

**North Dakota Medicaid
Drug Utilization Review Board Meeting
September 6, 2023
Conference Room 210/212**

Meeting Notice

North Dakota Medicaid Drug Use Review Board

Wednesday, September 6th, 2023

1 to 4 p.m. Central Time

In-Person Information

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

Virtual Information

Join virtually: [Click here to join the meeting](#)

Join by phone: 701-328-0950, Conference ID: 617 220 993#

Agenda

1. Call to Order
2. Roll Call
3. Review and Approval of Minutes
4. Reports from Department
 - Administrative Report: Unwinding, Humira biosimilars, RSV
 - Financial Report: Budget, Top Drugs
 - Clinical Report:
 - Prior authorization update
 - Annual PDL Review Criteria Updates for Gout, Chronic Kidney Disease, Heart Failure, Long-Acting Opioid Analgesics, Opioid Use Disorder, Clostridioides difficile-associated diarrhea (CDAD), Medications over \$3000
 - Retrospective DUR report
5. Unfinished Business
 - Update to Hyperparathyroidism (Sensipar)
6. New business
 - First Review of Diuretics (triamterene)
 - First Review of Menopause (Veoza)
 - Review of retrospective DUR criteria recommendations
7. Announcements
 - Next Meeting (December 6th, 2023)
8. Adjourn

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

Meeting Minutes
North Dakota Medicaid Drug Use Review (DUR) Board
Meeting Date: June 7th, 2023
Time and Location: 1:00 pm CST in Bismarck, North Dakota

Board Members:

Present: Andrea Honeyman, Gabriela Balf, Amy Werremeyer, Laura Kroetsch, Kevin Martian, Kristen Peterson, Josh Askvig, Stephanie Antony, Jennifer Iverson

Absent: Tanya Schmidt, Kathleen Traylor

Quorum Present: Yes

Medicaid Pharmacy Department:

Present: Brendan Joyce, LeNeika Roehrich, Alexi Murphy

Absent: Jeff Hostetter

Call to Order:

A regular quarterly meeting of the North Dakota Medicaid Drug Use Review (DUR) Board meeting was convened at 1:02 pm CST. with pro tem Presiding Officer K. Martian presiding, and DUR Board Coordinator, C. Stauter recording minutes. In Presiding Officer T. Schmidt's absence, K. Martian served as Presiding Officer pro tem.

Approval of Meeting Minutes:

The minutes of the March 1, 2023, meeting were approved as distributed.

Reports:

Administrative Report: Legislative Update provided by A. Murphy

A. Murphy shared with the Board all changes made affecting the DUR Board from Senate Bill 2156, effective August 1, 2023. These changes can be found in the handout.

Administrative Report: Robert's Rules of Order provided by A. Murphy

A. Murphy shared with the Board all changes made affecting the DUR Board elections, debate, minutes, old business, first and second reviews, and adjournment. These changes can be found in the handout.

Administrative Report: Member Update provided by A. Murphy

A. Murphy introduced the new Board Member S. Antony. L. Morgan introduced the new DUR Board Coordinator C. Stauter.

Financial Report: Budget provided by A. Murphy

A. Murphy shared with the Board the history of ND Medicaid pharmacy spending and rebates. These specifics can be found in the handout.

Financial Report: Top Drugs provided by L. Morgan

L. Morgan 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.

Clinical Report: Prior Authorization Update provided by A. Murphy

A. Murphy shared with the Board new medications requiring prior authorizations. This list can be found in the handout.

Clinical Report: Criteria Update

Update to Hepatitis C provided by A. Murphy

A. Murphy discussed the changes to the hepatitis C section to the PDL. L. Morgan presented the updated prior authorization form and consent forms for discussion. These changes can be found in the handout.

Update to Chronic Kidney Disease (Filspari) provided by L. Morgan

L. Morgan discussed the changes to the chronic kidney disease section to the PDL for discussion. These changes can be found in the handout.

Retrospective Drug Utilization Review (RDUR) Report: C. Stauter reviewed the quarterly RDUR criteria that were selected for review of each month. This material can be found in the handout.

Special Orders:

Presiding Officer and Vice-Presiding Officer Elections

Nomination by J. Askvig for T. Schmidt as Presiding Officer, motion was seconded, **motion carried.**

Nomination by J. Askvig for A. Honeyman as Vice-Presiding Officer, motion was seconded, **motion carried.**

New Business:

L. Morgan presented an overview of hyperparathyroidism, influenza, neuromyelitis optica spectrum disorder, and urea cycle agents. The presented material can be found in the handout.

RDUR criteria recommendations were reviewed. The presented material can be found in the handout.

Second Review of Hyperparathyroidism:

Motion: Moved by K. Martian for the Department to adopt criteria as distributed for hyperparathyroidism, motion was seconded. **Motion carried.**

Second Review of Influenza:

Motion: Moved by K. Martian for the Department to adopt criteria as distributed for influenza, motion was seconded. **Motion carried.**

Second Review of Neuromyelitis Optica Spectrum Disorder:

Motion: Moved by J. Askvig for the Department to adopt criteria as distributed for neuromyelitis optica spectrum disorder, motion was seconded. **Motion carried.**

Second Review of Urea Cycle Agents:

Motion: Moved by K. Martian for the Department to adopt criteria as distributed for urea cycle agents, motion was seconded. **Motion carried.**

Retrospective Drug Utilization Review (RDUR) Criteria Recommendations:

Motion: Moved by J. Askvig to approve the RDUR criteria, motion was seconded. **Motion carried.**

Announcements:

Next meeting is September 6th, 2023.

Adjournment:

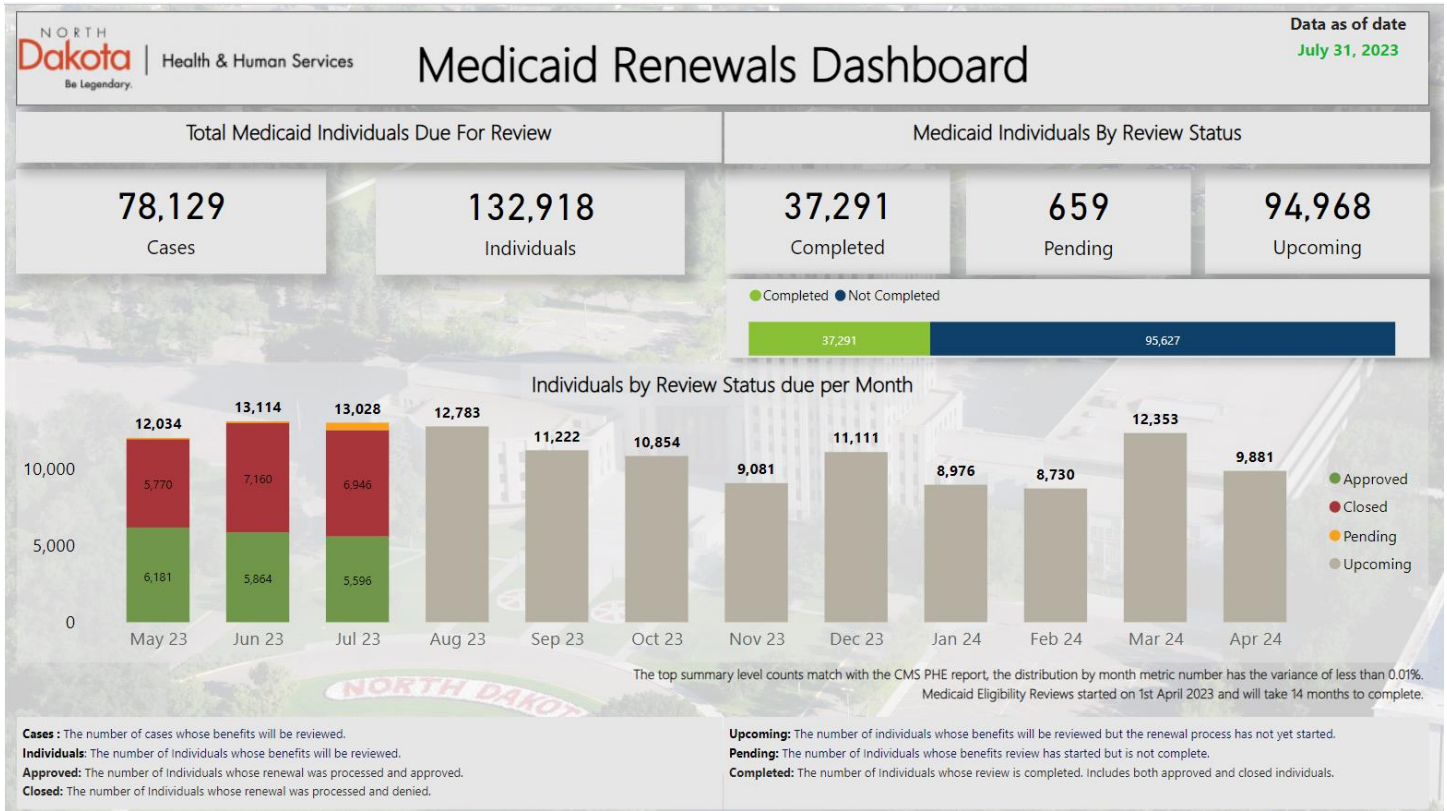
Meeting adjourned by K. Martian at 2:25 pm CST.

Date of Minutes Approval:

Minutes submitted by: Claire Stauter, Kepro

Unwinding:

<https://www.hhs.nd.gov/medicaid/data> > Medicaid Renewals:



RSV:

[ACIP and AAP Recommendations for Nirsevimab | Red Book Online | American Academy of Pediatrics](#)

Advisory Committee on Immunization Practices (ACIP) Recommendations:

On August 3, 2023, the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC) recommended use of nirsevimab as indicated in its FDA package insert:

- Infants aged <8 months born during or entering their first Respiratory Syncytial Virus (RSV) season are recommended to receive one dose of nirsevimab (50 mg for infants <5 kg and 100 mg for infants ≥5 kg).
- Children aged 8–19 months who are at increased risk of severe RSV disease and entering their second RSV season are recommended to receive one dose of nirsevimab (200 mg).

The ACIP also voted for inclusion of nirsevimab in the Vaccines for Children (VFC) program.

American Academy of Pediatrics (AAP) Recommendations

American Academy of Pediatrics Recommendations for the 2023–2024 RSV season with regard to palivizumab versus nirsevimab administration for high-risk infants during the same RSV season:

- If nirsevimab is administered, palivizumab should not be administered later that season.
- If palivizumab was administered initially for the season and <5 doses were administered, the infant should receive 1 dose of nirsevimab. No further palivizumab should be administered.
- If palivizumab was administered in season 1 and the child is eligible for RSV prophylaxis in season 2, the child should receive nirsevimab in season 2, if available. If nirsevimab is not available, palivizumab should be administered as previously recommended.

No recommendations from AAP/ACIP for use with monoclonal antibody prophylaxis:

Vaccine for respiratory syncytial virus (RSV) : Abrysvo

- For protection of infants from the virus from birth to 6 months of age to be given between weeks 32 and 36 of pregnancy (Approved August 2023)
- For protection of people aged 60 years and older (Approved May 2023)

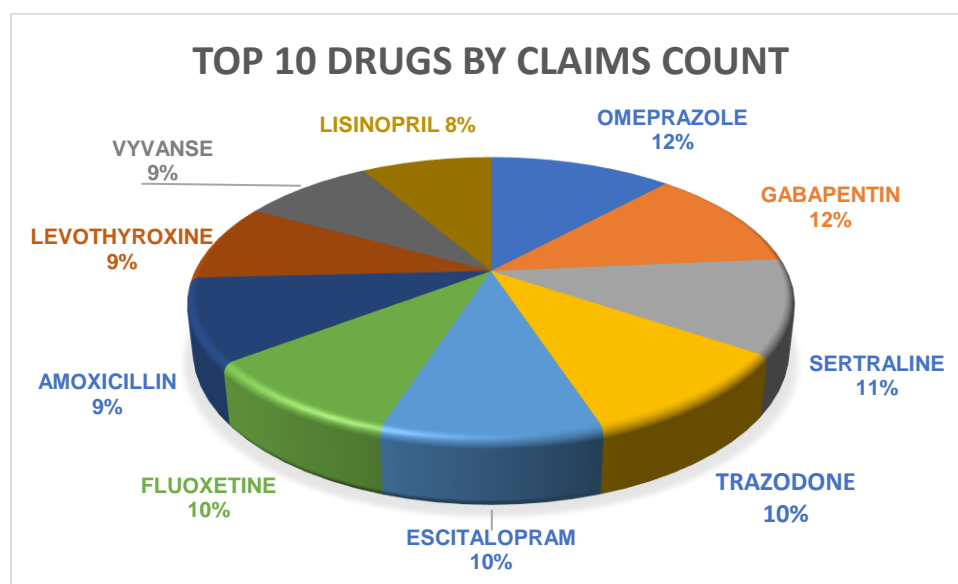
North Dakota Medicaid Plan

- Beyfortus (nirsevimab) is expected to be available in the U.S. ahead of the upcoming 2023-2024 RSV season.
- The North Dakota Department of Health and Human Services Immunization Unit supplies free vaccines for children who are eligible for the Vaccines for Children (VFC) program.
- ND Medicaid will not provide RSV prophylaxis (Synagis or Beyfortus) coverage for infants eligible to receive Beyfortus through the VFC program.
- Continue to monitor AAP/ACIP recommendations for updates regarding use of Abrysvo.

Top 25 Drugs Based on Number of Claims from 04/01/2023 – 06/30/2023

Drug	Claims	Claims Cost	Patients	Cost / Claim	% Total Claims	Dif.
1. OMEPRAZOLE	4,780	\$61,334.67	2,452	\$12.83	1.8%	NC
2. GABAPENTIN	4,756	\$70,617.96	2,047	\$14.85	1.8%	NC
3. SERTRALINE HCL	4,438	\$60,082.07	2,548	\$13.54	1.7%	NC
4. TRAZODONE HCL	4,034	\$54,266.42	2,068	\$13.45	1.5%	NC
5. ESCITALOPRAM	4,029	\$54,166.97	2,369	\$13.44	1.5%	↑1
6. FLUOXETINE HCL	3,967	\$52,665.49	2,178	\$13.28	1.5%	↑1
7. AMOXICILLIN	3,745	\$53,781.88	3,529	\$14.36	1.4%	↓2
8. LEVOTHYROXINE	3,558	\$56,732.96	1,904	\$15.95	1.3%	↑1
9. VYVANSE	3,445	\$959,714.37	1,456	\$278.58	1.3%	↓1
10. LISINOPRIL	3,408	\$44,206.91	2,082	\$12.97	1.3%	NC
11. ATORVASTATIN	3,311	\$46,943.20	1,978	\$14.18	1.2%	NC
12. BUPROPION XL	3,269	\$55,023.40	1,806	\$16.83	1.2%	NC
13. PANTOPRAZOLE	3,142	\$43,799.50	1,565	\$13.94	1.2%	NC
14. VENTOLIN HFA	3,049	\$195,110.70	3,023	\$63.99	1.1%	↑9
15. HYDROCODONE-APAP	2,812	\$40,883.63	1,788	\$14.54	1.0%	↓1
16. CYCLOBENZAPRINE	2,730	\$31,639.66	1,737	\$11.59	1.0%	↓1
17. DULOXETINE HCL	2,722	\$44,150.27	1,448	\$16.22	1.0%	↓1
18. CLONIDINE HCL	2,688	\$32,921.20	1,355	\$12.25	1.0%	NC
19. HYDROXYZINE HCL	2,653	\$35,848.70	1,667	\$13.51	1.0%	↑2
20. PREDNISONE	2,623	\$31,457.70	2,148	\$11.99	1.0%	NC
21. LAMOTRIGINE	2,597	\$36,996.03	1,116	\$14.25	1.0%	↑3
22. AMOXICILLIN-CLAV	2,487	\$44,172.95	2,336	\$17.76	0.9%	↓5
23. BUP-NALOXONE	2,472	\$105,145.74	667	\$42.53	0.9%	↓1
24. BUSPIRONE HCL	2,371	\$36,045.20	1,329	\$15.20	0.9%	↑1
25. AMLODIPINE	2,350	\$30,116.93	1,363	\$12.82	0.9%	↑4

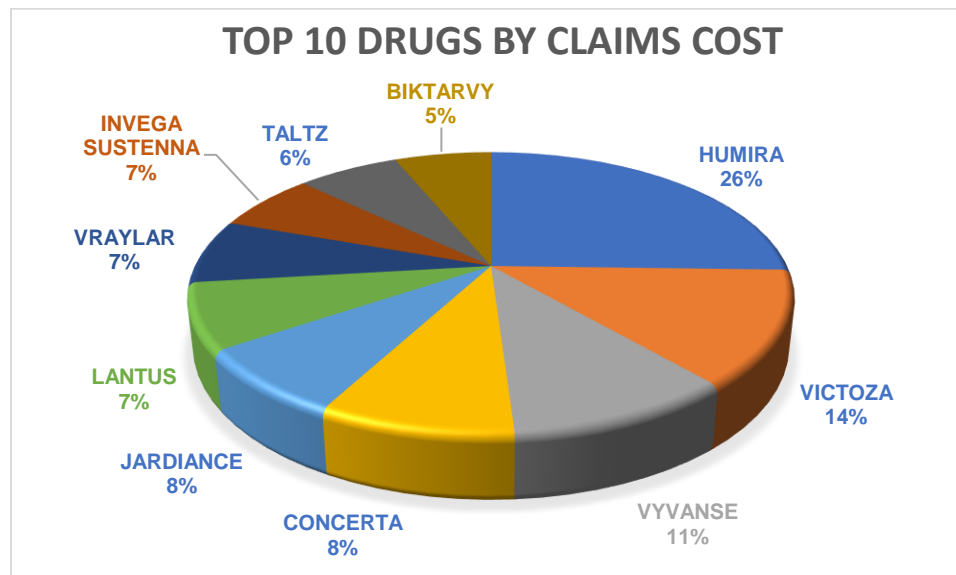
Total Claims	268,762
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Top 25 Drugs Based on Total Claims Cost from 04/01/2023 – 06/30/2023

Drug	Claims	Claims Cost	Patients	Cost / Patient	% Total Cost	Dif.
1. HUMIRA	298	\$2,369,800.15	129	\$36,805.07	6.8%	NC
2. VICTOZA	1,440	\$1,280,526.06	722	\$3,437.17	3.7%	NC
3. VYVANSE	3,445	\$959,714.37	1,456	\$659.14	2.8%	NC
4. CONCERTA	2,021	\$742,939.96	878	\$846.17	2.1%	NC
5. JARDIANCE	1,054	\$719,714.34	562	\$1,280.63	2.1%	↑1
6. LANTUS SOLOSTAR	1,315	\$674,274.62	815	\$827.33	1.9%	↓1
7. VRAYLAR	627	\$606,021.84	267	\$2,269.74	1.7%	↑5
8. INVEGA SUSTENNA	234	\$603,537.30	94	\$6,420.61	1.7%	↓1
9. TALTZ	90	\$563,834.38	37	\$15,238.77	1.6%	↓1
10. BIKTARVY	246	\$474,504.98	121	\$3,921.53	1.4%	NC
11. STELARA	19	\$449,263.66	16	\$28,078.98	1.3%	↓2
12. ADDERALL XR	2,210	\$407,926.75	972	\$419.68	1.2%	↑2
13. MAVYRET	33	\$404,248.01	21	\$19,249.91	1.2%	↓3
14. ELIQUIS	706	\$398,791.14	341	\$1,169.48	1.1%	↓1
15. TRIKAFTA	19	\$396,954.88	8	\$49,619.36	1.1%	↑4
16. SYMBICORT	1,100	\$386,516.13	640	\$603.93	1.1%	NC
17. NORDITROPIN	85	\$359,585.00	40	\$8,989.63	1.0%	↑4
18. ADVAIR DISKUS	914	\$342,726.20	506	\$677.32	1.0%	↓1
19. NOVOLOG FLEXPEN	452	\$340,017.54	287	\$1,184.73	1.0%	↓1
20. ABILIFY MAINTENA	121	\$288,510.77	49	\$5,887.97	0.8%	NC
21. DUPIXENT PEN	88	\$281,760.55	38	\$7,414.75	0.8%	↑1
22. SOFO-VELPATASVIR	35	\$273,263.30	15	\$18,217.55	0.8%	↑17
23. XIFAXAN	93	\$251,608.20	45	\$5,591.29	0.7%	NC
24. SUBLOCADE	129	\$249,351.84	60	\$4,155.86	0.7%	↑10
25. LEVEMIR FLEXPEN	403	\$248,682.67	251	\$990.77	0.7%	↑2

Total Claims Cost	\$34,870,800.35
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Top 15 Therapeutic Classes Based on Number of Claims from 04/01/2023 – 06/30/2023

Therapeutic Class Description	Claims	Claims Cost	Patients	Cost/Claim	% Total Claims	Dif.
1. ANTIDEPRESSANTS	30,485	\$660,732.16	13,096	\$21.67	11.3%	NC
2. ANTICONVULSANTS	13,862	\$551,732.40	5,065	\$39.80	5.2%	NC
3. ANTIPSYCHOTICS	9,672	\$2,433,160.77	3,922	\$251.57	3.6%	NC
4. PPI'S	8,322	\$157,833.32	4,160	\$18.97	3.1%	NC
5. ANXIOLYTICS, SEDATIVES, HYPNOTICS	7,696	\$111,802.75	4,041	\$14.53	2.9%	NC
6. AMPHETAMINES	7,175	\$1,423,056.31	3,065	\$198.34	2.7%	NC
7. OPIATE AGONISTS	6,865	\$108,986.71	3,680	\$15.88	2.6%	↑1
8. PENICILLIN ANTIBIOTICS	6,564	\$103,267.77	5,932	\$15.73	2.4%	↓1
9. NSAIDS	6,416	\$89,525.82	4,314	\$13.95	2.4%	NC
10. STATINS	5,910	\$85,875.84	3,491	\$14.53	2.2%	↑1
11. RESP/CNS STIMULANTS	5,723	\$957,880.83	2,250	\$167.37	2.1%	↓1
12. BETA BLOCKING AGENTS	5,566	\$99,228.03	3,125	\$17.83	2.1%	NC
13. ADRENALS	4,374	\$59,273.88	3,505	\$13.55	1.6%	NC
14. BETA AGONISTS	4,333	\$261,176.56	3,970	\$60.28	1.6%	NC
15. ACE INHIBITORS	4,238	\$67,143.00	2,567	\$15.84	1.6%	NC

Top 15 Therapeutic Classes Based on Claims Cost from 04/01/2023 – 06/30/2023

Therapeutic Class Description	Claims	Claims Cost	Patients	Cost/Patient	% Total Cost	Dif.
1. DMARDS	652	\$3,867,842.27	272	\$14,220.01	11.1%	NC
2. ANTIPSYCHOTICS	9,672	\$2,433,160.77	3,922	\$620.39	7.0%	NC
3. SKIN AGENTS	702	\$2,061,210.88	420	\$4,907.64	5.9%	NC
4. INSULINS	3,609	\$1,902,722.57	1,451	\$1,311.32	5.5%	NC
5. INCRETIN MIMETICS	1,646	\$1,461,430.59	756	\$1,933.11	4.2%	↑2
6. ANTINEOPLASTICS	634	\$1,436,618.88	267	\$5,380.60	4.1%	↓1
7. AMPHETAMINES	7,175	\$1,423,056.31	3,065	\$464.29	4.1%	↓1
8. CORTICOSTEROID (RESP)	3,705	\$1,102,822.73	2,242	\$491.89	3.2%	↑1
9. SGLT-2 INHIBITORS	1,470	\$978,569.30	782	\$1,251.37	2.8%	↑2
10. RESP/CNS STIMULANTS	5,723	\$957,880.83	2,250	\$425.72	2.7%	NC
11. ANTIRETROVIRALS	736	\$946,848.72	291	\$3,253.78	2.7%	↓3
12. HCV ANTIVIRALS	68	\$677,511.31	36	\$18,819.76	1.9%	↑1
13. ANTIDEPRESSANTS	30,485	\$660,732.16	13,096	\$50.45	1.9%	↓1
14. IMMUNOMODULATORY	88	\$586,616.81	36	\$16,294.91	1.7%	↑2
15. ANTICOAGULANTS	1,508	\$558,295.57	649	\$860.24	1.6%	NC

PA / PDL Update	PA Status	Class
Fabior (tazarotene) foam	PA	Acne
Carac (fluorouracil) cream	PA	Actinic Keratosis
Suflave	PA	Bowel Prep Agents
Rinvoq	PA	Crohn's
alosectron	PA	Diarrhea - IBS
Miebo	PA	Dry Eye Disease
Olumiant	PA	Eczema/Atopic Dermatitis
Menest	PA	Estrogens
travoprost	PA	Glaucoma
apraclonidine	PA	Glaucoma
tafluprost	PA	Glaucoma
Sogroya	PA	Growth Hormone
Rayaldee ER	PA	Hyperparathyroidism
doxercalciferol	PA	Hyperparathyroidism
Xofluza	PA	Influenza
Zavzpret	PA	Migraine
Fosamax D	PA	Osteoporosis
Elepsia XR	PA	Preferred Dosage Forms
Spritam	PA	Preferred Dosage Forms
Sympazan	PA	Preferred Dosage Forms
olanzapine/fluoxetine	PA	Preferred Dosage Forms
Cotempla XR - ODT	PA	Preferred Dosage Forms
amphetamine ER Suspension	PA	Preferred Dosage Forms
Pexeva	PA	Preferred Dosage Forms
Liqrev	PA	Pulmonary Hypertension
Pandel	PA	Topical Steroids
Fluocinonide-E cream	PA	Topical Steroids
Olpruva	PA	Urea Cycle Disorders
Symproic	remove PA	Constipation (Opioid-Induced)
Simponi	remove PA	Cytokine Modulators
Nivestym	remove PA	Hematopoietic, Colony Stimulating Factor
Releuko	remove PA	Hematopoietic, Colony Stimulating Factor
Nexletol	remove PA	Lipid-Lowering Agents
Nexlizet	remove PA	Lipid-Lowering Agents
gatifloxacin eye drops	remove PA	Ophthalmic - Antiinfectives
Airduo Respiclick	remove PA	Steroid/LABA combination inhalers
Tlando	remove PA	Testosterone
clocortolone cream	remove PA	Topical Steroids
halobetasol ointment	remove PA	Topical Steroids
desoximetasone cream	remove PA	Topical Steroids

Chronic Kidney Disease

Prior Authorization Criteria

Initial Criteria - Approval Duration: 12 months

- If member is on renal dialysis, Medicare eligibility must be ruled out.

Filspari Only

- The member must have eGFR ≥ 30 .
- The member must be experiencing proteinuria ≥ 1 gram/day or UPCR ≥ 1.5 g/g (documentation must be attached) despite 3-month trials with good compliance of the following at the target or maximally tolerated dose, as evidenced by paid claims or pharmacy printouts:
 - ACE inhibitor or an ARB
 - A SGLT-2 inhibitor

Inpefa Only:

- The requested medication must be prescribed by, or in consult with, a cardiologist or nephrologist.
- If member is on renal dialysis, Medicare eligibility must be ruled out.
- The member has type 2 diabetes and chronic kidney disease.
- The member has a history of a cardiovascular event (e.g., heart failure, myocardial infarction, cerebrovascular event) or two or more risk factors (e.g., elevated cardiac and inflammatory biomarker, obesity, hyperlipidemia, hypertension)
- The member is receiving concurrent Entresto, a beta-blocker, a SGLT-2 Inhibitor, and a mineralocorticoid receptor antagonist.
- Clinical justification must be provided explaining why the member is unable to use Farxiga and Jardiance (subject to clinical review)

Kerendia Only

- The member must have history of diabetes
- The member must be on the following at the target or maximally tolerated dose, as evidenced by paid claims or pharmacy printouts:
 - An ACE-inhibitor or an ARB
 - A SGLT-2 inhibitor
- The member has an estimated glomerular filtration rate (eGFR) ≥ 25 mL/min/1.73 m² AND one of the following (1 or 2):
 1. Urinary albumin-to-creatinine ratio (UACR) ≥ 30 mg/g (≥ 3 mg/mmol)
 2. Albuminuria ≥ 300 mg/day

Korsuva Only

- The member must have failed a 90-day trial of pregabalin or gabapentin, as evidenced by paid claims or pharmacy printouts.

Tarpeyo Only

- The member must have eGFR ≥ 30 .
- The member must be experiencing proteinuria > 1 gram/day or UPCR ≥ 1.5 g/g (documentation must be attached) despite 6-month trials with good compliance of the following at the target or maximally tolerated dose, as evidenced by paid claims or pharmacy printouts:
 - ACE inhibitor or an ARB
 - A SGLT-2 inhibitor
 - Prednisone or methylprednisolone

Renewal Criteria - Approval Duration: 12 months

- The member must have experienced meaningful clinical benefit since starting treatment with the requested medication, as evidenced by medical documentation (e.g., chart notes) attached to the request (subject to clinical review) including one of the following scores and symptoms:
 - *Filspari and Tarpeyo Only*: proteinuria <1 gram/day or UPCR < 1.5 g/g
 - *Kerendia Only*: albuminuria <1 gram/day or UACR < 1.5 g/g

References:

1. Rossing, Peter, et al. "KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease." *Kidney international* 102.5 (2022): S1-S127.
2. de Boer, Ian H., et al. "Diabetes management in chronic kidney disease: a consensus report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO)." *Diabetes care* 45.12 (2022): 3075-3090.

Heart Failure

First Line Agents

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
ACE (angiotensin-converting enzyme) inhibitors - <i>all oral agents preferred</i>	INPEFA (sotagliflozin)
ARBs (angiotensin receptor blockers) - <i>all oral agents preferred</i>	
Beta blockers - <i>all oral agents preferred</i>	
ENTRESTO (sacubitril/valsartan)	
FARXIGA (dapagliflozin)	
JARDIANCE (empagliflozin)	

Second Line Agents

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
CORLANOR (ivabradine)	
VERQUVO (vericiguat)	

Electronic Diagnosis Verification

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

Prior Authorization Criteria

Initial Criteria - Approval Duration: 12 months

- Corlanor Only:
 - The requested medication must be prescribed by, or in consult with, a cardiologist.
 - The member must have a resting HR \geq 70 beats per minute on maximally tolerated or target beta blocker dose in sinus rhythm.
- 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, a SGLT-2 Inhibitor, and a mineralocorticoid receptor antagonist.
 - 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.
 - Clinical justification must be provided explaining why the member is unable to use Farxiga and Jardiance (subject to clinical review)
- 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.
 - Documentation of a recent hospitalization or need for IV diuretics within the past 6 months must be provided with request.
 - The member is receiving concurrent Entresto, a beta-blocker, a SGLT-2 Inhibitor, and a mineralocorticoid receptor antagonist.

Opioid Analgesics

Opioid Analgesics – Long Acting

Partial Agonist/Antagonist Opioids

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
BELBUCA (buprenorphine)	buprenorphine patches
Butorphanol	
BUTRANS (buprenorphine) PATCHES - <i>Brand Required</i>	

Abuse Deterrent Formulations/Unique Mechanisms from Full Agonists Opioids

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
NUCYNTA ER (tapentadol)	CONZIP (tramadol ER) CAPSULES
OXYCONTIN (oxycodone) – <i>Brand Required</i>	hydrocodone ER tablets
tramadol ER Tablets	HYSINGLA ER (hydrocodone)
	levorphanol
	methadone
	MORPHABOND ER (morphine)
	tramadol ER capsules
	XTAMPZA ER (oxycodone)

Full Agonist Opioids Without Abuse Deterrent Formulations

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
fentanyl 12 mcg/hr, 25 mcg/hr, 50 mcg/hr, 75 mcg/hr, 100 mcg/hr	fentanyl patch 37.5 mcg/hr, 62.5 mcg/hr, 87.5 mcg/hr
morphine ER tablets	hydrocodone ER capsules
	hydromorphone ER tablets
	morphine ER capsules
	MS CONTIN (morphine)
	oxycodone ER
	oxymorphone ER tablets

Prior Authorization Criteria

[Prior Authorization Form – Opioid Analgesics](#)

Initial Criteria - Approval Duration: 12 months

- The past 3 months of the member's North Dakota PDMP reports must have been reviewed.
- One of the following criteria must be met:
 - The member has access to Narcan and has been counseled on overdose risk
 - The member resides in a facility with skilled nursing care
- One of the following criteria must be met:
 - The member is currently on a long-acting opioid therapy
 - The member must have received opioid therapy during hospitalization requiring post discharge maintenance or tapering
 - Both of the following are met:

- The member must have a diagnosis of cancer pain, palliative care, or sickle cell disease
- The member must currently be on around-the-clock opioid therapy of at least 60 Morphine Milligram equivalents (MME) for at least a week, as evidenced by paid claims or pharmacy printouts
 - If member is unable to swallow (e.g., mucositis, head/neck radiation, head/neck cancers, uncontrollable vomiting) and has severe pain (>6/10), fentanyl patch 12.5 mcg/hr may be considered for approval for opioid naïve members (subject to clinical review).
- Both of the following are met:
 - The member has established opioid tolerability by using short acting opioids daily for at least 90 days prior to request for long-acting opioid as evidenced by paid claims or pharmacy printouts
 - The member has not achieved therapeutic goal with non-narcotic medication (NSAIDs, TCAs, SNRIs, corticosteroids, etc.) and non-medication alternatives (weight loss, physical therapy, cognitive behavioral therapy, etc.).
- One of the following criteria must be met:
 - The member resides in a facility with skilled nursing care
 - The member must have taper plan of one or both agents
 - The opioid medication must be prescribed by, or in consult with, with an oncologist or pain management specialist with a pain management contract (with treatment plan including goals for pain and function, and urine and/or blood screens) if the cumulative daily dose of opioids exceeds 90 MME/day

Fentanyl Patch:

- The member must have a BMI ≥ 17

Non-Preferred Agents Criteria:

- Clinical justification must be provided explaining why the member is unable to use other opioid and non-opioid analgesic agents (subject to clinical review).

Renewal Criteria - Approval Duration: 12 months

- One of the following must be met:
 - Documentation noting progress toward therapeutic goal must be included with request (e.g., improvement in pain level, quality in life, or function).
 - The member must be stable on long-acting opioid medication for 2 years or longer

Opioid Use Disorder

Mono Product

Oral Agents

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
	buprenorphine tablets++

++ Clinically Non-Preferred: Naloxone is added to buprenorphine to prevent misuse. When taken correctly, a baby will have little to no absorption of naloxone which a growing body of evidence show is safe. Taking combination product during pregnancy or breastfeeding means that products don't need to be switched to a different medication after the baby is born during this high anxiety time. Risk of withdrawal to a neonate is a labeled warning on each product. Pregnancy and breastfeeding are not listed as contraindications on either product.

References:

1. *Opioid use and opioid use disorder in pregnancy. Committee Opinion No. 711. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;130:e81–94.*
2. *Perry, Briana N. MD; Vais, Simone BA; Miller, Melissa BA; Saia, Kelley A. MD. Buprenorphine-Naloxone Versus Buprenorphine for Treatment of Opioid Use Disorder in Pregnancy [07E]. Obstetrics & Gynecology 135():p 51S, May 2020. | DOI: 10.1097/01.AOG.0000663444.50960.74*
3. *Substance Abuse and Mental Health Services Administration. Clinical Guidance for Treating Pregnant and Parenting Women With Opioid Use Disorder and Their Infants. HHS Publication No. (SMA) 18-5054. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2018.*

Prior Authorization Criteria

Prior Authorization Form – Opioid Dependence

Initial Criteria - Approval Duration: 1 year

- Clinical justification must be provided explaining why the member is unable to use the preferred agents (subject to clinical review)
 - Pregnancy or breastfeeding will not be approved as clinical justification based on the clinically non-preferred information provided above.
 - Allergy to oral naloxone is extremely rare and must be well documented.
 - Any request for transmucosal buprenorphine should include justification why long-acting injectable buprenorphine can't be used (while need for long-term transmucosal stability will not be considered, limited approval may be granted to allow for recommended pre-treatment and titration prior to initiation of long-acting buprenorphine product - maximum of 14 days for Sublocade, and 1 dose for Brixadi)

Non-Oral Agents

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
BRIXADI (buprenorphine)	
SUBLOCADE (buprenorphine)	

Combination Product

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
buprenorphine-naloxone tablets	BUNAVAIL FILM (buprenorphine/naloxone)
	buprenorphine/naloxone film
	SUBOXONE FILM (buprenorphine/naloxone)
	ZUBSOLV (buprenorphine/naloxone)

Prior Authorization Criteria

- See [DAW \(Dispense As Written\) Criteria](#)

Clostridioides difficile-associated diarrhea (CDAD)

Prevention

Fecal Microbiota

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
REBYOTA (fecal microbiota, live-jslm) SUSPENSION – <i>Medical Billing Only</i>	
VOWST (fecal microbiota spores, live-brpk) CAPSULE	

Monoclonal Antibody

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
ZINPLAVA (bezlotoxumab) – <i>Medical Billing Only</i>	

Electronic Duration Verification:

- Rebyota and Vowst is payable every 6 months.

Prior Authorization Criteria

Initial Criteria - Approval Duration: 12 months

- The member has one of the following (1 or 2):
 3. The member has had at least two episodes of diarrhea with a positive stool test for *C.difficile* toxin within the last year
 4. The member has had at least one previous episodes of diarrhea with a positive stool test for *C.difficile* toxin within the last year AND one of the following
 - *C. difficile* infection was severe (defined as ZAR score ≥ 2)
 - Member is immunocompromised

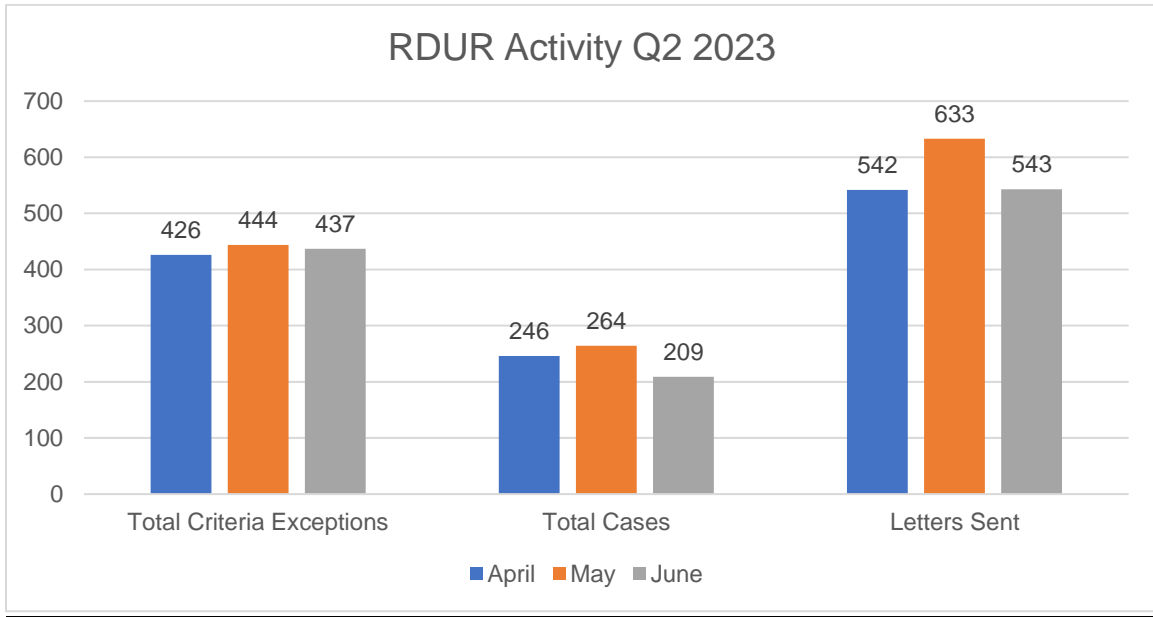
Medications that cost over \$3000/month

Prior Authorization Criteria

Initial Criteria - Approval Duration: 6 months

- The member must meet FDA-approved label for use (e.g., use outside of studied population will be considered investigational)
- The requested medication must be prescribed by, or in consult with, a specialist in the member's treated diagnosis
- As applicable, documentation must be attached to confirm serum marker or pathogenic gene variants amenable to treatment
- Documentation of the baseline labs, signs or symptoms that can be utilized for comparison to show member has experienced clinical benefit upon renewal has been submitted with request

RDUR Activity Overview: Q2 2023



April Cases by Type of Criteria

Criteria Description	# of Cases	% of Cases
Clinical Appropriateness	45	18.3%
Drug-Disease Interactions	148	60.2%
Drug-Drug Conflicts	53	21.5%

May Cases by Type of Criteria

Criteria Description	# of Cases	% of Cases
Adverse Effects	13	4.9%
Drug-Disease Interactions	251	95.1%

June Cases by Type of Criteria

Criteria Description	# of Cases	% of Cases
Drug-Disease Interactions	38	18.2%
Drug-Drug Conflicts	169	80.9%
Therapeutic Duplication	2	1.0%

Hyperparathyroidism

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
calcitriol	doxercalciferol
paricalcitol	HECTOROL (doxercalciferol)
	RAYALDEE ER (calcifediol)
	ROCALTROL (calcitriol)
	SENSIPAR (cinacalcet)
	ZEMPLAR (paricalcitol)

++ cinacalcet is associated with hypocalcemia, increased urinary calcium excretion, and increased serum phosphate levels

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 member must have failed a 30-day trial of each preferred medication
- Clinical justification must be provided explaining why the member is unable to use the preferred agents (subject to clinical review).

Cinacalcet Only:

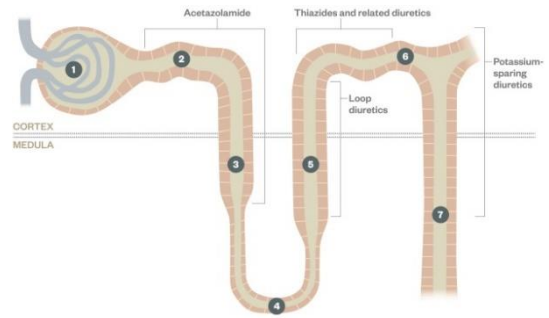
- If member is on renal dialysis, Medicare eligibility must be ruled out.

References:

1. Quarles LD. Management of secondary hyperparathyroidism in adult non-dialysis patients with chronic kidney disease. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA, 2023

REVIEW OF DIURETICS

Diuretics are oftentimes used in heart failure (HF) and hypertension (HTN) due to their ability to increase excretion of sodium and water. Diuretics consist of different classes based on their mechanism of action including loop, thiazide, potassium sparing, and carbonic anhydrase inhibitors. Carbonic anhydrase inhibitors are not included in the chart below due to their limited use as diuretics.



Per the Pharmaceutical Journal, Diuretic Therapy Explained

	Loop	Thiazides	Potassium (K)-Sparing	
Drugs	Bumetanide Ethacrynic acid Furosemide Torsemide	Chlorthalidone Hydrochlorothiazide Indapamide Metolazone	Amiloride Triamterene	Spirolactone Eplerenone
Mechanism	Inhibits sodium-chloride (Na-Cl) reabsorption in the ascending loop of Henle	Inhibits Na reabsorption in the distal tubule	Inhibits Na reabsorption in exchange for K at the distal tubule	Aldosterone antagonist
Primary use	HF : fluid retention	HTN	Added to limit hypokalemia caused by other diuretics	<ul style="list-style-type: none"> Resistant HTN HF: ascites
Key notes	<ul style="list-style-type: none"> Sulfonamide derivatives (except ethacrynic acid) Electrolyte imbalances (including hypokalemia) 		<ul style="list-style-type: none"> Risk of hyperkalemia, requires monitoring of K levels in patients at higher risk 	

Triamterene

FDA Approval

Triamterene: 505(j) Abbreviated New Drug Application (ANDA) pathway, standard

Cost of Potassium-Sparing Diuretics Per Year

Amiloride: \$109.50 • Plus HCTZ (\$10.95): \$120.45 • Amiloride/HCTZ combination: \$251	Spirolactone: \$36.50 Plus HCTZ (\$10.95): \$47.45 • Spirolactone/HCTZ combination: \$427.05
Triamterene: \$4,872.75 • Plus HCTZ (\$7.30): \$4,880.05 • Triamterene/HCTZ combination: \$73	Eplerenone: \$474.50 • No combination products

Based on adult dosing at lowest per unit WAC cost.

Advantages	Disadvantages
<ul style="list-style-type: none"> Limits hypokalemia when used alongside other diuretics 	<ul style="list-style-type: none"> Mono product increases pill burden and may decrease adherence Cost is higher for mono product, and the most frequent use is in combination with HCTZ Not a first line agent for HTN per guideline recommendations Risk of hyperkalemia

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1. Brater DC, Ellison DH. Mechanism of action of diuretics. UpToDate, November 30, 2022. https://www.uptodate.com/contents/mechanism-of-action-of-diuretics?search=diuretic&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1
2. Brater DC, Ellison DH. Loop diuretics: Dosing and major side effects. UpToDate, January 24, 2023. https://www.uptodate.com/contents/loop-diuretics-dosing-and-major-side-effects?search=diuretic&topicRef=2338&source=see_link
3. Loop Diuretics. Drug Facts And Comparisons, March 9, 2020. https://fco.factsandcomparisons.com/lco/action/doc/retrieve/docid/fc_dfc/5545873?cesid=3hUS8YbzYwE&searchUrl=%2Ffco%2Faction%2Fsearch%3Fq%3Dloop%2Bdiuretics%26t%3Dname%26acs%3Dtrue%26acq%3Dloop%26nq%3Dtrue
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14. Hydrochlorothiazide and Triamterene Oral. Drug Facts And Comparisons, June 28, 2023. https://fco.factsandcomparisons.com/lco/action/doc/retrieve/docid/fc_dfc/5548990?cesid=3JXlba1okTA&searchUrl=%2Ffco%2Faction%2Fsearch%3Fq%3Dtriamterene%2Band%2BhydroCHLOROthiazide%26t%3Dname%26acs%3Dtrue%26acq%3Dtriamt%26nq%3Dtrue
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REVIEW OF MENOPAUSE

Menopause is caused by decreased ovarian production of estrogen and other hormones with age. Patients may experience vasomotor symptoms (VMS) and genitourinary syndrome (GSM) which can decrease quality-of-life (QOL).

VMS: hot flashes	GSM: vulvovaginal atrophy (dryness, dyspareunia)
First line: systemic hormonal therapy * Non-hormonal treatment is recommended for women who are unable to take first line agents due to contraindications, comorbidities, or patient preference	First line: local therapies <ul style="list-style-type: none"> • Low-dose vaginal estrogens • Ospemifene • Lubricants

Hormonal Therapy			
<ul style="list-style-type: none"> • Most effective for VMS and GSM • Shown to prevent bone loss and fractures 			
Drug class	Estrogen	Estrogen-progestin	Estrogen-SERM: Duavee
Patient population	Women who have had a hysterectomy	Women who have an intact uterus	Women who cannot tolerate progestin
Formulations	Multiple formulations for systemic and local use		Oral
Warnings	Risk of cardiovascular disease (CVD), hormonal cancer, lipid effects		
Cost per year	Ranges from approximately \$21.92 [±] to \$3,660.95 [‡]		\$2,325.05
Contraindications	<ul style="list-style-type: none"> • History of hormone dependent cancer • History of venous thromboembolism (VTE), myocardial infarction (MI) or transient ischemic attack (TIA) • Liver disease • Unexplained vaginal bleeding, thrombophilia disorders • Pregnancy 		
Non-Hormonal Therapy			
<ul style="list-style-type: none"> • Indicated for VMS • Recommended for patients who cannot take or are hesitant to take hormonal therapies 			
Medication	Paroxetine	Veozah	
Mechanism	SSRI	Neurokinin-3 (NK3) receptor antagonist	
Key Points	Beneficial for patients also suffering from depression	<ul style="list-style-type: none"> • Liver function tests are needed every 3 months within the first year due to the risk of hepatic impairment • Contraindicated in liver and kidney impairment 	
Cost per year	\$1,671.70	\$6,690.45	

Based on adult dosing at lowest per unit WAC cost. ± Oral estradiol ‡ Activella

*** Medications that do not have an FDA approved indication for menopause but are used off-label: selective serotonin reuptake inhibitors (SSRIs), selective norepinephrine reuptake inhibitors (SNRIs), gabapentin, clonidine, oxybutynin.

Veozah

FDA Approval

Veozah: 505(b) New Drug Application (NDA) pathway, Type 1 – New Molecular Entity, PRIORITY

Advantages	Disadvantages
<ul style="list-style-type: none"> • Alternative for patients who are unable or hesitant to take hormonal therapy • No risk of VTE or cancer 	<ul style="list-style-type: none"> • Cost • Liver dysfunction • Frequent liver function tests required • Minimal data and long-term effects are unknown • No head-to-head trials • Doesn't treat GSM symptoms

References:

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2. *New Drug Review: Veozah (fezolinetant)*. IPD Analytics. Aventura, FL, 2021. June 2023. <https://www.ipdanalytics.com>.
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NORTH DAKOTA MEDICAID RETROSPECTIVE DRUG UTILIZATION REVIEW CRITERIA RECOMMENDATIONS 3RD QUARTER 2023

Criteria Recommendations

Approved Rejected

1. Elacestrant / Overuse

Alert Message: Orserdu (elacestrant) may be over-utilized. The recommended dosage of elacestrant is 345 mg taken orally with food once daily until disease progression or unacceptable toxicity occurs.

Drugs/Diseases

Util A Util B Util C
Elacestrant

Max Dose: 345 mg/day

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Orserdu Prescribing Information, Jan. 2023, Stemline Therapeutics, Inc.

2. Elacestrant / Therapeutic Appropriateness

Alert Message: The safety and effectiveness of Orserdu (elacestrant) in pediatric patients have not been established.

Drugs/Diseases

Util A Util B Util C
Elacestrant

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Orserdu Prescribing Information, Jan. 2023, Stemline Therapeutics, Inc.

3. Elacestrant / Severe Hepatic Impairment

Alert Message: Avoid the use of Orserdu (elacestrant) in patients with severe hepatic impairment (Child-Pugh C). Elacestrant has not been studied in patients with severe hepatic impairment.

Drugs/Diseases

Util A Util B Util C
Elacestrant Cirrhosis
 Liver Failure

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Orserdu Prescribing Information, Jan. 2023, Stemline Therapeutics, Inc.

Criteria Recommendations

Approved Rejected

4. Elacestrant 345 mg / Moderate Hepatic Impairment

Alert Message: Patients who have moderate hepatic impairment (Child-Pugh B) taking Orserdu (elacestrant) should receive a reduced dose. The recommended dose of elacestrant in patients with moderate hepatic impairment is 258 mg once daily. In pharmacokinetic studies, the AUC of elacestrant increased in subjects with moderate hepatic impairment (Child-Pugh B) by 83%. There were no clinically significant differences in the C_{max} and AUC of elacestrant in subjects with mild hepatic impairment (Child-Pugh A).

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Elacestrant	Moderate Hepatic Impairment	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Orserdu Prescribing Information, Jan. 2023, Stemline Therapeutics, Inc.

5. Elacestrant / Dyslipidemia

Alert Message: In clinical trials, hypercholesterolemia and hypertriglyceridemia occurred in patients taking Orserdu (elacestrant) at an incidence of 30% and 27%, respectively. The incidence of Grade 3 and 4 hypercholesterolemia and hypertriglyceridemia were 0.9% and 2.2%, respectively. Monitor lipid profile prior to starting and periodically while taking elacestrant.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Elacestrant	Hypercholesterolemia Hypertriglyceridemia	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Orserdu Prescribing Information, Jan. 2023, Stemline Therapeutics, Inc.

6. Elacestrant / Strong and Moderate CYP3A4 Inducers

Alert Message: The concurrent use of Orserdu (elacestrant) with a moderate or strong CYP3A4 inducer should be avoided. Elacestrant is a CYP3A4 substrate, and concomitant use with a strong or moderate CYP3A4 inducer may decrease elacestrant exposure, which may decrease the effectiveness of elacestrant.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Elacestrant	Apalutamide Bosentan Carbamazepine Efavirenz Etravirine Phenobarbital Phenytoin Primidone Rifabutin Rifampin Rifapentine	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Orserdu Prescribing Information, Jan. 2023, Stemline Therapeutics, Inc.

Criteria Recommendations

Approved Rejected

7. Elacestrant / Strong and Moderate CYP3A4 Inhibitors

Alert Message: The concurrent use of Orserdu (elacestrant) with a moderate or strong CYP3A4 inhibitor should be avoided. Elacestrant is a CYP3A4 substrate, and concomitant use with a strong or moderate CYP3A4 inhibitor may increase elacestrant exposure, which may increase the risk of elacestrant-related adverse reactions.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Elacestrant	Atazanavir	Fosamprenavir
	Aprepitant	Idelalisib
	Cimetidine	Itraconazole
	Ciprofloxacin	Ketoconazole
	Clarithromycin	Nefazodone
	Clotrimazole	Nelfinavir
	Cobicistat	Posaconazole
	Crizotinib	Ritonavir
	Cyclosporine	Tipranavir
	Diltiazem	Verapamil
	Dronedarone	Voriconazole
	Erythromycin	
	Fluconazole	
	Fluvoxamine	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

Orserdu Prescribing Information, Jan. 2023, Stemline Therapeutics, Inc.

8. Elacestrant / BCRP Substrates

Alert Message: Orserdu (elacestrant) is a BCRP inhibitor. In drug interaction studies, the concomitant use of elacestrant with a BCRP substrate increased the plasma concentrations of a BCRP substrate. Concurrent use of elacestrant with a BCRP substrate may increase the risk for adverse reactions associated with a BCRP substrate. Reduce the dosage of BCRP substrates per the BCRP substrate prescribing information when minimal concentration changes may lead to serious or life-threatening adverse reactions.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Elacestrant	Alpelisib	Prazosin
	Atorvastatin	Rosuvastatin
	Dantrolene	Sulfasalazine
	Dolutegravir	Talazoparib
	Methotrexate	Tenofovir
	Pazopanib	Topotecan
	Pibrentasvir	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

Orserdu Prescribing Information, Jan. 2023, Stemline Therapeutics, Inc.

Criteria Recommendations

Approved Rejected

9. Elacestrant / P-gp Substrates

Alert Message: Orserdu (elacestrant) is a P-gp inhibitor. In drug interaction studies, concomitant use of elacestrant with a P-gp substrate increased the concentrations of P-gp substrate. Concurrent use of elacestrant with a P-gp substrate may increase the risk for adverse reactions associated with a P-gp substrate. Reduce the dosage of P-gp substrates per the P-gp substrate prescribing information when minimal concentration changes may lead to serious or life-threatening adverse reactions.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Elacestrant	Cyclosporine Digoxin Sirolimus Tacrolimus	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Orserdu Prescribing Information, Jan. 2023, Stemline Therapeutics, Inc.

10. Elacestrant / Pregnancy / Pregnancy Negating

Alert Message: Based on findings in animals and its mechanism of action, Orserdu (elacestrant) can cause fetal harm when administered to a pregnant woman. Administration of elacestrant to pregnant rats resulted in adverse developmental outcomes, including embryo-fetal mortality and structural abnormalities, at maternal exposures below the recommended dose based on the area under the curve (AUC). Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with elacestrant and for 1 week after the last dose.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negate)</u>
Elacestrant	Pregnancy	Abortion Delivery Miscarriage

Gender: Female

Age Range: 11 – 50 yoa

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Orserdu Prescribing Information, Jan. 2023, Stemline Therapeutics, Inc.

11. Elacestrant / Lactation

Alert Message: There are no data on the presence of Orserdu (elacestrant) in human milk, its effects on milk production, or the breastfed child. Because of the potential for serious adverse reactions in the breastfed child, advise lactating women to not breastfeed during treatment with elacestrant and for 1 week after the last dose.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Elacestrant	Lactation	

Gender: Female

Age Range: 11 – 50 yoa

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Orserdu Prescribing Information, Jan. 2023, Stemline Therapeutics, Inc.

Criteria Recommendations

Approved Rejected

12. Elacestrant / Therapeutic Appropriateness

Alert Message: Advise females of reproductive potential to use effective contraception during treatment with Orserdu (elacestrant) and for 1 week after the last dose. Based on findings in animals and its mechanism of action, elacestrant can cause fetal harm when administered to a pregnant woman.

Drugs/Diseases

Util A Util B Util C (Negating)
Elacestrant Contraceptives

Gender: Female

Age Range: 11 – 50 yoa

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

Orserdu Prescribing Information, Jan. 2023, Stemline Therapeutics, Inc.

13. Elacestrant / Therapeutic Appropriateness

Alert Message: Advise male patients with female partners of reproductive potential to use effective contraception during treatment with Orserdu (elacestrant) and for 1 week after the last dose.

Drugs/Diseases

Util A Util B Util C
Elacestrant

Gender: Male

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

Orserdu Prescribing Information, Jan. 2023, Stemline Therapeutics, Inc.

14. Elacestrant / Non-adherence

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

Drugs/Diseases

Util A Util B Util C
Elacestrant

References:

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

Ruddy K, Mayer E, Partridge A. Patient Adherence and Persistence With Oral Anticancer Treatment. CA Cancer J Clin 2009;59:56-66.

Barillet M, Prevost V, Joly F, Clarisse B. Oral Antineoplastic Agents: How do We Care About Adherence?. Br J Clin Pharmacol. 2015;80(6):1289–1302. doi:10.1111/bcp.12734

Greer JA, Amoyal N, Nisotel L, et al. Systemic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist. 2016;21:354-376.

Criteria Recommendations

Approved Rejected

15. Betamethasone Spray / Therapeutic Appropriateness - Pediatric

Alert Message: The safety and effectiveness of Sernivo (betamethasone spray) in patients younger than 18 years of age have not been studied. Pediatric patients may be more susceptible to systemic toxicity due to their larger skin surface-to-body mass ratios. The use of betamethasone spray is not recommended in pediatric patients.

Drugs/Diseases

Util A

Util B

Util C

Betamethasone Spray

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.

16. Betamethasone Spray / Therapeutic Appropriateness - Duration

Alert Message: The use of Sernivo (betamethasone spray) is recommended for up to 4 weeks of treatment. Treatment with betamethasone spray beyond 4 weeks is not recommended.

Drugs/Diseases

Util A

Util B

Util C

Betamethasone Spray

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.

17. Betamethasone Spray / Glaucoma, Cataracts & IOP

Alert Message: The use of topical corticosteroids, including Sernivo (betamethasone spray), may increase the risk of posterior subcapsular cataracts and glaucoma. Cataracts, glaucoma, and intraocular pressure have been reported postmarketing with the use of topical corticosteroid products, including betamethasone dipropionate. Advise patients to avoid contact with betamethasone spray with the eyes and to report any visual symptoms.

Drugs/Diseases

Util A

Util B

Util C

Betamethasone Spray

Cataracts
Glaucoma

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.

18. Betamethasone Spray / Therapeutic Appropriateness

Alert Message: Sernivo (betamethasone spray) can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency. This may occur during or after the withdrawal of treatment. Factors that predispose to HPA axis suppression include the use of high-potency corticosteroids, large treatment surface areas, prolonged use, use of occlusive dressings, altered skin barrier, liver failure, and young age.

Drugs/Diseases

Util A

Util B

Util C

Betamethasone Spray

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.

Criteria Recommendations

Approved Rejected

19. Betamethasone Spray / Lactation

Alert Message: There are no data regarding the presence of betamethasone dipropionate in human milk, the effects on the breastfed infant, or the effects on milk production after topical application of Sernivo (betamethasone spray) to women who are breastfeeding. It is possible that topical administration of betamethasone dipropionate could result in sufficient systemic absorption to produce detectable quantities in human milk. The developmental and health benefits of breastfeeding should be considered, along with the mother’s clinical need for betamethasone spray and any potential adverse effects on the breastfed infant from betamethasone spray or the underlying maternal condition.

Drugs/Diseases

Util A Util B Util C
Betamethasone Spray Lactation

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.

20. Atorvastatin Suspension / Overuse

Alert Message: Atorvaliq (atorvastatin suspension) may be over-utilized. The maximum recommended dose of atorvastatin suspension in adults is 80 mg per day.

Drugs/Diseases

Util A Util B Util C
Atorvastatin Suspension

Max Dose: 80 mg/day
Age Range: 18 – 999 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Atorvaliq Prescribing Information, Feb. 2023, CMP Pharma Inc.

21. Atorvastatin Suspension / Overuse

Alert Message: Atorvaliq (atorvastatin suspension) may be over-utilized. The maximum recommended dose of atorvastatin suspension in pediatric patients 10 years of age and older with homozygous familial hypercholesterolemia (HoFH) is 80 mg per day. The maximum recommended dose of atorvastatin suspension in pediatric patients 10 years of age and older with heterozygous familial hypercholesterolemia (HeFH) is 20 mg per day.

Drugs/Diseases

Util A Util B Util C
Atorvastatin Suspension

Max Dose: 80 mg/day
Age Range: 10 – 17 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Atorvaliq Prescribing Information, Feb. 2023, CMP Pharma Inc.

Criteria Recommendations

Approved Rejected

22. Atorvastatin Suspension / Therapeutic Appropriateness

Alert Message: The safety and effectiveness of Atorvaliq (atorvastatin suspension) have not been established in pediatric patients younger than 10 years of age with HeFH or HoFH, or in pediatric patients with other types of hyperlipidemia (other than HeFH or HoFH).

Drugs/Diseases

Util A Util B Util C
Atorvastatin Suspension

Age Range: 0 - 9 yoa

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Atorvaliq Prescribing Information, Feb. 2023, CMP Pharma Inc.

23. Rosuvastatin / Darolutamide

Alert Message: In patients taking Nubeqa (darolutamide), the dose of rosuvastatin should not exceed 5 mg once daily. Rosuvastatin is a BCRP substrate, and concurrent use with darolutamide, a BCRP inhibitor, has been shown to elevate rosuvastatin concentrations, increasing the risk of statin-associated adverse reactions.

Drugs/Diseases

Util A Util B Util C
Rosuvastatin Darolutamide

Max Dose: 5 mg/day

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.

24. Rosuvastatin / Regorafenib

Alert Message: In patients taking regorafenib, the dose of rosuvastatin should not exceed 10 mg once daily. Rosuvastatin is a BCRP substrate, and concurrent use with regorafenib, a BCRP inhibitor, has been shown to elevate rosuvastatin concentrations increasing the risk of statin-associated adverse reactions.

Drugs/Diseases

Util A Util B Util C
Rosuvastatin Regorafenib

Max dose: 10 mg/day

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.

Criteria Recommendations**Approved Rejected****25. Atogepant / Severe Hepatic Impairment**

Alert Message: Due to the potential for liver injury in patients with severe hepatic impairment, avoid the use of Qulipta (atogepant) in this patient population. In pharmacokinetic studies, atogepant exposure was increased by 38% in patients with severe (Child-Pugh Class C) hepatic impairment compared to patients with normal hepatic function.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Atogepant	Cirrhosis	Hepatic Failure

References:

Qulipta Prescribing Information, April 2023, AbbVie.
Clinical Pharmacology, 2023 Elsevier/Gold Standard.

26. Tucatinib / Overuse

Tukysa (tucatinib) may be over-utilized. The recommended daily dosage of tucatinib is 300 mg orally twice daily.

Alert Message:

Drugs/Disease

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negate)</u>
Tucatinib		Cirrhosis Hepatic Failure

Max Dose: 600 mg/day

Reference:

Clinical Pharmacology, 2023, Elsevier/Gold Standard.
Tukysa Prescribing Information, Jan. 2023, Seagen Inc.

27. Tucatinib / Overuse – Hepatic Impairment

Alert Message: Tukysa (tucatinib) may be over-utilized. For patients with severe hepatic impairment (Child-Pugh C), the recommended dosage of tucatinib is 200 mg orally twice daily.

Drugs/Disease

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Tucatinib		Cirrhosis Hepatic Failure

Max Dose: 400 mg/day

Reference:

Clinical Pharmacology, 2023, Elsevier/Gold Standard.
Tukysa Prescribing Information, Jan. 2023, Seagen Inc.

28. Tucatinib / Therapeutic Appropriateness

Alert Message: The safety and effectiveness of Tukysa (tucatinib) in pediatric patients have not been established.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Tucatinib		

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.

Criteria Recommendations

Approved Rejected

29. Tucatinib / Strong CYP3A4 Inducers or Moderate 2C8 Inducers

Concomitant use of Tukysa (tucatinib) with a strong CYP3A or moderate CYP2C8 inducer decreased tucatinib plasma concentrations, which may reduce tucatinib activity. Avoid the concomitant use of tucatinib with a strong CYP3A inducer or a moderate CYP2C8 inducer. If concomitant use with a strong CYP2C8 inhibitor cannot be avoided, reduce the recommended dosage to 100 mg orally twice daily.

Alert Message:

Drugs/Disease

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Tucatinib	Apalutamide Carbamazepine Enzalutamide Mitotane	Phenobarbital Phenytoin Primidone Rifampin

Reference:

Clinical Pharmacology, 2023, Elsevier/Gold Standard.
Tukysa Prescribing Information, Jan. 2023, Seagen Inc.

30. Tucatinib / Strong CYP2C8 Inhibitors

Alert Message: The concurrent use of Tukysa (tucatinib) with strong CYP2C8 inhibitors should be avoided. If concomitant use with a strong CYP2C8 inhibitor cannot be avoided, reduce the recommended dosage to 100 mg orally twice daily. After discontinuation of the strong CYP2C8 inhibitor for 3 elimination half-lives, resume the tucatinib dose that was taken prior to initiating the inhibitor.

Drugs/Disease

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Tucatinib	Gemfibrozil	

Reference:

Clinical Pharmacology, 2023, Elsevier/Gold Standard.
Tukysa Prescribing Information, Jan. 2023, Seagen Inc.

31. Tucatinib / CYP3A Substrates w/ NTI

Alert Message: In drug interaction studies, concomitant use of Tukysa (tucatinib) with a CYP3A substrate increased the plasma concentrations of the CYP3A substrate, which may increase the toxicity associated with a CYP3A substrate. Avoid concomitant use of tucatinib with CYP3A substrates, where minimal concentration changes may lead to serious or life-threatening toxicities. If concomitant use is unavoidable, decrease the CYP3A substrate dosage in accordance with approved product labeling.

Drugs/Disease

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

Reference:

Clinical Pharmacology, 2023, Elsevier/Gold Standard.
Tukysa Prescribing Information, Jan. 2023, Seagen Inc.

Criteria Recommendations

Approved Rejected

32. Tucatinib / P-gp w/ NTI

_____ Alert Message:

In drug interaction studies, concomitant use of Tukysa (tucatinib) with a P-gp substrate increased the plasma concentrations of the P-gp substrate, which may increase the toxicity associated with a P-gp substrate. Consider reducing the dosage of P-gp substrates, where minimal concentration changes may lead to serious or life-threatening toxicities.

Drugs/Disease

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Tucatinib	Cyclosporine Digoxin Everolimus	Sirolimus Tacrolimus

Reference:

Clinical Pharmacology, 2023, Elsevier/Gold Standard.
Tukysa Prescribing Information, Jan. 2023, Seagen Inc.

33. Tucatinib / Diarrhea

_____ Alert Message:

Tukysa (tucatinib) can cause severe diarrhea. If diarrhea occurs, administer antidiarrheal treatment as clinically indicated. Perform diagnostic tests as clinically indicated to exclude other causes of diarrhea. Based on the severity of the diarrhea, interrupt dose, then dose reduce or permanently discontinue tucatinib.

Drugs/Disease

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Tucatinib	Diarrhea	

Reference:

Clinical Pharmacology, 2023, Elsevier/Gold Standard.
Tukysa Prescribing Information, Jan. 2023, Seagen Inc.

34. Tucatinib / Hepatotoxicity

Alert Message: Tukysa (tucatinib) can cause severe hepatotoxicity. Monitor ALT, AST, and bilirubin prior to starting tucatinib, every 3 weeks during treatment, and as clinically indicated. Based on the severity of hepatotoxicity, interrupt dose, then dose reduce or permanently discontinue tucatinib.

Drugs/Disease

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Tucatinib		

Reference:

Clinical Pharmacology, 2023, Elsevier/Gold Standard.
Tukysa Prescribing Information, Jan. 2023, Seagen Inc.

Criteria Recommendations

Approved Rejected

35. Tucatinib / Pregnancy / Pregnancy Negating

Alert Message: Based on findings from animal studies and its mechanism of action, Tukysa (tucatinib) can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of tucatinib to pregnant rats and rabbits during organogenesis caused embryo-fetal mortality, reduced fetal weight and fetal abnormalities at maternal exposures >= 3 times the human exposure (AUC) at the recommended dose. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with tucatinib and for at least 1 week after the last dose.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>
Tucatinib	Pregnancy	Abortion Delivery Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023, Elsevier/Gold Standard.
Tukysa Prescribing Information, Jan. 2023, Seagen Inc.

36. Tucatinib / Lactation

Alert Message: There are no data on the presence of Tukysa (tucatinib) or its metabolites in human or animal milk or its effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment with tucatinib, and for 1 week after the last dose. Tucatinib is used in combination with trastuzumab and capecitabine. Refer to the full prescribing information of trastuzumab and capecitabine for lactation information.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Tucatinib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023, Elsevier/Gold Standard.
Tukysa Prescribing Information, Jan. 2023, Seagen Inc.

37. Tucatinib / Therapeutic Appropriateness

Alert Message: Advise females of reproductive potential to use effective contraception during treatment with Tukysa (tucatinib) and for at least 1 week after the last dose. Based on findings from animal studies and its mechanism of action, Tukysa (tucatinib) can cause fetal harm when administered to a pregnant woman.

Drugs/Disease

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Tucatinib		

Gender: Female
Age Range: 11 – 50 yoa

Reference:
Clinical Pharmacology, 2023, Elsevier/Gold Standard.
Tukysa Prescribing Information, Jan. 2023, Seagen Inc.

Criteria Recommendations

Approved Rejected

38. Tucatinib / Therapeutic Appropriateness

_____ Alert Message:

Advise male patients with female partners of reproductive potential to use effective contraception during treatment with Tukysa (tucatinib) and for 1 week after the last dose.

Drugs/Disease

Util A Util B Util C
Tucatinib

Gender: Male

Reference:

Clinical Pharmacology, 2023, Elsevier/Gold Standard.
Tukysa Prescribing Information, Jan. 2023, Seagen Inc.

39. Tucatinib / Non-adherence

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

Drugs/Diseases

Util A Util B Util C
Tucatinib

References:

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

40. Mavacamten / Black Box Warning

Alert Message: Camzyos (mavacamten) reduces systolic contraction and can cause heart failure or totally block ventricular function. Patients who experience a serious intercurrent illness (e.g., serious infection) or arrhythmia (e.g., atrial fibrillation or other uncontrolled tachyarrhythmia) are at greater risk of developing systolic dysfunction and heart failure. New or worsening arrhythmia, dyspnea, chest pain, fatigue, palpitations, leg edema, or elevations in N-terminal pro B-type natriuretic peptide (NT-proBNP) may be signs and symptoms of heart failure and should also prompt an evaluation of cardiac function.

Drugs/Diseases

Util A Util B Util C
Mavacamten Heart Failure
 Arrhythmias
 Dyspnea
 Angina
 Palpitations
 Localized Edema

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Camzyos Prescribing Information, September 2022, Bristol-Myers Squibb.

Criteria Recommendations**Approved Rejected****41. Mavacamten / Contraindication (Black Box)**

Alert Message: Concomitant use of Camzyos (mavacamten) with a moderate to strong CYP2C19 inhibitor or a strong CYP3A4 inhibitor is contraindicated. Concomitant use with a moderate to strong CYP2C19 or a strong CYP3A4 inhibitor increases mavacamten exposure, which may increase the risk of heart failure due to systolic dysfunction.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Mavacamten	Cobicistat	Ketoconazole
	Clarithromycin	Nefazodone
	Esomeprazole	Nelfinavir
	Felbamate	Posaconazole
	Fluconazole	Ritonavir
	Fluvoxamine	Ticlopidine
	Fluoxetine	Voriconazole
	Itraconazole	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
 Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
 Camzyos Prescribing Information, September 2022, Bristol-Myers Squibb.

42. Mavacamten / Contraindication (Black Box)

Alert Message: Concomitant use of Camzyos (mavacamten) with a moderate to strong CYP2C19 inducer or a moderate to strong CYP3A4 inducer is contraindicated. Concomitant use with a moderate to strong CYP2C19 inducer or a moderate to strong CYP3A4 inducer decreases mavacamten exposure, which may reduce the efficacy of mavacamten. The risk of heart failure due to systolic dysfunction may increase with discontinuation of these inducers as the levels of induced enzyme normalize.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Mavacamten	Apalutamide	Phenytoin
	Bosentan	Rifabutin
	Butalbital	Rifampin
	Carbamazepine	Rifapentine
	Efavirenz	
	Enzalutamide	
	Etravirine	
	Mitotane	
	Phenobarbital	
	Primidone	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
 Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
 Camzyos Prescribing Information, September 2022, Bristol-Myers Squibb.

Criteria Recommendations

Approved Rejected

43. Mavacamten / Weak CYP2C19 Inhibitors & Moderate 3A4 Inhibitors

Alert Message: Concomitant use of Camzyos (mavacamten) with a weak CYP2C19 inhibitor or a moderate CYP3A4 inhibitor increases mavacamten exposure, which may increase the risk of adverse drug reactions. Initiate mavacamten at the recommended starting dosage of 5 mg orally once daily in patients who are on stable therapy with a weak CYP2C19 inhibitor or a moderate CYP3A4 inhibitor. Reduce dose of mavacamten by one level (i.e., 15 to 10 mg, 10 to 5 mg, or 5 to 2.5 mg) in patients who are on mavacamten treatment and intend to initiate a weak CYP2C19 inhibitor or a moderate CYP3A4 inhibitor. Avoid initiation of concomitant weak CYP2C19 and moderate CYP3A4 inhibitors in patients who are on stable treatment with 2.5 mg of mavacamten because a lower dose is not available.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Mavacamten	Aprepitant Ciprofloxacin Cimetidine Conivaptan Crizotinib Cyclosporine Diltiazem	Erythromycin Esomeprazole Imatinib Omeprazole Verapamil

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Camzyos Prescribing Information, September 2022, Bristol-Myers Squibb.

44. Mavacamten / Therapeutic Appropriateness

Alert Message: The safety and effectiveness of Camzyos (mavacamten) have not been established in pediatric patients.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Mavacamten		

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Camzyos Prescribing Information, September 2022, Bristol-Myers Squibb.

45. Mavacamten / Disopyramide

Alert Message: Avoid concomitant use of Camzyos (mavacamten) in patients on disopyramide or disopyramide in combination with verapamil or diltiazem. Concurrent use of mavacamten and disopyramide will have additive negative inotropic effects. Concomitant use of mavacamten with disopyramide in combination with verapamil or diltiazem has been associated with left ventricular systolic dysfunction and heart failure symptoms in patients with obstructive HCM.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Mavacamten	Disopyramide	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Camzyos Prescribing Information, September 2022, Bristol-Myers Squibb.

Criteria Recommendations**Approved Rejected****46. Mavacamten / Ranolazine**

Alert Message: Coadministration of ranolazine with Camzyos (mavacamten) is contraindicated due to decreased ranolazine exposure and efficacy. Ranolazine is a CYP3A substrate, and mavacamten is a moderate CYP3A inducer. Patients on therapy with ranolazine were excluded from the clinical trial of mavacamten in obstructive HCM (EXPLORER-HCM).

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Mavacamten	Ranolazine	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
 Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
 Ranexa Prescribing Information, Oct. 2019, Gilead Sciences, Inc.

47. Mavacamten / Combined Hormonal Contraceptives

Alert Message: Concomitant use of Camzyos (mavacamten) with hormonal contraceptives that are CYP3A4 substrates may lead to contraceptive failure or an increase in breakthrough bleeding. Mavacamten is a CYP3A4 inducer and can induce the metabolism of progestin and ethinyl estradiol. Advise patients to use a contraceptive method that is not affected by CYP450 enzyme induction (e.g., intrauterine system) or add nonhormonal contraception (such as condoms) during concomitant use and for 4 months after the last dose of mavacamten.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Mavacamten	Contraceptives	

Gender: Female

Age Range: 11 – 50 yoa

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
 Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
 Camzyos Prescribing Information, September 2022, Bristol-Myers Squibb.

48. Mavacamten / Pregnancy / Pregnancy Negating

Alert Message: Camzyos (mavacamten) may cause fetal toxicity when administered to a pregnant female, based on findings in animal studies. Confirm the absence of pregnancy in females of reproductive potential prior to treatment and advise patients to use effective contraception during treatment with mavacamten and for 4 months after the last dose. Mavacamten may reduce the effectiveness of combined hormonal contraceptives (CHCs). Advise patients using CHCs to use an alternative contraceptive method that is not affected by CYP450 enzyme induction or to add nonhormonal contraception.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negate)</u>
Mavacamten	Pregnancy	Abortion Delivery Miscarriage

Gender: Female

Age Range: 11 – 50 yoa

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
 Camzyos Prescribing Information, September 2022, Bristol-Myers Squibb.

Criteria Recommendations

Approved Rejected

49. Mavacamten / Lactation

Alert Message: The presence of Camzyos (mavacamten) in human or animal milk, the drug's effects on the breastfed infant, and the effects on milk production are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for mavacamten and any potential adverse effects on the breastfed child from mavacamten or from the underlying maternal condition.

Drugs/Diseases

Util A Util B Util C
Mavacamten Lactation

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Camzyos Prescribing Information, September 2022, Bristol-Myers Squibb.

50. Baclofen Granules / Overuse

Alert Message: Lyvispah (baclofen granules) may be over-utilized. The maximum recommended dosage of baclofen granules is 80 mg daily (20 mg four times a day).

Drugs/Diseases

Util A Util B Util C
Baclofen granules

Max Dose: 80 mg/day

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lyvispah Prescribing Information, Nov. 2021, Saol Therapeutics.

51. Baclofen Granules / Therapeutic Appropriateness

Alert Message: The safety and effectiveness of Lyvispah (baclofen granules) in pediatric patients below the age of 12 have not been established.

Drugs/Diseases

Util A Util B Util C
Baclofen granules

Age Range: 0 – 11 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lyvispah Prescribing Information, Nov. 2021, Saol Therapeutics.

Criteria Recommendations**Approved Rejected****52. Baclofen Granules / Renal Impairment**

Alert Message: Because baclofen is primarily excreted unchanged through the kidneys, Lyvispah (baclofen granules) should be given with caution to patients with renal impairment, and it may be necessary to reduce the dosage.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Baclofen granules	Renal Impairment	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lyvispah Prescribing Information, Nov. 2021, Saol Therapeutics.

53. Baclofen Granules / Pregnancy / Pregnancy Negating

Alert Message: There are no adequate data on the risk of major birth defects, miscarriages, or other maternal adverse outcomes associated with the use of Lyvispah (baclofen granules) in pregnant women. There are adverse effects on fetal outcomes associated with withdrawal from baclofen after delivery. Oral administration of baclofen to pregnant rats resulted in an increased incidence of fetal structural abnormalities at a dose which was also associated with maternal toxicity.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negate)</u>
Baclofen granules	Pregnancy	Abortion Delivery Miscarriage

Gender: Female

Age Range: 11 – 50 yoa

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lyvispah Prescribing Information, Nov. 2021, Saol Therapeutics.

54. Baclofen Granules / Lactation

Alert Message: At recommended oral doses, Lyvispah (baclofen) is present in human milk. Withdrawal symptoms can occur in breastfed infants when maternal administration of baclofen is stopped, or when breastfeeding is stopped. There are no adequate data on other effects of baclofen on the breastfed infant. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for baclofen and any potential adverse effects on the breastfed infant from baclofen or from the underlying maternal condition.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Baclofen granules	Lactation	

Gender: Female

Age Range: 11 – 50 yoa

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lyvispah Prescribing Information, Nov. 2021, Saol Therapeutics.

Criteria Recommendations

Approved Rejected

55. Perampanel /Therapeutic Appropriateness

Alert Message: The safety and effectiveness of Fycompa (perampanel) in pediatric patients less than 4 years of age have not been established.

Drugs/Diseases

Util A

Util B

Util C

Perampanel

Age Range: 0 – 3 yoa

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.