1.12%	↑5
16	INGREZZA	50	$408,209.86	21	$19,438.56	1.02%	NC
17	SUBLOCADE	158	$347,928.22	89	$3,909.31	0.87%	NC
18	ENBREL	39	$330,368.35	19	$17,387.81	0.83%	NC
19	VICTOZA	456	$311,006.08	263	$1,182.53	0.78%	↑13
20	KESIMPTA PEN	30	$309,104.83	11	$28,100.44	0.77%	↑3
21	ABILIFY MAINTENA	115	$307,308.18	43	$7,146.70	0.77%	↓2
22	ELIQUIS	719	$292,388.53	353	$828.30	0.73%	↓7
23	VERZENIO	15	$258,855.30	6	$43,142.55	0.65%	↑3
24	INSULIN LISPRO	1008	$251,720.88	612	$411.31	0.63%	↓2
25	OXERVATE	4	$239,800.76	1	$239,800.76	0.60%	N/A

Top 25 Drugs Based on Number of Claims from 1/1/26 – 3/31/26

Total Number of Claims - 72,687

#	Drug Name	Claims	Claims Cost	Patients	Cost/Claim	% Claims	Dif
1	GABAPENTIN	4340	$64,771.48	1838	$14.92	1.71%	NC
2	AMOXICILLIN	3760	$58,414.07	3505	$15.54	1.49%	↑4
3	TRAZODONE	3754	$49,761.72	2012	$13.26	1.48%	NC
4	SERTRALINE	3737	$51,235.12	2105	$13.71	1.48%	↓2
5	VYVANSE	3542	$1,071,806.59	1420	$302.60	1.40%	NC
6	FLUOXETINE	3372	$44,873.39	1880	$13.31	1.33%	↓2
7	ESCITALOPRAM	3249	$43,157.02	1873	$13.28	1.28%	NC
8	CLONIDINE	3079	$37,352.00	1563	$12.13	1.22%	NC
9	HYDROXYZINE	2958	$40,527.38	1805	$13.70	1.17%	↑4
10	VENTOLIN HFA	2835	$184,948.25	2807	$65.24	1.12%	↓1
11	LEVOTHYROXINE	2819	$39,666.52	1539	$14.07	1.11%	↓1
12	BUPROPION XL	2792	$45,978.99	1590	$16.47	1.10%	NC
13	OMEPRAZOLE	2784	$38,364.03	1752	$13.78	1.10%	↓2
14	METHYLPHENIDATE ER	2717	$76,326.30	1129	$28.09	1.07%	↑1
15	ONDANSETRON ODT	2687	$41,177.65	2109	$15.32	1.06%	↑5
16	AMOXICILLIN-CLAV	2676	$45,927.19	2491	$17.16	1.06%	↑2
17	DEXTROAMP-AMPH ER	2623	$71,517.22	1101	$27.27	1.04%	↓1
18	PREDNISONE	2617	$30,020.45	2121	$11.47	1.03%	↓1
19	ATORVASTATIN	2516	$35,865.07	1529	$14.25	0.99%	↓5
20	LAMOTRIGINE	2360	$32,352.26	985	$13.71	0.93%	↑2
21	PANTOPRAZOLE	2329	$33,699.83	1401	$14.47	0.92%	↓1
22	GUANFACINE HCL ER	2324	$32,083.12	904	$13.81	0.92%	↑5
23	ARIPIPRAZOLE	2285	$34,139.54	1132	$14.94	0.90%	↑1
24	LISINOPRIL	2277	$31,744.07	1456	$13.94	0.90%	↓5
25	BUSPIRONE	2255	$34,594.15	1201	$15.34	0.89%	↓2

Top 15 Therapeutic Classes Based on Number of Claims from 1/1/26 – 3/31/26

Total Number of Claims = 112,870

#	Therapeutic Class Description	Claims	Claims Cost	Patients	Cost/Claim	% Claims	Dif
1	ANTIDEPRESSANTS	25777	$677,715.83	10974	$26.29	10.18%	NC
2	ANTIPSYCHOTICS	9996	$3,151,643.99	4086	$315.29	3.95%	NC
3	AMPHETAMINES	7917	$1,198,403.35	3200	$151.37	3.13%	NC
4	RESPIRATORY AND CNS STIMULANTS	7325	$337,710.20	2841	$46.10	2.89%	NC
5	GABA-MEDIATED ANTICONVULSANTS	6799	$146,214.51	2807	$21.51	2.69%	NC
6	PENICILLIN ANTIBIOTICS	6695	$108,707.19	5889	$16.24	2.64%	↑1
7	CENTRAL ALPHA-AGONISTS	6114	$84,895.30	2755	$13.89	2.42%	↑2
8	BETA-ADRENERGIC AGONISTS	5890	$792,389.71	4204	$134.53	2.33%	↓2
9	NSAIDS	5592	$77,398.32	3857	$13.84	2.21%	↑1
10	OPIOID AGONISTS	5564	$109,227.40	2845	$19.63	2.20%	↓2
11	PROTON-PUMP INHIBITORS	5527	$100,966.02	3316	$18.27	2.18%	NC
12	ANTICONVULSANTS	5105	$369,556.95	2095	$72.39	2.02%	↑1
13	ADRENALS	5105	$166,182.46	3794	$32.55	2.02%	↓1
14	STATINS	4751	$68,573.37	2917	$14.43	1.88%	↑1
15	BETA-BLOCKERS	4713	$79,326.47	2722	$16.83	1.86%	↓1

Top 15 Therapeutic Classes Based on Claims Cost from 1/1/26 – 3/31/26

Total Claims Cost = $21,157,789.54

#	Therapeutic Class Description	Claims	Claims Cost	Patients	Cost/Patient	% Cost	Dif
1	ANTIPSYCHOTIC	9996	$3,151,643.99	4,086	$771.33	7.88%	↑1
2	TNF INHIBITORS	432	$3,030,087.56	183	$16,557.86	7.58%	↓1
3	INCRETIN MIMETICS	2322	$2,136,773.53	1,068	$2,000.72	5.34%	↑2
4	ANTINEOPLASTIC AGENTS	610	$1,759,962.07	254	$6,928.98	4.40%	↓1
5	INTERLEUKIN-MEDIATED AGENTS	204	$1,621,299.34	91	$17,816.48	4.05%	↓1
6	HCV ANTIVIRALS	52	$1,200,328.32	51	$23,535.85	3.00%	↑5
7	AMPHETAMINES	7917	$1,198,403.35	3,200	$374.50	3.00%	NC
8	ANTIRETROVIRALS	782	$1,191,291.55	304	$3,918.72	2.98%	↑2
9	SKIN AGENTS	288	$1,036,372.71	141	$7,350.16	2.59%	↑3
10	IMMUNOMODULATORY AGENTS	241	$923,359.16	191	$4,834.34	2.31%	↓2
11	CFTR CORRECTORS	38	$916,238.52	15	$61,082.57	2.29%	↓2
12	BETA-ADRENERGIC AGONISTS	5890	$792,389.71	4,204	$188.48	1.98%	↑1
13	PITUITARY	376	$765,083.12	157	$4,873.14	1.91%	↑1
14	SGLT2 INHIBITORS	1600	$756,840.78	854	$886.23	1.89%	↓8
15	ANTIDEPRESSANTS	25777	$677,715.83	10,974	$61.76	1.69%	NC

RDUR Report: Q1 2026

Date	Total Criteria Exceptions	Total Cases	Letters Sent
January 2026	425	243	540
February 2026	0	0	800
March 2026	440	233	544

January 2026 Cases by Type of Criteria

Criteria Description	# of Cases	% of Cases
Drug Disease Precaution	112	46.09%
Drug-Drug Marker and/or Diagnosis	82	33.74%
Drug-Drug Interactions	47	19.34%
Therapeutic Appropriateness	2	0.82%

March 2026 Cases by Type of Criteria

Criteria Description	# of Cases	% of Cases
Drug Disease Precaution	123	48.62%
Underutilization	76	30.04%
Drug-drug Interactions	24	9.49%
Therapeutic Appropriateness	20	7.91%
Drug-Drug Marker and/or Diagnosis	9	3.56%
High Dose Alert	1	0.40%

February 2026 Special Mailing

800 Letters Sent

Dear Prescriber,

SUBJECT: Required Prescription Drug Monitoring Program (PDMP) Use for ND Medicaid

In accordance with the SUPPORT ACT under Section 5042, Medicaid providers are required to assess prescription drug history from a qualified PDMP before prescribing controlled substances to Medicaid members. Exclusions to this requirement include prescriptions written for members:

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

ACTION REQUIRED: Please respond to the attached questionnaire regarding your use of the PDMP for the period of October 1, 2024 through September 30, 2025, and fax to 866-798-4904.

State Medicaid programs must report provider PDMP usage to CMS annually. A recent review of claims data indicated that you have written a controlled substance prescription for a Medicaid member during this timeframe. If there appears to be an error in this information, please note the discrepancy on the questionnaire. Thank you for your professional consideration.

Sincerely,

ND Medicaid

References:

1. Library of Congress. H.R. 6—SUPPORT for Patients and Communities Act, 115th Congress (2017–2018). Congress.gov. Published 2017. Accessed January 27, 2026. https://www.congress.gov/bill/115th-congress/house-bill/6/text
2. US Department of Health and Human Services. Frequently asked questions: SUPPORT for Patients and Communities Act, Section 5042—Medicaid PARTNERSHIP Act. Centers for Medicare & Medicaid Services website. Published May 15, 2019. Accessed January 27, 2026. https://www.hhs.gov/guidance/sites/default/files/hhs-guidance-documents/faq051519_199.pdf

Clinical Report

Prior Authorization Updates

Drug	PA Status	Class
Atmeksi	PA	Muscle Relaxants
Avtozma	PA	Biosimilars
Contepo	PA	Urinary Tract Infections
Desmoda	PA	Non-preferred Dosage Forms
Forzinity	PA	Medications that cost > $3000
Icotyde	PA	Plaque Psoriasis
ivabradine	Remove PA	Heart Failure
Kygevvi	PA	Medications that cost > $3000
Lerochol	PA	Lipid-Lowering Agents
Nypozi	PA	Biosimilars
Orladeyo Pellet	PA	Hereditary Angioedema
Palsonify	PA	Medications that cost > $3000
Qivigy	PA	Immune Globulins
Relgaabi	PA	Non-preferred Dosage Forms
Sephience	PA	Phenylketonuria
tapentadol	PA	Opioid Analgesic
tapentadol ER	PA	Opioid Analgesic
Tonmya	PA	Muscle Relaxants
Yuvezzi	PA	Presbyopia
Zelvysia	PA	Phenylketonuria

Summary of Changes

Alzheimer's Disease

After the discussion at the previous meeting, the Therapeutic Duplication section has been divided to add a Drug-Drug Interaction section to better explain the effects of both types of medications and why they are not covered together. Not residing in skilled nursing care criteria has been limited to extended-release medications.

Solid Dosage Forms

Cholinesterase Inhibitors

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
donepezil 5 mg, 10 mg tablet	ARICEPT (donepezil)
galantamine tablet	donepezil 23 mg tablet
galantamine ER	donepezil ODT
rivastigmine capsule	RAZADYNE (galantamine)
this space intentionally left blank	RAZADYNE ER (galantamine)
this space intentionally left blank	ZUNVEYL (benzgalantamine)

Non-Solid Dosage Forms

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
EXELON (rivastigmine) PATCH – *Brand Required*	ADLARITY (donepezil) PATCH
this space intentionally left blank	galantamine oral solution
this space intentionally left blank	rivastigmine patch

NMDA Receptor Antagonists

Solid Dosage Forms

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
memantine	NAMENDA (memantine)

Non-Solid Dosage Forms

PREFERRED AGENTS (PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
memantine ER capsule sprinkle	memantine oral solution
this space intentionally left blank	NAMENDA XR (memantine) CAPSULE SPRINKLE

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
this space intentionally left blank	memantine/donepezil
this space intentionally left blank	NAMZARIC (memantine/donepezil)

Cholinesterase Inhibitors / NMDA Receptor Antagonist Combinations

Therapeutic Duplication

- One memantine medication is allowed at a time

Drug-Drug Interaction

- Anticholinergic medications are not covered with acetylcholinesterase inhibitors (e.g., donepezil, rivastigmine, galantamine, benzgalantamine).
  - The effects of an anticholinergic (blocks the effect of acetylcholine) and acetylcholinesterase inhibitors (prevents breakdown of acetylcholine) oppose each other, and the therapeutic effect of both products is diminished.

Electronic Diagnosis Verification

- Memantine: Pharmacy must submit prescriber supplied diagnosis with the claim at point of sale

Electronic Age Verification

- Submit chart notes to verify diagnosis for members less than 30 years old

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months

- The member must have failed a 30-day trial of a pharmaceutically equivalent preferred agent, as evidenced by paid claims or pharmacy printouts.
- Zunveyl Only:
  - The member must have experienced gastrointestinal side effects with galantamine (lasting longer than 6 days after dose increase) that were unable to be mitigated despite gradual titration, adequate fluid intake, and being taken with meals.
  - Clinical justification must be provided explaining why the member is unable to use another preferred products (subject to clinical review).
- Donepezil 23 mg Only:
  - Clinical justification must be provided explaining why the member is unable to use the preferred products (subject to clinical review).
  - The member must not reside in facility where medications are managed such as skilled nursing care.
- Extended release and non-solid dosage forms:
  - The member must not reside in facility where medications are managed such as skilled nursing care.
- Non-solid dosage forms: Must meet Non-Solid Dosage Forms criteria

Heart Failure

A step was added for second line agents: generic ivabradine is now preferred with no PA required. PA criteria was also added for ivabradine oral solution, which is now preferred, but PA is required.

Solid Dosage Forms

First Line Agents

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
ACE (angiotensin-converting enzyme) inhibitors – *all oral agents preferred*	dapagliflozin
ARBs (angiotensin receptor blockers) – *all oral agents preferred*	ENTRESTO (sacubitril/valsartan)
Beta blockers – *all oral agents preferred*	INPEFA (sotagliflozin)
Diuretics	SAMSCA (tolvaptan)
FARXIGA (dapagliflozin) – *Brand Required*	tolvaptan
JARDIANCE (empagliflozin)	this space intentionally left blank
sacubitril/valsartan	this space intentionally left blank

Second Line Agents

PREFERRED AGENTS (NO PA REQUIRED)	PREFERRED AGENTS (PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
ivabradine tablet	ivabradine oral solution	CORLANOR (ivabradine)
this space intentionally left blank	KERENDIA (finerenone)	this space intentionally left blank
this space intentionally left blank	VERQUVO (vericiguat)	this space intentionally left blank

Non-Solid Dosage Forms

First Line Agents

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
enalapril oral solution	ENTRESTO (sacubitril/valsartan) SPRINKLE
this space intentionally left blank	EPANED (enalapril) SOLUTION

Electronic Diagnosis Verification

- Ivabradine, Entresto, and Verquvo: Pharmacy must submit prescriber supplied diagnosis with the claim at point of sale.

Electronic Duration Verification:

- tolvaptan is payable for 30 days every year.

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months

- Ivabradine Only (oral solution only):
  - The requested medication must be prescribed by, or in consult with, a cardiologist.

- The member's heart rate must not be determined exclusively by a pacemaker
- The member has a diagnosis of heart failure with left ventricular ejection fraction of ≤ 45%
- For members 6 years old and older: The member must have a resting HR ≥ 70 beats per minute despite a 30-day trial of each of the following on maximally tolerated or target beta blocker dose in sinus rhythm, as evidenced by paid claims or pharmacy printouts:
  - Metoprolol
  - Bisoprolol
  - Carvedilol
- For children less than 18 years old: The member must have a resting HR per minute as indicated below despite a 30-day trial of a maximally tolerated or target beta blocker dose in sinus rhythm, as evidenced by paid claims or pharmacy printouts:
  - HR ≥ 105 bpm in the age-subset 6–12 months.
  - HR ≥ 95 bpm in the age-subset 1–3 years.
  - HR ≥ 75 bpm in the age-subset 3–5 years

- Entresto Sprinkle
  - See Non-Solid Dosage Form criteria
  - The member has a diagnosis of heart failure with left ventricular ejection fraction of ≤ 45 %
  - The member has failed a 3-month trial of enalapril, as evidenced by paid claims or pharmacy printouts and a NT-proBNP that failed to decrease by 60%.
- Inpefa Only:
  - The requested medication must be prescribed by, or in consult with, a cardiologist or nephrologist.
  - The member is receiving concurrent Entresto, a beta-blocker, and a mineralocorticoid receptor antagonist as evidenced by paid claims or pharmacy printouts.
  - The member must have diabetes type 2, and must not have diabetes type 1
  - The member has failed 30-day trials of dapagliflozin and empagliflozin, as evidenced by paid claims or pharmacy printouts. Failure is defined by being admitted to the hospital, a heart failure unit, infusion center, or emergency department for worsening heart failure within the past 3 months.
- Kerendia Only:
  - The requested medication must be prescribed by, or in consult with, a cardiologist.
  - The member has a diagnosis of heart failure with left ventricular ejection fraction of ≥ 40%
  - The member has been admitted to the hospital, a heart failure unit, infusion center, or emergency department for worsening heart failure within the past 3 months despite 2-month trials each of spironolactone and eplerenone in combination with a SLGT-2 inhibitor (and a GLP-1 agonist if BMI is > 30 kg/m^2), as evidenced by paid claims or pharmacy printouts.
- Tolvaptan Only:
  - The requested medication must be prescribed by, or in consult with, a cardiologist
  - The member is experiencing sodium levels less than 120 mEq/L despite a 30-day trial of an ACE inhibitors or ARBs in combination with a loop diuretic, as evidenced by paid claims or pharmacy printouts.
  - The member does not have liver disease.
- Verquvo Only:
  - The requested medication must be prescribed by, or in consult with, a cardiologist.

- The member must have left ventricular ejection fraction (LVEF) < 45% at initiation.
- The member must have had a hospitalization or need for IV diuretics within the past 3 months despite 2-month trial of Entresto, a beta-blocker, a SGLT-2 Inhibitor, a mineralocorticoid receptor antagonist, and vasodilator therapy (e.g., isosorbide and hydralazine or amlodipine)

Imcivree

A new indication for hypothalamic obesity was added to PA criteria and to renewal criteria.

PA REQUIRED
IMCIVREE (setmelanotide)

Prior Authorization Criteria

Initial Criteria – Approval Duration: 4 months (6 months for Bardet-Bidel syndrome)

- The member must have a diagnosis of obesity (BMI > 30 kg/m2 for adults or > 95th percentile using growth chart assessments for pediatric members)
- The member's weight and body mass index (BMI) must be provided within the last 60 days.
- The requested medication must be prescribed by, or in consult with, endocrinologist or medical geneticist.
- The member's obesity must be due to one of the following:
- Genetic testing confirms one of the following variants that is pathogenic, likely pathogenic, or of unknown significance:
    - Proopiomelanocortin (POMC) deficiency
    - Proprotein convertase subtilisin/kexin type 1 (PCSK1) deficiency
    - Leptin receptor (LEPR) deficiency
  - Bardet-Biedl syndrome as evidenced by three or more of the following:
    - Rod-cone dystrophy
    - Polydactyly
    - Genital anomalies
    - Renal anomalies
    - Intellectual impairment
  - Hypothalamic obesity due to injury to the ventromedial or paraventricular region of the hypothalamus or the amygdala.

Renewal Criteria – Approval Duration: 12 months

For Bardet-Biedl Syndrome

- One of the following must be met since starting treatment with Imcivree:
  - Members ≥ 18 years old:
    - First renewal – a weight reduction has been achieved or maintained.
    - Subsequent renewal – a 5% weight reduction has been achieved or maintained.
  - Members < 18 years old:
    - First renewal – a weight reduction has been achieved or maintained.
    - Subsequent renewal - a 5% reduction in BMI has been achieved or maintained.

For POMC, PCSK1, or LEPR deficiency and Hypothalamic obesity

- One of the following must be met since starting treatment with Imcivree:
  - Members ≥ 18 years old:
    - First renewal – a 5% weight reduction has been achieved or maintained.
    - Subsequent renewal – a 10% weight reduction has been achieved or maintained.
  - Members < 18 years old: a 5% reduction in BMI has been achieved or maintained.

Mounjaro

An adjustment was made to the criteria requirements to meet triple therapy. If Ozempic cannot be tolerated for triple therapy, liraglutide, Rybelsus, and Trulicity must also be trialed along with metformin and SGLT-2 inhibitor or insulin before Mounjaro will be approved.

PA REQUIRED
MOUNJARO (tirzepatide)

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months

- One of the following is met (A or B):
  - The member meets both of the following (1 and 2):
    1. The member has been unable to achieve goal, defined as meeting either A1C (≤ 7%) or TIR (>70%), despite a 90-day trial of triple combination therapy consisting of Ozempic injection (liraglutide, Rybelsus, and Trulicity must be trialed if Ozempic is not tolerated), along with metformin, SGLT-2 inhibitor or insulin, as evidenced by paid claims or pharmacy printouts (subject to clinical review).
       - If triple therapy cannot be met with liraglutide, Ozempic, Rybelsus, or Trulicity, 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*)
    2. 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 GLP-1 agonist, 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, chart documentation must be submitted that the following approaches have been trialed for at least two months:
  - Dietary changes (e.g., eating apples, crackers, or mint- or ginger based drinks 30 minutes after administering the GLP-1 Receptor Agonist)
  - Reduction in meal size, eating slower, decreased intake of greasy, high-fat or spicy food, refrain from laying down after eating.

- Prescription antiemetics
- Dose adjustment of GLP-1 Receptor Agonist

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

Second Review

Acromegaly

PREFERRED AGENTS (NO PA REQUIRED)	PREFERRED AGENTS (PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
bromocriptine capsule	SOMAVERT (pegvisomant) INJECTION	BYNFEZIA (octreotide) PEN
lanreotide injection – *Medical Billing*	this space intentionally left blank	MYCAPSSA (octreotide) CAPSULE
octreotide injection	this space intentionally left blank	PALSONIFY (paltusotine) TABLET
octreotide depot injection – *Medical Billing*	this space intentionally left blank	SANDOSTATIN (octreotide) INJECTION
SIGNIFOR (pasireotide) INJECTION	this space intentionally left blank	SANDOSTATIN (octreotide) DEPOT – *Medical Billing*
this space intentionally left blank	this space intentionally left blank	SOMATULINE (lanreotide) DEPOT – *Medical Billing*

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, an endocrinologist and/or a neurosurgeon.
- Baseline IGF-1 and GH levels must be submitted
- The member must have had one or more of the following:
  - An inadequate response to surgery
  - An inadequate response to radiation therapy
  - Surgery or radiation therapy is not appropriate for the member, subject to clinical review
- The member must have failed a 3-month trial of octreotide or lanreotide, as evidenced by paid claims or printouts

Bynfezia and Mycapssa Only:

- The member must have failed a 3-month trial of both octreotide AND lanreotide, as evidenced by paid claims or printouts

Palsonify Only:

- The member must have failed a 3-month trial of each preferred and non-preferred agent of a unique ingredient, as evidenced by paid claims or printouts

Renewal Criteria – Approval Duration: 12 months

- The member must have experienced one of the following:
  - Serum IGF-1 concentration ≤ 1.0 x ULN for the member's age and gender

- Serum GH concentration ≤ 1 mcg/L

Calcium Channel Blockers

Solid oral dosage forms

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
amlodipine	diltiazem 12HR ER capsule
CARTIA XT (diltiazem) capsule	diltiazem ER(LA) tablet
diltiazem tablet	levamlodipine tablet
diltiazem ER(CD) capsule	isradipine capsule
diltiazem ER(XR) capsule	MATZIM LA (diltiazem) ER tablet
DILT-XR (diltiazem) capsule	nicardipine capsule
felodipine ER	nisoldipine ER
nifedipine	NORVASC (amlodipine)
nifedipine ER	PROCARDIA XL (nifedipine)
nimodipine capsule	SULAR ER (nisoldipine)
TIADYLT ER (diltiazem)	verapamil ER PM
verapamil tablet	this space intentionally left blank
verapamil ER/SR capsule	this space intentionally left blank
verapamil ER tablet	this space intentionally left blank

Non-solid oral dosage forms

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
NORLIQVA (amlodipine) SOLUTION	KATERZIA (amlodipine) SUSPENSION
nimodipine solution – *PA required for non-solid dosage form*	NYMALIZE (nimodipine) SOLUTION

Prior Authorization Criteria

- The member must meet FDA-approved label for use (e.g., use outside of studied population will be considered investigational)
- The member must have failed a 30-day trial of each preferred medication of the same subtype (e.g., dihydropyridine, non-dihydropyridine), as evidenced by paid claims or pharmacy printouts.
- Clinical justification must be provided explaining why the member is unable to use the preferred agents (subject to clinical review).

Electronic Diagnosis Verification

- Nimodipine: Pharmacy must submit prescriber supplied diagnosis with the claim at point of sale

Graft vs Host Disease

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
JAKAFI (ruxolitinib)	REZUROCK (belumosudil)

JAKAFI XR (ruxolitinib ER)	NIKTIMVO (axatilimab-csfr) – *Medical Billing*

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, an oncologist
- The member must have life expectancy > 6 months
- The member must have failed a 3-month trial of Jakafi WITH concurrent corticosteroids or corticosteroid taper following NCCN treatment guidelines
- Request must include all affected organs or sites of involvement and current scoring per Chronic GVHD: Grading in the NCCN guidelines

Renewal Criteria – Approval Duration: 12 months

- The member must have experienced improvement in at least 1 organ or site without progression in any other organ or site as evidenced by current scoring per Chronic GVHD: Grading in the NCCN guidelines

Malaria

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
chloroquine	atovaquone/proguanil
hydroxychloroquine	COARTEM (artemether/lumefantrine)
quinine	KRINTAFEL (tafenoquine)
this space intentionally left blank	MALARONE (atovaquone/proguanil)
this space intentionally left blank	mefloquine
this space intentionally left blank	primaquine
this space intentionally left blank	SOVUNA (hydroxychloroquine)

Prior Authorization Criteria

Initial Criteria – Approval Duration: 7 days

- The request must be for treatment of malaria (*NOT covered for prophylaxis)*
- One of the following criteria must be met (A or B):
  A. The member is continuing treatment upon discharge from an acute care facility.
  B. The requested medication must be prescribed by, or in consult with, an infection disease specialist and clinical justification has been provided explaining why the preferred agents are not an option due to susceptibility, previous failed trials, or other contraindications (subject to clinical review)

Renewal Criteria – Approval Duration: 5 days

- It is medically necessary to continue treatment course after re-evaluation of the member's condition.

- The total requested duration of use must not be greater than manufacturer labeling or treatment guideline recommendations (whichever is greater).

First Review of Familial Chylomicronemia Syndrome (FCS)

Overview

Purpose of Review: New to market/review – Redemplo and Tryngolza

Definition[1]: A rare, autosomal recessive genetic disease characterized by very high triglyceride levels. It is caused by genetic changes that impair the normal breakdown of triglycerides (TG) to chylomicrons. The most common gene affected is the Lipoprotein Lipase (LPL) gene. Diagnosis is often delayed due to similar symptoms as familial combined hyperlipidemia and poorly controlled diabetes.

Prevalence[1]**:**

- Affects 1 out of every 1 million people (3,000 to 5,000 people worldwide).
- Higher incidence in Quebec, Canada and the Cayman Islands

Clinical Features[1]**:**

- Triglyceride levels > 750 mg/dL
  - Typically occurs at a younger age than in those with other causes.
- Increased risk of acute pancreatitis
  - Affects approximately 70% of patients with FCS
- Recurrent abdominal pain, nausea, and vomiting
- Visible fat deposits in the skin
- Fatigue
- Difficulty concentrating
- Lipemia retinalis – milky appearance in retinal veins
- Often have no atherosclerotic cardiovascular disease (ASCVD) due to the lipid-rich

  atherosclerotic plaque in the arterial wall being mostly cholesteryl ester and not triglyceride.[2]

Diagnosis[1]**:** Based on medical history, clinical exam, and lab tests showing TG levels greater than 750 mg/dL. Patients have extremely high triglyceride levels at a younger age and do not have the classic conditions associated with high triglycerides (e.g. obesity and diabetes). Genetic testing can help to identify gene variants but may not always find disease-causing variants.

FDA Approval

Redemplo (plozasiran): November 18, 2025; 505(b) New Drug Application (NDA) pathway; Type 1 – New Molecular Entity; Standard; Orphan

Tryngolza (olezarsen): December 19, 2024; 505(b) New Drug Application (NDA) pathway; Type 1 – New Molecular Entity; Priority; Orphan

Current Utilization

Quarter 1 2025 – Quarter 4 2025

Medication	Rx Count	% of Rx	Reimb Amount

Redemplo (plozasiran)	**0**	**0**	**0**
Tryngolza (olezarsen)	**0**	**0**	**0**

Treatment Overview

- Primary treatment is a highly restrictive low-fat diet
  - Less than 10-15% of daily calories or no more than 15 to 20 grams of fat per day
  - Avoid alcohol
  - Avoid processed, sugary foods
- Pharmacotherapy
  - Medications that lower TG levels for non-genetic causes are not effective for FCS.
  - Tryngolza (olezarsen)
  - Redemplo (plozasiran)

Medication Overview:

- Redemplo (plozasirin)[4, 7]
  - Mechanism of action: siRNA conjugated with GaINAc that degrades the apoC-III mRNA through RNA interference mechanism resulting in reduced levels of hepatic and serum apC-III protein which leads to increased clearance of serum TG.
  - Dosing: 25mg subcutaneous once every 3 months
  - Clinical Trials: The median difference between Redemplo 25mg and placebo on percent change of fasting TG from baseline at month 10 was 58.7%.[4]
  - Cost (WAC) per 30 days: $15,000.00
- Tryngolza (olezarsen)[6, 8]
  - Mechanism of action: ASO-GaINAc$_3$ conjugate that binds to apoC-III mRNA leading to mRNA degradation and resulting in a reduction in serum apoC-III protein which leads to increased clearance of plasma TG and VLDL.
  - Dosing: 80 mg subcutaneous once monthly
  - Clinical Trials: The Tryngolza group had a 42.5% drop in fasting triglycerides from baseline to month 6 compared to the placebo group. Trials also showed that olezarsen reduced the incidence of acute pancreatitis by 85%.
  - Cost (WAC) per 30 days: $49,584.00

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First Review of Nausea and Vomiting

Overview

Purpose of Review: New to market -- Nereus

Pathophysiology[1]:

- **Nausea**: There is a shift in the normal three-cycle-per-minute gastric myoelectrical activity. This can be increased frequency (tachygastria) or reduced frequency (bradygastria).
    - Tachygastria typically precedes nausea in motion sickness.
- **Vomiting**: a reflex that allows a person to rid itself of ingested toxins or poisons. Can be activated by central or peripheral neuronal stimuli or by humoral stimuli.

Acute disorders[1]:

- Secondary to common cold for cause of lost productivity.
- Mainly caused by viruses but may also be caused by bacterial and parasitic pathogens.

Chronic disorders[1]:

- Functional nausea and vomiting disorders
    - Symptom onset 6 months before diagnosis and fulfills Rome IV criteria for at least 3 months
    - Chronic nausea and vomiting syndrome
    - Cyclic vomiting syndrome
    - Cannabinoid hyperemesis syndrome
- Rumination syndrome
    - Characterized by persistent or recurrent regurgitation of recently ingested food into the mouth with subsequent spitting or remastication and swallowing.
    - Primary treatment is behavioral modification.
- Nausea and vomiting of pregnancy
    - Occurs in 74% of pregnant individuals

Motion Sickness[2]:

- Syndrome that occurs in response to real or perceived motion, which can include gastrointestinal, CNS, and autonomic symptoms.
- Physiological form of dizziness which occurs when vestibular, visual, and somatosensory information cues are not congruent.
- Females are more susceptible that males

Chemotherapy-induced nausea and vomiting (CINV)[3]:

- Three types of CINV
    - Acute emesis – begins within one to two hours of chemotherapy and peaks in four to six hours.
    - Delayed emesis – occurs more than 24 hours after chemotherapy
    - Anticipatory emesis – occurring prior to treatment in patients who have developed significant nausea and vomiting during previous cycles of chemotherapy

FDA Approval

Akynzeo (netupitant/palonestron)[4]: October 10, 2014; New Drug Application; Type 1 – New Molecular Entity and Type 4 – New Combination; Standard

Nereus (tradipitant)[5]: December 30, 2025; New Drug Application; Type 1 – New Molecular Entity; Standard

Diclegis (doxylamine/pyridoxine)[6]: April 8, 2013. New Drug Application; Type 5 – New Formulation or New Manufacturer; Standard

Bonjesta (doxylamine/pyridoxine)[7]: November 7, 2016. New Drug Application; Type 5 – New Formulation or New Manufacturer; Standard

Current Utilization

Quarter 1 2025 – Quarter 4 2025

Medication	Rx Count	% of Rx	Reimb Amount
Akynzeo	**0**	**0%**	**$0**
Aprepitant	**3**	**0.0015**	**$1,023.34**
Bonjesta	**0**	**0%**	**$0**
Diclegis	**47**	**0.02%**	**$5,724.25**
Dronabinol	**11**	**0.004%**	**$1,247.23**
Emend	**1**	**0.000%**	**$435.81**
Granisetron	**13**	**0.005%**	**$953.87**
Meclizine	**556**	**0.22%**	**$7,358.35**
Nereus	**0**	**0%**	**0**
Ondansetron	**12,868**	**5.084%**	**$182,685.54**
Sancuso	**0**	**0%**	**0**
Scopolamine	**480**	**0.190%**	**$20,085.27**

Treatment Overview

Motion Sickness[2]:

- Prevention:
  - Scopolamine or antihistamines
    - Used for patients with recurrent motion sickness despite environmental modifications and complementary or alternative treatments
    - Preferred antihistamines include dimenhydrinate or meclizine
  - Tradipitant (Nereus)[8]
    - Used for patients who are symptomatic despite scopolamine or antihistamines
    - A neurokinin-1 receptor antagonist approved for motion-induced vomiting in December 2025.
    - Dosing: 85mg or 170mg as a single dose approximately 60 minutes prior to an event to cause vomiting induced by motion. Max one dose in 24 hours.
    - Mechanism of action: exact mechanism unknown but it crosses the blood brain barrier and occupies brain NK-1 receptors. High-affinity antagonist of human

substance P/neurokinin-1 (NK-1) receptors. No affinity for NK2, NK3, 5-HT3, D2, cholinergic, or H1 receptors.
        - Use with strong CYP3A4 inhibitors may increase somnolence and fatigue.
        - The incidence of vomiting during a boat trip was significantly less in the tradipitant group 10-20% compared to placebo group (38-44%).
        - Cost: $255 to $510 per dose

Chemotherapy-induced nausea and vomiting[3]:

- Drug classes
    - 5-HT3 Receptor antagonists
        - First generation - Granisetron, ondansetron
            - All appear to be equally effective for prevention of CINV
            - Can cause ECG changes within 1 to 2 hours after a dose but typically resolve within 24 hours.
            - Can cause potentially fatal cardiac arrhythmias including torsade de pointes and QTc prolongation.
                - Dolasetron should be avoided in patients with congenital long QT syndrome
        - Second generation – palonosetron
            - Has a 30- to 100-fold higher affinity for the 5-HT3 receptor and significantly longer half-life (40 hours) than first-generation agents.
            - More effective than ondansetron and dolasetron as a single agent and provides superior control when combined with a glucocorticoid.
    - Neurokinin-1 receptor antagonists
        - Aprepitant
        - Netupitant plus palonosetron (Akynzeo)[9]
            - Dose: Netupitant 300mg/palonestron 0.5mg) 1 hour prior to chemotherapy
            - Avoid use in patients with end-stage renal disease and Child-Pugh score greater than 9.
            - Can cause serotonin syndrome when administered with other serotonergic medications.
            - Mechanism of action: prevents acute emesis by stimulating 5-HT3 receptors and delayed emesis blocking substance P/NK1 receptors.
            - Cost: $690.10 per dose
    - Glucocorticoids
        - Dexamethasone can be used as a single agent or in combination with other drug classes
    - 5-HT2 receptor antagonist and dopamine D2 receptor antagonist
        - Olanzapine
        - Effective for prevention of acute and delayed nausea and vomiting
    - Cannabinoids[10]
        - Dronabinol
        - Used for patients with refractory nausea and vomiting to conventional antiemetic treatments.
- Highly emetogenic chemotherapy (>90% risk of emesis)
    - Recommend a combination of an NK1R antagonist, a 5-HT3 receptor antagonist, dexamethasone, and olanzapine
- Moderately emetogenic chemotherapy (> 30 to 90% risk of emesis)

    - Recommend a combination of an NK1R antagonist, a 5-HT3 receptor antagonist, and dexamethasone
- Low emetogenic chemotherapy (10 to 30% risk of emesis)
    - Recommend dexamethasone or a 5-HT3 receptor antagonist
- Minimally emetogenic chemotherapy (< 10% risk of emesis)
    - Routine antiemetic therapy is not recommended

Nausea and vomiting of pregnancy:[11]

- Pyridoxine (vitamin B6) monotherapy
    - Initial treatment
    - Dose: 10 to 25mg every 6 to 8 hours as needed
    - Helps improve mild to moderate nausea
    - No significant effect on vomiting
- Doxylamine-pyridoxine (Diclegis, Bonjesta)
    - To be used if pyridoxine alone is ineffective
    - Dose: two 10mg/10mg tablets or one 20mg/20mg tablet at bedtime. May be increased to a total of 4 tablets over the course of a day.
    - Clinical trials showed the combination appears to be more effective than either medication alone.
- Antihistamines (H1 antagonists) – diphenhydramine, dimenhydrinate
    - May be added as second-line therapy in patients who are vomiting.
    - Avoid concurrent use with ondansetron due to potential QT prolongation.
    - Provide direct inhibition of histamine at the H1 receptor, an indirect effect on the vestibular system by decreasing stimulation of the vomiting center and inhibit muscarinic receptors which may mediate the emetic response.
- Dopamine antagonists – metoclopramide, promethazine, prochlorperazine, and droperidol
    - Promote gastric motility and emptying which produces antiemetic effects. They also block emetic signaling by blocking dopamine 2 receptors.
    - Droperidol is rarely used due to maternal safety concerns
- Serotonin antagonists – ondansetron and granisetron
    - Ondansetron is preferred.
- Acid-reducing agents
    - Antacids containing aluminum, calcium, or magnesium are safe
    - H2 blockers – cimetidine and ranitidine
    - Proton pump inhibitors – lansoprazole, omeprazole, and esomeprazole
- Medications for refractory symptoms
    - Corticosteroids
    - Chlorpromazine
    - Droperidol – rarely used
    - Gabapentin
    - Mirtazapine and olanzapine

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First Review of Thrombotic Microangiopathies (TMA)

Overview

Purpose of Review: Expanding category, new to market – Yartemlea

Definition[1]: A specific pathologic lesion in which abnormalities in the arterioles and capillaries lead to microvascular thromboses.

Type of Thrombotic thrombocytopenic purpura (TTP)[2,3,4]**:**

- Thrombotic thrombocytopenic purpura (TTP) – defined by a severe deficiency of ADAMTS13
  - Immune TTP (iTTP)[2] – autoantibodies against ADAMTS13
    - Occurs in 2 to 6 per 1 million adults per year.
    - Typically affects adults
    - More commonly affects females
    - 30-fold more common than congenital TTP
  - Congenital TTP (cTTP) [2, 3] – Severe lifelong deficiency of ADAMTS12 due to biallelic pathogenic variants in the ADAMTS13 gene
    - Also known as hereditary TTP, inherited TTP, familial TTP, and Upshaw-Schulman syndrome.
    - Autosomal recessive
    - Very rare in adults (< 5% of all TTP)
    - More common in infants and young children
    - Typically presents as severe bilirubinemia in newborns.
    - Overall affects 0.5 to 2 patients per one million population
- Transplant-associated thrombotic microangiopathy (TA-TMA)[4] – can present with acute kidney injury after hematopoietic cell transplant (HCT).
  - Typically presents within the first 100 days after transplantation.
  - Common cause of CKD in this patient population.
  - Incidence rate of 2 to 39 percent.
- Complement-mediated TMA – abnormality of proteins that normally regulate the alternative pathway of complement or that accelerate activation of this pathway.
- Metabolism-mediated TMA – disorders of intracellular vitamin B12 metabolism.
- Coagulation-mediated TMA – causes thromboembolism in large vessels rather than systemic microvascular thrombosis.
- Infection-associated TMS
  - Shiga toxin mediated HUS (ST-HUS) is the most common. Caused by toxins produced by *S. dysenteriae* and some serotypes of *E. coli.* Large outbreaks are associated with sanitation or food contamination.
  - *S. pneumoniae*
- Drug-induced TMA (DITMA)
  - Immune-mediated – drug-dependent antibodies that react with platelets, neutrophils, endothelial cells, and/or other cells
  - Dose-dependent, non-immune – primarily caused by chemotherapeutic agents (gemcitabine, mitomycin), immunosuppressive agents (cyclosporine, tacrolimus), vascular endothelial growth factor inhibitors (bevacizumab), opioids taken inappropriately.
  - Hematopoietic stem cell or organ transplantation – manifests as kidney dysfunction and/or unexplained neurologic dysfunction with intravascular hemolysis.

        - Typically develops 20 to 100 days after transplantation.
- Systemic autoimmune disorders – systemic lupus erythematosus, systemic sclerosis, Sjogren's disease, vasculitides, and antiphospholipid syndrome can cause TMA that affects the kidney.
    - Should treat the underlying autoimmune disorder
- Pregnancy - preeclampsia

Outdated terminology[1]:

- Atypical hemolytic uremic syndrome (aHUS)
    - Used historically to describe children with microangiopathic hemolytic anemia (MAHA), thrombocytopenia, and kidney failure not associated with diarrhea
    - Non-specific term and provides no insight to the underlying pathology of the TMA
- Idiopathic
    - Historically used to imply ADAMTS13 deficiency in patients who did not have other recognized conditions that may cause TMA
- Primary or secondary no longer used as there are now mechanisms and causes of TMA available.

Diagnosis[1]:

- iTTP should be suspected when a patient presents with microangiopathic hemolytic anemia (hemoglobin < 10 g/dL) and severe thrombocytopenia (platelet count < 30, 000/microL).[2]
- When to suspect cTTP[3]:
    - Severe neonatal hyperbilirubinemia
    - Recurrent thrombocytopenia in a child or young adult
    - Transient neurologic symptoms or stroke, especially in a child or young adult
    - If a sibling has confirmed cTTP
    - TTP without an ADAMTS13 or antibody
- TA-TMA[4]
    - Elevated LDH level
    - Presence of schistocytes on blood smear
    - Decrease in hemoglobin concentration
    - Thrombocytopenia (platelet count <50,000/microL or ≥50 percent reduction from previous counts)
    - Decrease in serum haptoglobin
    - Negative Coombs test

Clinical Features:

- iTTP[2]
    - Initial symptoms – fatigue, dyspnea, petechiae, bleeding, or neurologic symptoms
- cTTP[3]
    - Some patients are asymptomatic with excellent health into adulthood
    - Mild, nonspecific symptoms – lethargy, headache, loss of concentration, abdominal discomfort
    - Acute, severe episodes – thrombocytopenia and MAHA, kidney failure, stroke
- TA-TMA should be suspected if HCT recipients present with one or more of the following: [4]
    - Elevated serum LDH level
    - Elevated serum creatinine (or reduction in estimated GFR)
    - New-onset or increasing proteinuria

    - Hypertension that is out of proportion to what would be expected from CNI and glucocorticoid therapy or volume overload (e.g., requiring ≥ antihypertensive medications)
    - Sudden requirement for more transfusion support than previously needed to maintain stable blood cell and platelet counts
- Can have anuric acute kidney injury or normal kidney function
    - Absence of kidney injury or minimal injury suggests a diagnosis of congenital or immune TTP
    - Sudden, severe kidney injury supports immune-mediated drug-induced TMA or acute dose-dependent, non-immune DITMA. Complement-mediated TMA may also be associated with sudden-onset kidney injury.
    - Onset over days supports a diagnosis of ST-HUS, complement-mediated TMA, or metabolism-mediated or coagulation-mediated TMA.
    - Onset over weeks to months suggests DITMA caused by toxic chemotherapeutic or immunosuppressive drugs.
- May occur at any age
    - Infants/young children: Shiga toxin-related hemolytic uremic syndrome is the most common TMA syndrome
        - Children may also be affected by complement-mediated TMA, congenital TTP, and hereditary metabolism -mediated or coagulation-mediated TMA.
    - Adults can be affected by any acquired or hereditary TMA syndromes.
        - Immune TTP, drug-induced TMA, and complement-mediated TMA are the most common forms in adults.
- Onset of complement-mediated TMA is generally sudden where other forms present gradually over several days.
- DITMA can present within hours of drug exposure.
    - Most common drugs that cause DITMA – rifampin, sulfisoxazole, trimethoprim-sulfamethoxazole, valproic acid, several cancer therapies, cocaine, oxycodone, MDMA, emicizumab, several immunosuppressive therapies, and quinine[5].

Laboratory Testing:

- Complete blood count with platelet count
- Lactate dehydrogenase and bilirubin
- Serum creatinine
- Blood smear for schistocytes
- Prothrombin time, partial thromboplastin time, and fibrinogen level
- Liver functions tests
- Electrocardiogram and cardiac troponin
- ADAMTS13
- May also complete homocysteine and methylmalonic acid testing, complement testing, stool cultures, genetic testing, and kidney biopsy.

FDA Approval

Adzynma (ADAMTS13, recombinant-krhn)[7]: November 9, 2023. Biologics License Application (BLA)

Cablivi (caplacizumab-yhdp)[8]: February 6, 2019; Biologics License Application (BLA); Orphan

Yartemlea (narsoplimab-wuug)[9]: December 23, 2025; Biologics License Application (BLA); Orphan

Current Utilization

Quarter 1 2025 – Quarter 4 2025

Medication	Rx Count	% of Rx	Reimb Amount
Adzynma	0	0	0
Cablivi	0	0	0
Yartemlea	0	0	0

Treatment Overview

iTTP[6]

- Therapeutic plasma exchange (TPE) – mainstay of treatment as it provides ADAMTS13 from the donor plasma and removes autoantibodies against ADAMTS13
  - Rituximab, if required, should be administered after TPE
  - Caplacizumab should be administered 15 minutes prior to TPE
  - Glucocorticoids and rituximab help improve outcome and reduce the duration of TPE.
- Glucocorticoids – should be given to all patients with a high PLASMIC score (5 to 7 points).
- Rituximab
  - Initiated in patients with ADAMTS13 > 10
- Caplacizumab
  - Reserved for individuals with ADAMTS13 < 10 and clinical features that warrant more aggressive initial therapy
    - Neurologic abnormalities (seizures, transient focal weakness, aphasia, dysarthria, confusion, coma)
    - Encephalopathy
    - High serum troponin levels
    - Thrombocytopenia due to TTP that does not improve after 2 to 3 days of TPR, a glucocorticoid, and rituximab.
  - May be preferred initial treatment in the following:
    - Patients who decline blood products
    - Those who have severe allergic reactions to plasma
  - Use should be discontinued when the ADAMTS13 activity is above 20 to 30 percent.
- Treatment should be initiated with a PLASMIC score of 5 or higher or if the patient has schistocytes and thrombocytopenia without another explanation
- TPE and glucocorticoids should be initiated in patients with an intermediate or high PLASMIC score before ADAMTS13 results are available.

cTTP[3]

- Acute episodes should be treated with a source of ADAMTS13
  - Adzynma (ADAMTS13, recombinant-krhn)
    - Provides ADAMTS13 protease without exposing the patient to donor plasma
  - Fresh frozen plasma (FFP) or thawed plasma
  - Plasma-derived clotting factor concentrate that contains ADAMTS13 (Alphanate, Humate-P, Wilate, 8Y, Koate-DVI)
  - The patient should receive whichever source of ADMATS13 is most readily available at the time of the acute attack.
    - rADAMTS13 (Adzynma) preferred over plasma if both are available

- Prophylaxis
    - Typically recommended for patients who have frequent recurrent acute episodes or severe symptoms or those who have significant morbidity from ongoing TTP activity.
    - Generally not recommended for asymptomatic patients, however, it may be helpful in protection against long-term organ damage such as stroke and kidney damage. Strong supportive evidence for prophylaxis in asymptomatic patients is lacking.
        - Asymptomatic patients who become pregnant should consider prophylaxis as this is a high-risk time that may trigger an acute episode.

TA-TMA[4]

- General supportive measures:
    - Management of hypertension
    - Withdrawal of offending agents (e.g., tacrolimus, cyclosporine, sirolimus)
    - Dialysis
- Severe disease – kidney, cardiac, pulmonary, gastrointestinal, or neurologic involvement
    - Eculizumab – initial treatment
    - Narsoplimab
        - Also, an appropriate initial treatment.
        - Preferred in patients who do not respond to eculizumab
    - Rituximab
        - Suggested to for use in patients with primarily kidney involvement and no evidence of complement activation
    - Defibrotide
        - Not commonly used.
        - Reserved for patients who do not respond to narsoplimab, eculizumab, or rituximab

Complement-mediated TMA

- Treat with anti-complement treatment urgently to prevent irreversible kidney damage
    - Eculizumab or ravulizumab are monoclonal antibodies directed against the C5 complement component. They block formation of the membrane attack complex (MAC) that is thought to mediate the microangiopathic changes and kidney injury seen in CM-TMA[10].
        - Eculizumab is preferred in pregnancy and breastfeeding.

Medication Overview:

rADAMTS13 (Adzynma)[11]

- Mechanism of action: Recombinant form of the endogenous ADAMTS13 that regulates the activity of von Willebrand factor (vWF) which reduces platelet binding properties of vWF and propensity to form microthrombi
- Dosing:
    - Prophylaxis: 40 IU/kg IV every other week
    - On-demand therapy: 40 IU/kg IV on day 1 followed by 20 IU/kg on day 2, then 15 IU/kg daily until 2 days after the acute event is resolved
- Cost (WAC) per 30 days: $27,680.00 (based on a 100kg weight) – prophylaxis dosing

Caplacizumab-yhdp (Cablivi)[12]

- Mechanism of action: vWF-directed antibody fragment that targets the A1-domain of the vWF and inhibits interaction between vWF and platelets, reducing vWF-mediated platelet adhesion and platelet consumption
- Dosing: 11mg IV bolus at least 15 minutes prior to TPE followed by 11mg SUBQ the day after TPE completion. 11mg daily for 30 days following the last daily TPE.
- Cost (WAC) per 30 days: $267,436.50

Narsoplimab-wuug (Yartemlea)[4,13]

- Mechanism of action: Inhibits MASP-2 which blocks lectin pathway activation
- Dosing:
  - 50kg or greater: 370mg IV once weekly
  - Less than 50kg: 4mg/kg IV once weekly
  - If inadequate response, may increase to twice weekly
- Special Considerations: Indicated for use in patients 2 years or older with TA-TMA
- Cost (WAC) per 30 days: $147,220.00

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NORTH DAKOTA MEDICAID

RETROSPECTIVE DRUG UTILIZATION REVIEW

CRITERIA RECOMMENDATIONS

2ND QUARTER 2026

1. Gepirone / Overuse
Alert Message: Exxua (gepirone) may be over-utilized. The maximum recommended daily dose of gepirone in adults 18 to 64 years of age is 72.6 mg once daily after a seven-day dose titration.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Exxua Prescribing Information, July 2025, Aytu Therapeutic.

2. Gepirone / Overuse – Geriatrics
Alert Message: Exxua (gepirone) may be over-utilized. The maximum recommended dose of gepirone in geriatric patients is 36.3 mg once daily after a seven-day dose titration.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Exxua Prescribing Information, July 2025, Aytu Therapeutic.

3. Gepirone / Overuse – Renal Impairment
Alert Message: Exxua (gepirone) may be over-utilized. The maximum recommended dose of gepirone in patients with renal impairment (creatinine clearance < 50 mL/min) is 36.3 mg once daily after a seven-day dose titration.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Exxua Prescribing Information, July 2025, Aytu Therapeutic.

4. Gepirone / Overuse – Moderate Hepatic Impairment
Alert Message: Exxua (gepirone) may be over-utilized. The maximum recommended dose of gepirone in patients with moderate hepatic impairment (Child-Pugh B) is 36.3 mg once daily after a seven-day dose titration. Gepirone use is contraindicated in patients with severe hepatic impairment. No dosage adjustment is required in patients with mild hepatic impairment.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Exxua Prescribing Information, July 2025, Aytu Therapeutic.

5. Gepirone / Therapeutic Appropriateness
Alert Message: The safety and efficacy of Exxua (gepirone) in pediatric patients have not been established.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Exxua Prescribing Information, July 2025, Aytu Therapeutic.

6. Gepirone / Contraindication – Severe Hepatic Impairment
Alert Message: Exxua (gepirone) use is contraindicated in patients with severe hepatic impairment (Child-Pugh C) due to the risk of elevated gepirone plasma concentrations and increased risk of gepirone-associated QTc interval prolongation.

Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Exxua Prescribing Information, July 2025, Aytu Therapeutic.

7. Gepirone / QT Prolongation - Contraindication
Alert Message: Exxua (gepirone) prolongs the QTc interval. The use of gepirone is contraindicated in patients with congenital long QT syndrome or with a prolonged QTc interval greater than 450 msec at baseline.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Exxua Prescribing Information, July 2025, Aytu Therapeutic.

8. Gepirone / Strong CYP3A4 Inhibitors - Contraindication
Alert Message: Exxua (gepirone) use is contraindicated in patients taking strong CYP3A4 inhibitors. Gepirone is a CYP3A4 substrate, and concomitant use of a strong CYP3A4 inhibitor may increase gepirone plasma concentrations 5-fold, increasing the risk of serious gepirone-related adverse reactions.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Exxua Prescribing Information, July 2025, Aytu Therapeutic.

9. Gepirone / MOAIs - (Contraindication)
Alert Message: Exxua (gepirone) use is contraindicated in patients taking MAOIs or in patients who have taken MAOIs within the preceding 14 days. Allow at least 14 days after stopping gepirone before starting an MAOI. Concomitant use of gepirone with an MAOI increases the risk of serious and possibly fatal drug interactions, including hypertensive crisis and serotonin syndrome.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Exxua Prescribing Information, July 2025, Aytu Therapeutic.

10. Gepirone / Bipolar Disorder
Alert Message: Antidepressant treatment, including Exxua (gepirone), can precipitate a manic, mixed, or hypomanic episode. The risk appears to be increased in patients with bipolar disorder.Prior to initiating treatment with gepirone, screen patients for a history of bipolar disorder and the presence of

risk factors for bipolar disorder (e.g., family history of bipolar disorder and suicide). Gepirone is not approved for use in treating bipolar depression.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Exxua Prescribing Information, July 2025, Aytu Therapeutic.

11. Gepirone / SSRIs, SNRIs, & TCA
Alert Message: Concurrent use of Exxua (gepirone) with serotonergic drugs may increase the risk of serotonin syndrome, a potentially life-threatening condition. If concomitant use of gepirone with other serotonergic medications is clinically warranted, inform patients of the increased risk for serotonin syndrome and monitor for symptoms. Discontinue gepirone and/or any concomitant serotonergic medications immediately if the symptoms of serotonin syndrome occur and initiate supportive symptomatic treatment.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Exxua Prescribing Information, July 2025, Aytu Therapeutic.

12. Gepirone / Strong CYP3A4 Inducers
Alert Message: Concurrent use of Exxua (gepirone) with strong CYP3A4 inducers should be avoided. Gepirone is a CYP3A4 substrate, and concomitant use of a strong CYP3A4 inducer may decrease gepirone exposure 20- to 29-fold.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Exxua Prescribing Information, July 2025, Aytu Therapeutic.

13. Gepirone / Drugs That Prolong QT Interval
Alert Message: Concurrent use of Exxua (gepirone) with drugs that prolong the QTc interval may add to the QTc-prolonging effects of gepirone and increase the risk of cardiac arrhythmias. Monitor patients on current therapy with ECGs more frequently.

References:
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Exxua Prescribing Information, July 2025, Aytu Therapeutic.

14. Gepirone/ Moderate CYP3A4 Inhibitors
Alert Message: If Exxua (gepirone) is used concurrently with a moderate CYP3A4 inhibitor, the gepirone dose should be reduced by 50%. Gepirone is a CYP3A4 substrate, and concomitant use of a moderate CYP3A4 inhibitor may increase gepirone exposure approximately 2-fold, increasing the risk of gepirone-related adverse effects.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.

Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Exxua Prescribing Information, July 2025, Aytu Therapeutic.

15. Gepirone / Pregnancy / Pregnancy Negating

Alert Message: Based on animal reproduction studies, Exxua (gepirone) has been shown to have adverse effects on embryo/fetal and postnatal development. Third trimester use of gepirone may increase risk of persistent pulmonary hypertension and symptoms of poor adaptation (respiratory distress, temperature instability, feeding difficulty, hypotonia, irritability) in the neonate.

References:

Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Exxua Prescribing Information, July 2025, Aytu Therapeutic.

16. Gepirone / Lactation

Alert Message: There are no data on the presence of Exxua (gepirone) in human milk, the effects on the breastfed infant, or the effects on milk production. In studies with rats, gepirone was present in rat milk. When a drug is present in animal milk, it is likely that the drug will be present in human milk. There are reports of breastfed infants exposed to serotonergic antidepressants experiencing irritability, restlessness, excessive somnolence, decreased feeding, and weight loss.

References:

Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Exxua Prescribing Information, July 2025, Aytu Therapeutic.

17. Gepirone / Non-adherence

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

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Iuga AO, McGuire MJ. Adherence and Health Care Costs. Risk Manag Healthc Policy. 2014 Feb 20;7:35-44.
Woldu H, Porta G, Goldstein T, et al. Pharmacokinetically and Clinician- Determined Adherence to an Antidepressant Regimen and Clinical Outcome in the TORDIA Trial. J Am Acad Child Adol Psy, 50;5:490-98. May 2011.
Keene MS. Confusion and Complaints: The True Cost of Noncompliance in Antidepressant Therapy. Medscape Psychiatry & Mental Health. 2005;10(2). Available at: http://www.medscape.com/viewarticle/518273
Chong WW, Aslani P, Chen TF. Effectiveness of Interventions to Improve Antidepressant Medication Adherence: A Systematic Review. Int J Clin Pract. 2011 Sep;65(9)954-975.

18. Mitapivat / Overuse

Alert Message: Pyrukynd (mitapivat) may be over-utilized. The maximum recommended dose of mitapivat is 100 mg/day (50 mg twice daily).

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

19. Mitapivat / Therapeutic Appropriateness
Alert Message: The safety and effectiveness of Pyrukynd (mitapivat) in pediatric patients have not been established.

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

20. Mitapivat / Therapeutic Appropriateness
Alert Message: Avoid the use of Pyrukynd (mitapivat) in patients with moderate and severe hepatic impairment. Mitapivat undergoes extensive hepatic metabolism. Moderate and severe hepatic impairment is expected to increase the systemic exposure to mitapivat.

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

21. Mitapivat / Strong CYP3A4 Inhibitors
Alert Message: The co-administration of Pyrukynd (mitapivat) with strong CYP3A4 inhibitors should be avoided. Mitapivat is a CYP3A4 substrate, and concurrent use of mitapivat with a strong CYP3A4 inhibitor may increase mitapivat plasma concentrations, increasing the risk of mitapivat-related adverse reactions.

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

22. Mitapivat / Strong CYP3A4 Inducers
Alert Message: The co-administration of Pyrukynd (mitapivat) with strong CYP3A4 inducers should be avoided. Mitapivat is a CYP3A4 substrate, and concurrent use of mitapivat with a strong CYP3A4 inducer may decrease mitapivat plasma concentrations, leading to decreased mitapivat efficacy.

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

23. Mitapivat / Moderate CYP3A4 Inhibitors
Alert Message: Pyrukynd (mitapivat) is a CYP3A substrate, and co-administration of mitapivat with moderate CYP3A4 inhibitors may increase mitapivat plasma concentrations. Do not titrate mitapivat beyond 20 mg twice daily when co-administered with a moderate CYP3A4 inhibitor. When

concurrent use is warranted, monitor Hb and for increased risks of mitapivat-related adverse reactions.

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

24. Mitapivat / Moderate CYP3A4 Inducers
Alert Message: Pyrukynd (mitapivat) is a CYP3A4 substrate, and co-administration of mitapivat with moderate CYP3A4 inducers may decrease mitapivat plasma concentrations and efficacy. Consider alternative therapies that are not moderate CYP3A4 inducers during treatment with mitapivat. If there are no alternative therapies, monitor Hb and titrate beyond 50 mg twice daily, if necessary, but do not exceed a maximum recommended dose of 100 mg twice daily.

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

25. Mitapivat / Sensitive CYP3A4 Substrates
Alert Message: Pyrukynd (mitapivat) induces CYP3A4, and co-administration of mitapivat will decrease systemic concentrations of drugs that are sensitive CYP3A4 substrates, including hormonal contraceptives. Monitor patients for loss of therapeutic effect of sensitive CYP3A4 substrates with a narrow therapeutic index when co-administered with mitapivat.

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Pyrukynd Prescribing Information, Jan. 2025, Agios Pharmaceuticals.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors, and Inducers. Available at: https://www.fda.gov/drugs/drug-interactions-labeling/drug-development-and-drug-interactions-table-substrates-inhibitors-and-inducers

26. Mitapivat / Hormonal Contraceptives
Alert Message: Pyrukynd (mitapivat) is a CYP3A4 inducer, and co-administration of mitapivat, with drugs that are sensitive CYP3A4 substrates, including hormonal contraceptives, may decrease substrate concentrations. Advise patients using hormonal contraceptives to use an alternative non-hormonal contraceptive method or add a barrier method of contraception during treatment with mitapivat.

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

27. Mitapivat / CYP2B6, CYP2C8, CYP2C9 & CYP2C19 Substrates
Alert Message: Pyrukynd (mitapivat) induces CYP2B6, CYP2C8, CYP2C9, and CYP2C19 enzymes in vitro, and may decrease systemic concentrations of drugs that are sensitive substrates of these enzymes. Monitor patients for loss of therapeutic effect of sensitive substrates of these enzymes with a narrow therapeutic index when co-administered with mitapivat.

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Pyrukynd Prescribing Information, Jan. 2025, Agios Pharmaceuticals.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors, and Inducers. Available at: https://www.fda.gov/drugs/drug-interactions-labeling/drug-development-and-drug-interactions-table-substrates-inhibitors-and-inducers

28. Mitapivat / Sensitive UGT1A1 Substrates
Alert Message: Pyrukynd (mitapivat) induces UGT1A1 in vitro and may decrease systemic concentrations of drugs that are UGT1A1 substrates. Monitor patients for loss of therapeutic effect of UGT1A1 substrates with a narrow therapeutic index when co-administered with mitapivat.

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

29. Mitapivat / P-gp Substrates
Alert Message: Pyrukynd (mitapivat) inhibits P-gp transporter in vitro, which may increase systemic concentrations of drugs that are P-gp substrates. Monitor patients for P-gp substrate-induced adverse reactions when a P-gp substrate is co-administered with mitapivat.

References:

Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Pyrukynd Prescribing Information, Jan. 2025, Agios Pharmaceuticals.

30. Mitapivat / Lactation
Alert Message: There are no data on the presence of Pyrukynd (mitapivat) or its metabolites in human or animal milk, the effects on the breastfed child, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for mitapivat and any potential adverse effects on the breastfed child from mitapivat or from the underlying maternal condition.

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

31. Mitapivat / Non-adherence
Alert Message: Based on refill history, your patient may be under-utilizing Pyrukynd (mitapivat). Nonadherence to the prescribed dosing regimen may result in subtherapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs. To reduce the risk of acute hemolysis, avoid abrupt interruption or abrupt discontinuation of mitapivat when possible. Taper the dose to gradually discontinue the medication. Monitor patients for signs of acute hemolysis and worsening anemia.

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Pyrukynd Prescribing Information, Feb 2022, Agios Pharmaceuticals.
Kleinsinger F. The Unmet Challenge of Medication Nonadherence. Perm Jrnl. 2018; 22:18-033. doi:10.7812/TPP/18-033.

Brown MT, Bussell J, Suparna D, et al. Medication Adherence: Truth and Consequences. Am J Med Sci. 2016 Apr;351(4):387-399.

32. Bumetanide Nasal Spray / Overuse
Alert Message: Enbumyst (bumetanide nasal spray) may be over-utilized. The recommended total daily dose of bumetanide nasal spray is 2 mg/day (total 4 sprays/day). Bumetanide nasal spray is not intended for chronic use and should be replaced with oral diuretics as soon as practical.

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Enbumyst Prescribing Information, Sept. 2025, Corstasis Therapeutics.

33. Bumetanide Nasal Spray / Therapeutic Appropriateness
Alert Message: The safety and effectiveness of Enbumyst (bumetanide nasal spray) has not been established in pediatric patients.

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Enbumyst Prescribing Information, Sept. 2025, Corstasis Therapeutics.

34. Bumetanide Nasal Spray / Nasal Obstruction & Congestion
Alert Message: Enbumyst (bumetanide nasal spray) has not been assessed in individuals with nasal mucosal or structural abnormalities. Avoid use in patients with significant nasal mucosal or structural abnormalities, such as acute episodes of rhinitis or congestion due to any cause. Consider alternative products or therapies in such patients.

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Enbumyst Prescribing Information, Sept. 2025, Corstasis Therapeutics.

35. Nerandomilast / Overuse
Alert Message: Jascayd (nerandomilast) may be over-utilized. The recommended dosage of nerandomilast is 18 mg twice daily, administered 12 hours apart.

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Jascayd Prescribing Information, Oct. 2025, Boehringer Ingelheim Pharmaceuticals, Inc.

36. Nerandomilast / Therapeutic Appropriateness
Alert Message: The safety and efficacy of Jascayd (nerandomilast) have not been established in pediatric patients.

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Jascayd Prescribing Information, Oct. 2025, Boehringer Ingelheim Pharmaceuticals, Inc.

37. Nerandomilast 18 mg / Strong CYP3A Inhibitors
Alert Message: Jascayd (nerandomilast) may be over-utilized. The recommended dosage of nerandomilast when used concomitantly with a strong CYP3A4 inhibitor is 9 mg twice daily, administered 12 hours apart. Nerandomilast is a CYP3A4 substrate, and when used concurrently with a strong CYP3A4 inhibitor, may result in increased nerandomilast exposure and increased risk of nerandomilast-related adverse effects.

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Jascayd Prescribing Information, Oct. 2025, Boehringer Ingelheim Pharmaceuticals, Inc.

38. Nerandomilast / Moderate & Strong CYP3A Inducers
Alert Message: The concurrent use of Jascayd (nerandomilast) with a moderate or strong CYP3A4 inducers should be avoided. Nerandomilast is a CYP3A4 substrate. Concomitant use of nerandomilast with a moderate or strong CYP3A4 inducer may result in decreased nerandomilast exposure, which may decrease nerandomilast efficacy.

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Jascayd Prescribing Information, Oct. 2025, Boehringer Ingelheim Pharmaceuticals, Inc.

39. Nerandomilast / Pregnancy / Pregnancy Negating
Alert Message: Based on findings from animal reproduction studies, Jascayd (nerandomilast) may increase the risk of fetal loss. Advise pregnant women and females of reproductive potential of the potential risk of fetal loss.

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Jascayd Prescribing Information, Oct. 2025, Boehringer Ingelheim Pharmaceuticals, Inc.

40. Nerandomilast / Lactation
Alert Message: There are no data on the presence of Jascayd (nerandomilast) or its metabolite in human milk, the effects on the breastfed infant, or the effects on milk production. Nerandomilast is present in animal milk. When a drug is present in animal milk, it is likely that the drug will be present in human milk.

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Jascayd Prescribing Information, Oct. 2025, Boehringer Ingelheim Pharmaceuticals, Inc.

41. Nerandomilast / End-Stage Renal Disease
Alert Message: The use of Jascayd (nerandomilast) is not recommended in patients with end stage renal disease (eGFR < 15mL/min/1.73m2). Nerandomilast has not been investigated in patients with end stage renal disease.

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.

Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Jascayd Prescribing Information, Oct. 2025, Boehringer Ingelheim Pharmaceuticals, Inc.

42. Nerandomilast / Severe Hepatic Impairment
Alert Message: The use of Jascayd (nerandomilast) is not recommended in patients with severe hepatic impairment (Child-Pugh Class C). Nerandomilast has not been investigated in patients with severe hepatic impairment.

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Jascayd Prescribing Information, Oct. 2025, Boehringer Ingelheim Pharmaceuticals, Inc.

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

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497
Kim J, Combs K, Downs J, Tillman F. Medication Adherence: The Elephant in the Room. US Pharm. 2018;43(1)30-34.

Kleinsinger, Fred. The Unmet Challenge of Medication Nonadherence. The Permanente Journal. Vol. 22 (2018): 18-033. doi:10.7812/TPP/18-033.

44. CGRPs Injection / CGRP Oral - Therapeutic Duplication
Alert Message: Therapeutic duplication of calcitonin gene-related peptide (CGRP) antagonists may be occurring.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.

45. Tirzepatide / Overuse – Pediatric Patients
Alert Message: Mounjaro (tirzepatide) may be over-utilized. The maximum recommended dose of tirzepatide in pediatric patients 10 years of age and older is 10 mg injected subcutaneously once weekly.

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Mounjaro Prescribing Information, Dec. 2025, Eli Lilly and Company.

46. Lamotrigine / Estrogen-containing Oral Contraceptives
Alert Message: The concurrent use of lamotrigine with estrogen-containing contraceptives may cause a decrease in the lamotrigine concentrations and a decrease in the pharmacologic effects of lamotrigine. A lamotrigine maintenance dose increase of up to 2-fold may be required during concomitant use of estrogen-containing oral contraceptives. During the oral contraceptive pill-free week, trough lamotrigine concentrations may increase an average of 2-fold, which may increase the risk for lamotrigine-related adverse effects. If lamotrigine-related adverse effects consistently occur during the pill-free week, the overall lamotrigine maintenance dose may need

to be reduced.

References:
Clinical Pharmacology, 2025 Elsevier/Gold Standard.
Facts & Comparisons, 2025 Updates, Wolters Kluwer Health.
Lamictal Prescribing Information, Oct. 2025, GlaxoSmithKline.
Lamictal XR Prescribing Information, Oct. 2025, GlaxoSmithKline.

47. Cariprazine / Overuse – Pediatrics Schizophrenia
Alert Message: Vraylar (cariprazine) may be over-utilized. The maximum recommended dose of cariprazine for the treatment of schizophrenia in pediatric patients 13 to 17 years of age is 4.5 mg once daily.

References:
Vraylar Prescribing Information, Dec. 2025, AbbVie.
Clinical Pharmacology, 2025, Elsevier/Gold Standard.

48. Cariprazine / Overuse – Pediatrics Bipolar I
Alert Message: Vraylar (cariprazine) may be over-utilized. The maximum recommended dose of cariprazine for the treatment of bipolar I manic or mixed episodes in pediatric patients 10 to 17 years of age is 4.5 mg per day.

References:
Vraylar Prescribing Information, Dec. 2025, AbbVie.
Clinical Pharmacology, 2025, Elsevier/Gold Standard.

49. Cariprazine / Therapeutic Appropriateness - Schizophrenia
Alert Message: The safety and efficacy of Vraylar (cariprazine) for the treatment of schizophrenia have not been established in pediatric patients less than 13 years of age.

References:
Vraylar Prescribing Information, Dec. 2025, AbbVie.
Clinical Pharmacology, 2025, Elsevier/Gold Standard.

50. Cariprazine / Therapeutic Appropriateness
Alert Message: The safety and efficacy of Vraylar (cariprazine) for the treatment of manic or mixed episodes associated with bipolar I disorder (bipolar depression) have not been established in pediatric patients less than 10 years of age.

References:
Vraylar Prescribing Information, Dec. 2025, AbbVie.
Clinical Pharmacology, 2025, Elsevier/Gold Standard.

51. Lorlatinib / Overuse – Severe Hepatic Impairment
Alert Message: Lorbrena (lorlatinib) may be over-utilized. The recommended dosage of lorlatinib in patients with severe hepatic impairment (Child-Pugh C) is 50 mg orally once daily.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Lorbrena Prescribing Information, Jan 2026, Pfizer, Inc.

52. Lorlatinib / Overuse – Severe Hepatic Impairment
Alert Message: Lorbrena (lorlatinib) may be over-utilized. The recommended dosage of lorlatinib in patients with a creatinine clearance (CLcr) of 15 to < 30 mL/min (estimated by Cockcroft-Gault) is 75 mg orally once daily. The pharmacokinetics of lorlatinib have not been studied in patients with end-stage renal disease requiring hemodialysis.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.
Lorbrena Prescribing Information, Jan 2026, Pfizer, Inc.

53. All Antipsychotics / Sedative/Hypnotics
Alert Message: Caution should be exercised when prescribing an antipsychotic with sedative/hypnotics. Concurrent use of these drugs can result in additive CNS depressant effects.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.

54. All Antipsychotics / Benzodiazepines
Alert Message: Caution should be exercised when prescribing an antipsychotic with benzodiazepines. Concurrent use of these drugs can result in additive CNS effects (e.g., drowsiness, somnolence, orthostatic hypotension).

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.

55. All Antipsychotics / Respiratory Conditions
Alert Message: Caution should be exercised when prescribing an antipsychotic to patients with a history of respiratory depression, asthma, COPD, or sleep apnea. Antipsychotics can cause adverse respiratory effects, including dyspnea, which may exacerbate respiratory conditions.

References:
Clinical Pharmacology, 2026 Elsevier/Gold Standard.
Facts & Comparisons, 2026 Updates, Wolters Kluwer Health.

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?