North Dakota Medicaid

Drug Utilization Review Board Meeting

March 6th, 2024

Conference Room 210/212

NORTH Dakota | Health & Human Services

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Meeting Notice

North Dakota Medicaid Drug Use Review Board

Wednesday, March 6th, 2024
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: 245 967 869 #

Agenda

1. Call to Order
2. Roll Call
3. Review and Approval of Minutes
4. Reports from Department
    - Administrative Report: COVID-19 treatment (Lagevrio & Paxlovid)
    - Financial Report: Budget, Top Drugs
    - Retrospective DUR Report
    - Clinical Report:
        - Prior authorization update
        - Criteria updates: Corticosteroids – Inhaled Criteria, Tardive Dyskinesia, Phenylketonuria
5. Unfinished business
    - Update to Hyperkalemia Criteria, Prophylaxis to Migraine, Eczema / Atopic Dermatitis, Cholestatis Pruritis
6. New business
    - First Review of potassium-competitive acid blockers (Voquezna)
    - First Review of Seborrheic Dermatitis (Zoryve)
    - First Review of Primary Hyperoxaluria Tyle 1 (Rivfloza)
    - First Review of Myasthenia Gravis (Ziibrysq)
    - First Review of Duchenne Muscular Dystrophy (Emflaza, Agamree)
    - First Review of Paroxysmal Nocturnal Hemoglobinuria (Empaveli, Fabhalta)
    - Review of retrospective DUR criteria recommendations
7. Announcements
    - Next Meeting (June 5, 2024)
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: December 6th, 2023
Time and Location: 1:00 pm CST in Bismarck, North Dakota

Call to Order:
A regular quarterly meeting of the North Dakota Medicaid Drug Use Review (DUR) Board meeting was convened at 1:06 pm CST. Motion moved by A. Werremeyer to have pro tem Presiding Officer K. Martian presiding and seconded by T. Schmidt. **Motion carried.**
DUR Board Coordinator, C. Stauter recording minutes.

Roll Call:
Board Members Voting:
Present: Stephanie Antony, Josh Askvig, Gabriela Balf, Kurt Datz, Andrea Honeyman, Laura Kroetsch, Kevin Martian, Kristen Peterson, Tanya Schmidt, Amy Werremeyer
Absent: Jennifer Iverson
Quorum Present: Yes

Board Members Non-Voting:
Absent: Kathleen Traylor

Medicaid Pharmacy Department:
Present: Brendan Joyce, Alexi Murphy, LeNeika Roehrich
Absent: Jeff Hostetter

Approval of Meeting Minutes:
Motion: Moved by L. Kroetsch to approve the minutes of the September 6th, 2023 meeting, motion was seconded by K. Peterson. **Motion carried.**
The minutes of the September 6th, 2023, meeting were approved as distributed.

Reports:
*Administrative Report***:** Rebates by A. Murphy
A. Murphy shared with the Board changes to rebate calculations. This information can be found in the handout.

Financial Report: Budget provided by B. Joyce
B. Joyce shared with the Board trends of pharmacy claims costing over $5000 from August 2023. 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 C. Stauter
C. Stauter reviewed the quarterly RDUR criteria that were selected for review of each month, including a special mailing letter from July 2023. This material can be found in the handout.

Clinical Report: Annual PDL Review and Criteria Updates by C. Stauter
C. Stauter discussed updates to the Preferred Drug List (PDL) throughout the year 2023, with emphasis on the following sections in the PDL: cholestasis pruritis, diabetes, and Hepatitis C. The presented information can be found in the handout. Testimony was provided by the following: Phong Pham from Ipsen Biopharmaceuticals on Bylvay; Shawn Hansen from Novo Nordisk on Ozempic and Rybelsus; Erin Nowak from Abbvie on Mavyret, Rinvoq, Skyrizi, and Ubrelvy; Phil Wettestad from Novartis on Leqvio and Cosentyx; Christine Dubé from Astrazeneca on Brilinta, Lokelma, and Fasenra; John Deason from Neurocrine Biosciences on Ingrezza.

New business:
Second Reviews provided by C. Stauter
C. Stauter presented group prior authorization criteria for diuretics and menopause. The presented material can be found in the handout.
Motion: Moved by K. Peterson to place diuretics on prior authorization, motion was seconded by K. Martian. **Motion carried.**
Motion: Moved by T. Schmidt to place agents for menopause on prior authorization, motion was seconded by A. Werremeyer. **Motion carried.**

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

Announcements:
Next meeting is March 6th, 2024.

Adjournment:
Meeting adjourned by K. Martian at 2:32 pm CST.

Date of Minutes Approval:
Minutes submitted by: Claire Stauter, Acentra Health

Administrative Report:

COVID-19 treatments:
https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/COVID19-Tx-Transition-Guide.aspx
COVID-19 Therapeutics Transition to Commercial Distribution: Frequently Asked Questions | HHS/ASPR

Under the American Rescue Plan, Medicaid plans must cover COVID-19 oral antivirals until the end of the third quarter of calendar year 2024.

On November 1, 2023, the manufacturers of Lagevrio and Paxlovid began a transition from distribution by the US Government to distribution through the commercial channel. To aid in this transition, the manufacturers have created patient assistance programs.

- **Paxlovid:** Through December 31, 2024, Medicaid members can obtain Paxlovid directly at the pharmacy *without having to enroll in the patient assistance program (PAP).*
  - How it works:
    1. Pharmacy bills commercial supply to Medicaid.
    2. The state collects a Pfizer calculated state-specific rebate to reimburse the Medicaid program for the cost of Paxlovid. To facilitate this, pharmacies may not use 340b stock.
  - For information on the Paxlovid PAP and to obtain Paxlovid at no cost: https://www.paxlovid.com/paxcess or call 1-877-219-7225 (1-877-C19-PACK).

- **Lagevrio:** Approved under emergency use authorization (EUA), Lagevrio should only be used in cases where Paxlovid is not an option, and the use of Lagevrio is a medically urgent need. Prior authorization will be used to verify that the FDA approved Paxlovid cannot be utilized.
  - Medicaid members cannot receive Lagevrio through the PAP operated by the manufacturer. Merck has published program information at https://www.merckhelps.com/LAGEVRIO or 1-800-727-5400.
  - For more information on use of EUA drugs during the COVID-19 pandemic - see Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1)

PDMP Use Survey:
- In accordance with the SUPPORT ACT under Section 5042 (effective October 1, 2021), all Medicaid providers authorized to prescribe controlled substances are required to assess qualified prescription drug monitoring programs (PDMPs) before prescribing controlled substances to most Medicaid members.
- A survey was sent to providers to assess their use of the PDMP to facilitate federally required reporting on PDMP utilization in February 2024.

Antipsychotic Weight Gain:
- Metformin is already allowed in the system and per the compendia
- Victoza has been added, and will be covered by using diagnosis code T43.505A

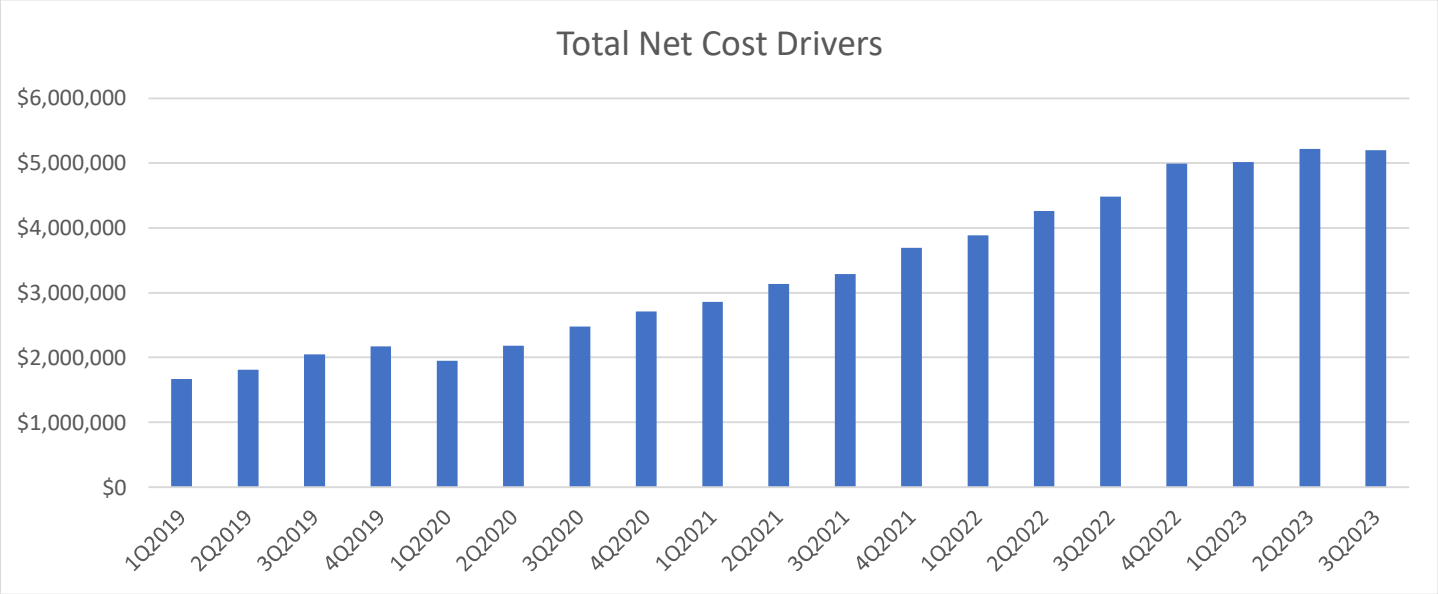
Cost Drivers:

- **Antipsychotics (more injectable use)**
  - 98.9% growth 1Q19 to 1Q23
  - $954,000 quarterly spend
- **Cystic Fibrosis (newest drugs are very effective)**
  - 268.7% growth 1Q19 to 1Q23
  - $621,000 quarterly spend
- **Eczema (Dupixent)**
  - 1,714% growth 1Q19 to 1Q23
  - $343,000 quarterly spend
- **Hemophilia (member no longer has TPL)**
  - 909.4% growth 3Q22 to 3Q23
  - $216,000 quarterly spend
- **Hepatitis C**
  - 14.6% growth 1Q19 to 1Q23
  - $212,000 quarterly spend
- **HIV**
  - 116.7% growth 1Q19 to 1Q23
  - $283,000 quarterly spend
- **Immunomodulators (Enbrel, Humira, etc)**
  - 574.4% growth 1Q19 to 1Q23
  - $1.1 million quarterly spend
- **Migraine**
  - 244.3% growth 1Q19 to 1Q23
  - $72,000 quarterly spend
- **Multiple Sclerosis**
  - 35.1% growth 1Q19 to 1Q23
  - $100,000 quarterly spend
- **Narcotic Treatment (more injectable use)**
  - 104.7% growth 1Q19 to 1Q23
  - $294,000 quarterly spend
- **Oncology**
  - 169.8% growth 1Q19 to 1Q23
  - $878,000 quarterly spend
- **Pulmonary HTN**
  - 779.4% growth 1Q19 to 1Q23
  - $200,000 quarterly spend
- **Tardive dyskinesia**
  - 720.2% growth 3Q19 to 3Q23
  - $140,000 quarterly spend

Summary:

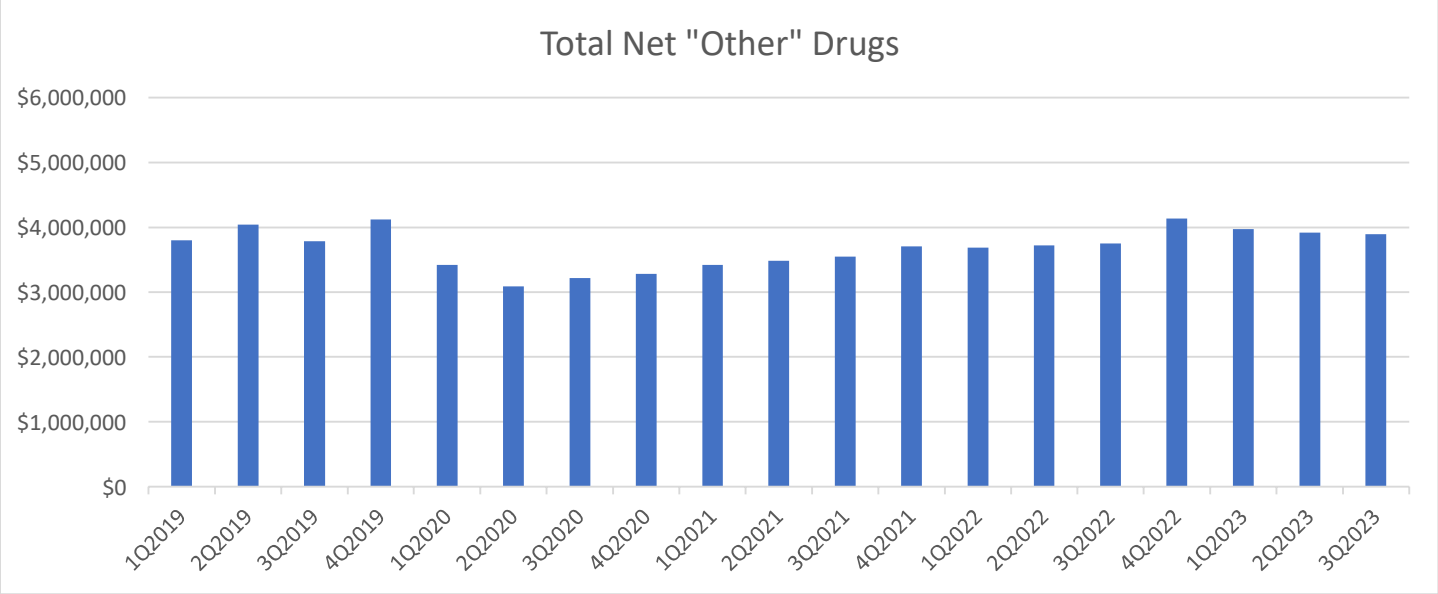
Cost Driver drug classes

- 200.7% growth 1Q19 to 1Q23
- $5.2 million quarterly spend



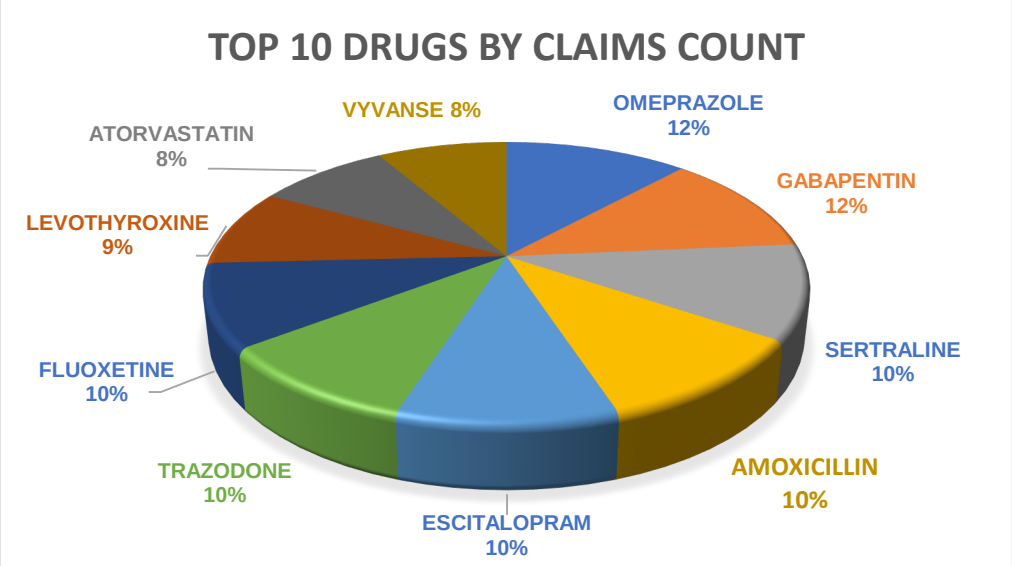
ALL OTHER DRUGS / ALL OTHER DRUG CLASSES

- 4.4% growth 1Q19 to 1Q23
- $3.9 million quarterly spend



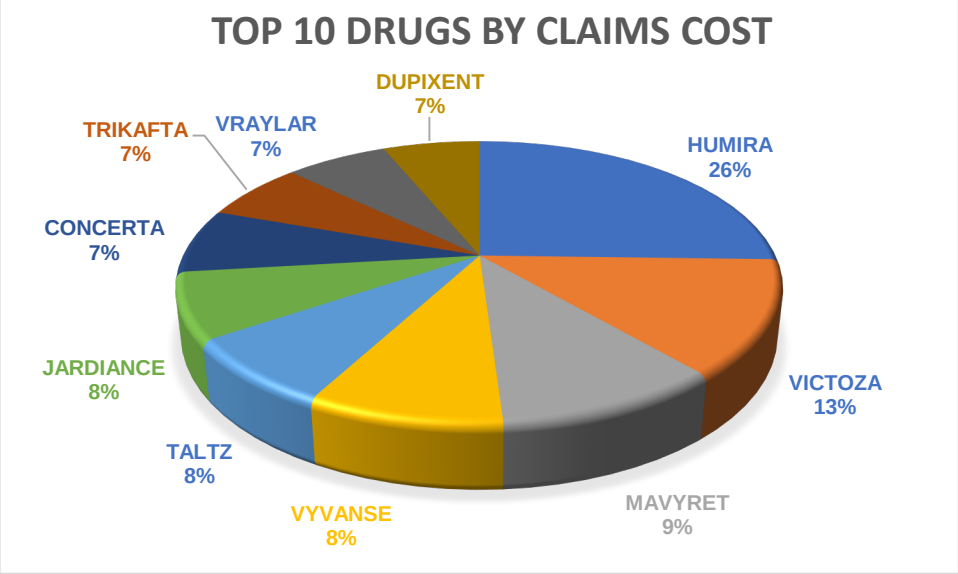
Top 25 Drugs Based on Number of Claims from 10/01/2023 – 12/31/2023

Drug	Claims	Claims Cost	Patients	Cost / Claim	% Total Claims	Dif.
1. GABAPENTIN	4,395	$64,864.30	1,899	$14.76	1.7%	↑1
2. OMEPRAZOLE	4,320	$55,568.18	2,134	$12.86	1.7%	↓1
3. SERTRALINE	3,820	$52,081.13	2,164	$13.63	1.5%	NC
4. AMOXICILLIN	3,799	$54,196.46	3,547	$14.27	1.5%	↑15
5. ESCITALOPRAM	3,661	$49,533.77	2,111	$13.53	1.4%	↓1
6. TRAZODONE	3,624	$49,004.33	1,890	$13.52	1.4%	↓1
7. FLUOXETINE	3,598	$48,039.16	1,957	$13.35	1.4%	↓1
8. LEVOTHYROXINE	3,189	$47,948.67	1,675	$15.04	1.3%	↓1
9. ATORVASTATIN	3,017	$42,944.04	1,808	$14.23	1.2%	NC
10. VYVANSE	3,009	$816,556.71	1,256	$271.37	1.2%	NC
11. VENTOLIN HFA	3,005	$194,077.31	2,970	$64.58	1.2%	NC
12. LISINOPRIL	3,003	$38,668.47	1,817	$12.88	1.2%	↓4
13. BUPROPION XL	2,917	$47,951.63	1,580	$16.44	1.2%	↓1
14. PANTOPRAZOLE	2,829	$39,259.28	1,420	$13.88	1.1%	↑1
15. AMOXICILLIN-CLAV	2,690	$47,483.81	2,506	$17.65	1.1%	↑16
16. PREDNISONE	2,666	$31,242.69	2,148	$11.72	1.1%	↑4
17. CLONIDINE	2,577	$31,882.66	1,280	$12.37	1.0%	↓2
18. NORCO	2,522	$37,413.25	1,560	$14.83	1.0%	↓4
19. DULOXETINE HCL	2,488	$40,954.73	1,311	$16.46	1.0%	↓3
20. LAMOTRIGINE	2,488	$35,557.37	1,043	$14.29	1.0%	↓3
21. CYCLOBENZAPRINE	2,420	$28,811.61	1,541	$11.91	1.0%	↓3
22. HYDROXYZINE	2,402	$33,371.03	1,498	$13.89	1.0%	↓1
23. BUSPIRONE	2,225	$33,601.71	1,204	$15.10	0.9%	NC
24. ONDANSETRON ODT	2,198	$30,962.28	1,739	$14.09	0.9%	↑8
25. ARIPIPRAZOLE	2,171	$32,296.35	1,052	$14.88	0.9%	↑1
Total Claims						**252,760**



Top 25 Drugs Based on Total Claims Cost from 10/01/2023 – 12/31/2023

Drug	Claims	Claims Cost	Patients	Cost / Patient	% Total Cost	Dif.
1. HUMIRA	293	$2,547,367.57	136	$18,730.64	7.3%	NC
2. VICTOZA	1,391	$1,254,889.13	688	$1,823.97	3.6%	NC
3. MAVYRET	52	$933,214.98	44	$21,209.43	2.7%	↑12
4. VYVANSE	3,009	$816,556.71	1,256	$650.12	2.3%	↓1
5. TALTZ	99	$749,738.54	39	$19,224.07	2.1%	↑2
6. JARDIANCE	1,100	$741,963.92	569	$1,303.98	2.1%	↓2
7. CONCERTA	2,070	$732,463.05	883	$829.52	2.1%	↓2
8. DUPIXENT	214	$726,444.93	101	$7,192.52	2.1%	↑1
9. TRIKAFTA	36	$703,839.86	14	$50,274.28	2.0%	↑3
10. VRAYLAR	700	$669,062.18	281	$2,381.00	1.9%	↓2
11. LANTUS	1,219	$633,244.71	772	$820.27	1.8%	↓1
12. BIKTARVY	258	$592,016.46	114	$5,193.13	1.7%	↓5
13. INVEGA SUSTENNA	204	$541,292.70	86	$6,294.10	1.5%	↓2
14. STELARA	20	$486,263.52	13	$37,404.89	1.4%	↑3
15. NORDITROPIN	82	$470,124.89	37	$12,706.08	1.3%	↑8
16. ADDERALL XR	2,164	$390,369.22	920	$424.31	1.1%	NC
17. ELIQUIS	680	$378,363.60	332	$1,139.65	1.1%	↓4
18. SYMBICORT	1,009	$363,704.15	578	$629.25	1.0%	NC
19. INGREZZA	47	$340,892.02	20	$17,044.60	1.0%	↑5
20. ENBREL	50	$316,541.07	24	$13,189.21	0.9%	NC
21. NOVOLOG	474	$314,345.38	303	$1,037.44	0.9%	↓7
22. ADVAIR DISKUS	796	$303,212.96	460	$659.16	0.9%	↓3
23. INSULIN ASPART	744	$298,030.93	453	$657.90	0.8%	NC
24. ABILIFY MAINTENA	123	$287,162.79	51	$5,630.64	0.8%	↓3
25. SUBLOCADE	146	$282,212.16	69	$4,090.03	0.8%	↓3
Total Claims Cost						**$35,100,930.83**



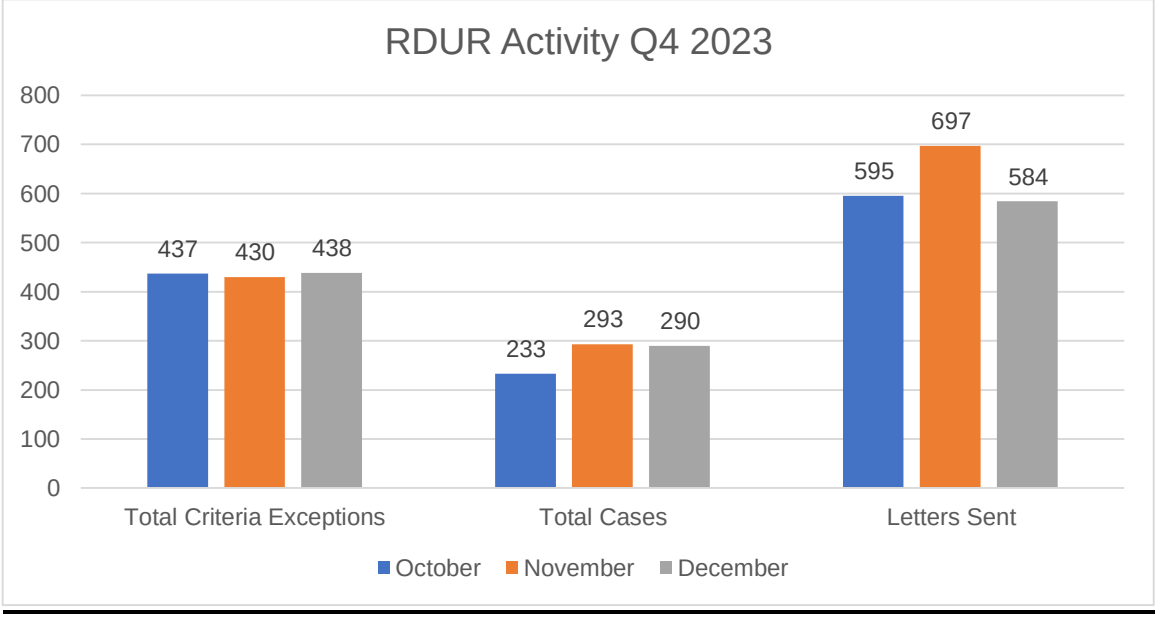
Top 15 Therapeutic Classes Based on Number of Claims from 10/01/2023 – 12/31/2023

Therapeutic Class Description	Claims	Claims Cost	Patients	Cost/Claim	% Total Claims	Dif.
1. ANTIDEPRESSANTS	27,364	$631,049.98	11,545	$23.06	10.8%	NC
2. ANTICONVULSANTS	13,231	$547,643.21	4,725	$41.39	5.2%	NC
3. ANTIPSYCHOTIC AGENTS	9,314	$2,512,358.06	3,689	$269.74	3.7%	NC
4. PPI'S	7,598	$165,525.72	3,729	$21.79	3.0%	NC
5. ANXIOLYTICS, SEDATIVES, HYPNOTICS	7,159	$104,901.98	3,680	$14.65	2.8%	NC
6. PENICILLIN ANTIBIOTICS	6,816	$107,096.35	6,028	$15.71	2.7%	↑6
7. AMPHETAMINES	6,810	$1,275,024.87	2,790	$187.23	2.7%	↓1
8. OPIATE AGONISTS	6,137	$98,341.35	3,179	$16.02	2.4%	↓1
9. NSAIDS	5,807	$79,769.80	3,867	$13.74	2.3%	↓1
10. RESP/CNS STIMULANTS	5,629	$976,379.37	2,144	$173.46	2.2%	NC
11. STATINS	5,414	$78,757.39	3,191	$14.55	2.1%	↓2
12. BETA BLOCKING AGENTS	4,998	$81,987.75	2,813	$16.40	2.0%	↓1
13. ADRENALS	4,548	$61,530.06	3,574	$13.53	1.8%	↑1
14. BETA AGONISTS	4,249	$251,818.70	3,890	$59.27	1.7%	↓1
15. BIGUANIDES	3,769	$53,049.25	2,217	$14.08	1.5%	↑1

Top 15 Therapeutic Classes Based on Claims Cost from 10/01/2023 – 12/31/2023

Therapeutic Class Description	Claims	Claims Cost	Patients	Cost/Patient	% Total Cost	Dif.
1. DMARDS	594	$3,585,936.02	248	$14,459.42	10.2%	NC
2. ANTIPSYCHOTIC AGENTS	9,314	$2,512,358.06	3,689	$681.04	7.2%	NC
3. SKIN AGENTS	650	$2,170,574.91	376	$5,772.81	6.2%	NC
4. INSULINS	3,201	$1,630,598.49	1,309	$1,245.68	4.6%	NC
5. INCRETIN MIMETICS	1,585	$1,424,354.23	715	$1,992.10	4.1%	NC
6. ANTINEOPLASTIC AGENTS	585	$1,406,890.82	246	$5,719.07	4.0%	↑1
7. AMPHETAMINES	6,810	$1,275,024.87	2,790	$457.00	3.6%	↓1
8. HCV ANTIVIRALS	68	$1,198,396.74	57	$21,024.50	3.4%	↑7
9. ANTIRETROVIRALS	709	$1,072,509.75	265	$4,047.21	3.1%	NC
10. CORTICOSTEROIDS (RESP)	3,462	$1,037,976.26	2,064	$502.90	3.0%	↓2
11. SGLT2 INHIBITORS	1,511	$1,004,789.63	781	$1,286.54	2.9%	↓1
12. RESP/CNS STIMULANTS	5,629	$976,379.37	2,144	$455.40	2.8%	↓1
13. CFTR CORRECTORS	36	$703,839.86	14	$50,274.28	2.0%	↑5
14. ANTIDEPRESSANTS	27,364	$631,049.98	11,545	$54.66	1.8%	↓2
15. PITUITARY	372	$609,256.69	149	$4,088.97	1.7%	↑2

RDUR Report: Q4 2023



October Cases by Type of Criteria		
Criteria Description	**# of Cases**	**% of Cases**
Clinical Appropriateness	7	3.0%
Drug-Disease Conflicts	38	16.3%
Drug-Drug Conflicts	188	80.7%

November Cases by Type of Criteria		
Criteria Description	**# of Cases**	**% of Cases**
Clinical Appropriateness	110	37.5%
Drug-Disease Conflicts	4	1.4%
Drug-Drug Conflicts	176	60.1%
Therapeutic Duplication	3	1.0%

December Cases by Type of Criteria		
Criteria Description	**# of Cases**	**% of Cases**
Clinical Appropriateness	268	92.4%
Drug-Disease Interactions	22	7.6%
Drug-Drug Conflicts	2	0.7%

Clinical Report

Prior Authorization Updates

Drug Name	PA Status	Class
Agamree	PA	Non-Preferred Dosage Forms
Betaseron	PA	Multiple Sclerosis - Interferons
Coxanto	PA	NSAIDs
Jesduvroq	PA	Chronic Kidney Disease
Jylamvo	PA	Non-Preferred Dosage Forms
Ogsiveo	PA	Medications Over $3000
Omvoh	PA	Ulcerative Colitis
Perseris	PA	Antipsychotics – Long Acting Injectable (LAI)
Rivfloza	PA	Medications Over $3000
Rykindo ER	PA	Antipsychotics – Long Acting Injectable (LAI)
Triamterene	PA	Diuretics
Veozah	PA	Menopause – Vasomotor Symptoms
Vevye	PA	Dry Eye Syndrome
Welireg	PA	Medications Over $3000
Xphozah	PA	Chronic Kidney Disease and Ulcerative Colitis
Zilbrysq	PA	Medications Over $3000
Zituvio	PA	Diabetes - DPP4 Inhibitors
Zimhi	Remove PA	Opioid Reversal Medications

Corticosteroids - Inhaled Summary of Changes:
Due to Medicaid Rebate CAP removal, Flovent Diskus and Flovent HFA are being discontinued. Because of this, Arnuity Ellipta has been moved to a preferred agent. PA criteria was added to Asmanex HFA, QVAR Redihaler, and fluticasone HFA to accommodate requests where the relatively higher inspiratory flow is required for preferred agents.

Corticosteroids – Inhaled

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
ARNUITY ELLIPTA (fluticasone)	ALVESCO (ciclesonide)
ASMANEX (mometasone) TWISTHALER	ARMONAIR DIGIHALER (fluticasone)
budesonide suspension	ASMANEX HFA (mometasone)
PULMICORT FLEXHALER (budesonide)	fluticasone HFA
	fluticasone diskus
	PULMICORT RESPULES (budesonide)
	QVAR REDIHALER (beclomethasone)

GINA and EPR-3 Guidelines – SMART:
- For steps 3-5, ICS-formoterol is preferred for use as an as needed and regular daily treatment
- Please consider SMART therapy instead of single agent inhaled corticosteroid.
    - Both Symbicort and Dulera are available as HFA products

Quantity Limits to accommodate SMART therapy:
- 2 Symbicort or Dulera inhalers per 30-day supply not to exceed a total of 9 inhalers per 365 days without prior approval.

References:

1. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2023. Updated July 2023. Available from: www.ginasthma.org
2. Cloutier, Michelle M., et al. "2020 focused updates to the asthma management guidelines: a report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group." Journal of Allergy and Clinical Immunology 146.6 (2020): 1217-1270. Available at: https://www.epa.gov/sites/default/files/2021-05/documents/_sites_default_files_publications_asthmamanagementguidelinesreport-2-4-21.pdf

Electronic Age Verification:
- Fluticasone HFA does not require PA for ages 4 and under

Electronic Duration Verification:
- Budesonide Suspension 1 mg/2 mL is payable for 30 days every 75 days. For diluted nasal rinses, please use 0.5 mg/2 mL instead of 1 mg/2 mL for doses 1 mg per day or higher.
- Guidelines recommend that once control is achieved, dose should be titrated down to minimum dose required to maintain control. For doses 1.5 mg per day or lower, please use 0.5 mg/2 mL strength.

Prior Authorization
Initial Criteria – Approval Duration: 12 months
- The member must have failed a 30-day trial of each preferred inhaler of a unique active ingredient, as evidenced by paid claims or pharmacy printouts.
- Armonair Digihaler Only:
    - The member must have failed a 30-day trial of Asmanex HFA, as evidenced by pharmacy claims or pharmacy printouts.
    - Clinical justification must be provided explaining why the member is unable to use the preferred products (subject to clinical review).

- Asmanex HFA and QVAR Redihaler Only:
  - Preferred agent trials may be bypassed if member meets one of the following criteria:
    - Member is unable to achieve inspiratory flow rate of 40 L/min.
    - Member is unable to achieve inspiratory flow rate of 60 L/min and has previously had adrenal insufficiency with fluticasone.
    - Permanent disability preventing use of a dry powder inhaler
- fluticasone HFA only:
  - Preferred agent trials may be bypassed if member meets one of the following criteria:
    - Member is unable to achieve inspiratory flow rate of 40 L/min.
    - Permanent disability preventing use of a dry powder inhaler

References:

1. Sannarangappa V, Jalleh R. Inhaled corticosteroids and secondary adrenal insufficiency. Open Respir Med J. 2014 Jan 31;8:93-100. doi: 10.2174/1874306401408010093. PMID: 25674179; PMCID: PMC4319207.
2. Saag KG, Furst DE, Barnes PJ . Major side effects of inhaled glucocorticoids In: *UpToDate*, Post TW (Ed), UpToDate, Waltham, MA, 2023

Tardive Dyskinesia - Summary of Changes:
With the requirement for specialist consulting on the diagnosis, removed diagnosis criteria to be able to use the general form instead of require attestation specific form to collect the information.

Tardive Dyskinesia

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
AUSTEDO (deutetrabenazine)	tetrabenazine 25 mg
AUSTEDO XR (deutetrabenazine)	XENAZINE (tetrabenazine)
INGREZZA (valbenazine)	
tetrabenazine 12.5 mg	

Electronic Step Therapy Required

- The Initiation Pack or 40 mg x 7 days is required for titration to 80 mg capsules.

Prior Authorization Criteria

Initial Criteria – Approval Duration: 12 months

- The requested medication must be prescribed by, or in consult with, a neurologist or psychiatrist.
- The member must have a history of treatment with dopamine receptor blocking agent (DRBA).
- ~~The member must have a diagnosis of tardive dyskinesia, including the following:~~
    - ~~Involuntary athetoid or choreiform movements~~
    - ~~History of treatment with dopamine receptor blocking agent (DRBA)~~
    - ~~The member must have symptom duration lasting longer than 4-8 weeks~~

Phenylketonuria - Summary of Changes:
With the addition of Palynziq, there is an option available for those with two null mutations in trans. Sapropterin is not effective in those with two null mutations in trans.

Phenylketonuria	
PREFERRED AGENTS (CLINICAL PA REQUIRED)	**NON-PREFERRED AGENTS (PA REQUIRED)**
JAVYGTOR (sapropterin)	KUVAN (sapropterin)
sapropterin	PALYNZIQ (pegvaliase-pqpz)

Underutilization

- Sapropterin and Palynziq must be used adherently and will reject on point of sale for late fill

Prior Authorization Criteria

Prior Authorization Form - Phenylketonuria

Initial Criteria - Approval Duration: 2 months (sapropterin); 12 months (Palynziq)

- The member must have been compliant with a PHE restricted diet for past 6 months (documentation must be attached).
- The requested medication must be prescribed by, or in consult with, a geneticist or endocrinologist.
- Baseline PHE levels must be attached
  - For members of childbearing potential and children ≤ 12 years old: PHE levels must be above 360 µmoles/liter (6 mg/dL)
  - For members without childbearing potential, and children > 12 years old: PHE levels must be above 600 µmoles/liter 10 mg/dL)
- Sapropterin Only:
  - The member's weight must be provided. Requested initial dose must be 10 mg/kg
  - The member must not have two null mutations in trans
- Palynziq Only: One of the following must be met:
  - PHE levels must be attached documenting the member was unable to achieve a PHE level less than 600 µmoles/liter (10 mg/dL) despite a 3-month trial of 20 mg/kg dose of sapropterin with good compliance, as evidenced by paid claims or pharmacy printouts.
  - The member is known to have two null mutations in trans

Renewal Criteria:

- For same or reduced dose from previous trial:
  Approval Duration: 12 months - if dose is the same or less than previous trial
  - PHE level must be between 60 and 600 µmoles per liter
  - Sapropterin Only: The member's weight must be provided.

- For a dose increase from previous trial
  Approval Duration: 4 months - for a dose increase from previous trial
  - PHE level must be attached that were taken after previous trial (1 month for Kuvan, 4 months for Palynziq)
    - For members of childbearing potential and children ≤ 12 years old: PHE levels must be above 360 µmoles/liter (6mg/dL)
    - For members without childbearing potential, and children > 12 years old: PHE levels must be above 600 µmoles/liter 10mg/dL)
  - Sapropterin Only: The member's weight must be provided.

Unfinished Business:

Hyperkalemia - Summary of Changes:
The KDIGO guidelines recommend that NSAIDs be discontinued with hyperkalemia. Renin–angiotensin–aldosterone system inhibitors (RAASi) and mineralocorticoid receptor antagonists (MRAs) should be continued unless other measures, including potassium binders, fail to lower potassium.

Hyperkalemia (Chronic)	
PREFERRED AGENTS (CLINICAL PA REQUIRED)	**NON-PREFERRED AGENTS (PA REQUIRED)**
LOKELMA (sodium zirconium cyclosilicate)	VELTASSA (patiromer)

Prior Authorization Criteria

Initial Criteria – Approval Duration: 3 months
- The requested medication must be prescribed by, or in consult with, a nephrologist.
- If member is on renal dialysis, Medicare eligibility must be ruled out *(6-month approval may be allowed to determine eligibility)*.
- The member's current serum potassium level must be exceeding the upper limit of normal, as evidenced by documentation from at least two separate lab values, submitted with the request.
- The member must have failed 30-day trials with at least two of the following products:
  - bumetanide, chlorothiazide, fludrocortisone, furosemide, hydrochlorothiazide, indapamide, metolazone, torsemide
- The member must not be receiving nonsteroidal anti-inflammatory drugs (NSAIDs)
  - ~~the medications known to cause hyperkalemia listed below, OR medical justification must be provided explaining why discontinuation of these agents would be clinically inappropriate in this member:~~
  - ~~angiotensin-converting enzyme inhibitor~~
  - ~~angiotensin II receptor blocker~~
  - ~~aldosterone antagonist~~
  - ~~nonsteroidal anti-inflammatory drugs (NSAIDs)~~

Non-Preferred Agent Criteria:
- The member must have failed a 30-day trial with Lokelma, as evidenced with paid claims or pharmacy print outs.

Renewal Criteria – Approval Duration: 12 months
- The member's current serum potassium level is within normal limits or has been significantly reduced from baseline, as evidenced by lab documentation submitted with the request.

Reference:

1. Rossing, Peter, et al. "KDIGO 2022 clinical practice guideline for diabetes management in chronic kidney disease." *Kidney International* 102.5 (2022): S1-S127.

Prophylaxis of Migraine - Summary of Changes
Timolol removed from qualifying trial medications. Although some references cite it as an effective medication, it does not have the level of support required for inclusion in the compendia.

Migraine

Prophylaxis of Migraine

Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonist

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
AJOVY (fremanezumab-vfrm) INJECTION	AIMOVIG (erenumab-aooe) INJECTION
EMGALITY (galcanazumab-gnlm) INJECTION	NURTEC ODT (rimegepant) TABLETS
	QULIPTA (atogepant) TABLETS
	VYEPTI (eptinezumab-jjmr) – *Medical Billing Only*

Prior Authorization Criteria
Prior Authorization Form – Migraine Prophylaxis/Treatment

Initial Criteria – Approval Duration: *6 months*
- The member must experience 3 or more migraine days per month.
- The member must have failed 2-month trials of at least two of the following agents from different therapeutic classes, as evidenced by paid claims or pharmacy printouts:
    - amitriptyline, atenolol, divalproex sodium, metoprolol, nadolol, propranolol, ~~timolol,~~ topiramate, venlafaxine

Non-Preferred Agents Criteria:
- The member must have failed a 3-month trial of two self-administered CGRPs (Ajovy, Emgality, and Aimovig), as evidenced by paid claims or pharmacy printouts.
- *Vyepti Only:*
    - The member must have failed a 3-month trial of Nurtec ODT, as evidenced by paid claims or pharmacy printouts.

Renewal Criteria – Approval Duration: *12 months*
- The member must have experienced at least a 50% reduction in migraine frequency, pain intensity, or duration from baseline.

Eczema / Atopic Dermatitis - Summary of Changes
Required length of trial for dupilumab was changed from 6 months to 4 months. Clinical trials SOLO-1 and SOLO-2 assessed dupilumab efficacy after 16 weeks. The following source recommends discontinuation if efficacy is not seen after 16 weeks: Dupilumab | Eczema Treatment | Eczema.org

Eczema / Atopic Dermatitis

Systemic

Interleukin (IL)-4/13 Inhibitor

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
DUPIXENT (dupilumab) INJECTION	

Interleukin (IL)-13 Inhibitor

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
ADBRY (tralokinumab-idrm) INJECTION	

Janus Kinase (JAK) inhibitor

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
CIBINQO (abrocitinib) TABLET	
OLUMIANT (baricitinib)	
RINVOQ ER (upadacitinib) TABLET	

Prior Authorization Criteria
Prior Authorization Form - Atopic Dermatitis

Initial Criteria - Approval Duration: 3 months
- Member must have failed a 6-week trial of tacrolimus or pimecrolimus as evidenced by paid claims or pharmacy printouts:
- One of the following must be met:
  - The member has failed a two 2-week trials of topical corticosteroids of medium or higher potency, as evidenced by paid claims or pharmacy printouts.
  OR
  - The member meets both of the following (1 AND 2):
    1. Affected area is on face, groin, axilla, or under occlusion.
    2. Member must have failed two 2-week trials of topical corticosteroids of low or higher potency, as evidenced by paid claims or pharmacy printouts.

Janus Kinase (JAK) Inhibitors Only:
- The member must have had a 4~~6~~-month trial with dupilumab.

Cholestatic Pruritis – Summary of Changes
Ileal bile acid transport inhibitors - Length of Therapy:
Long-term treatment (mean treatment duration 4.7 years) with maralixibat has been studied and shown to reduce event-free survival (EFS). EFS being variceal bleeding, ascites requiring therapy, surgical biliary diversion, liver transplantation, or death. Predictors of EFS include >1 point improvement in pruritus score, serum bilirubin <6.5 mg/dL, and bile acids <200 micromol/L. Long-term follow-up studies of odevixibat are ongoing (NCT05035030).

Cholestasis Pruritis

Alagille Syndrome (ALGS):

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED (PA REQUIRED)
LIVMARLI (maralixibat)	BYLVAY (odevixibat)

Progressive Familial Intrahepatic Cholestasis (PFIC):

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

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 hepatologist or gastroenterologist.
- Documentation must be provided to support the presence of moderate to severe pruritis.
- The member must have cholestasis, as evidenced by ≥ 1 of the following:
  - Serum bile acid > 3x upper limit of normal as defined by the reporting laboratory
  - Conjugated bilirubin > 1mg/dL
  - Fat soluble vitamin deficiency otherwise unexplainable
  - Gamma-glutamyl transferase > 3x the upper limit of normal
  - Intractable pruritus explainable only by liver disease
- The member must not have a history of liver transplant or decompensated cirrhosis.
- The member must not have history of biliary diversion surgery within the past 6 months.
- The member must have failed at least a 3-month trial of both of the following, as evidenced by paid claims or pharmacy printouts:
  - Ursodiol
  - agents to treat pruritis: cholestyramine, rifampin, antihistamines
- Bylvay Only:
  - ALGS:
    - Genetic testing confirms pathogenic variant (e.g., *JAG1* and *NOTCH2).*
    - The member has had a 6-month trial with Livmarli.
  - PFIC:
    - Genetic testing confirms pathogenic variant (e.g., ATP8B1, ABCB11, ABCB4, TJP2, NR1H4, and MYO5B).
    - Genetic testing does not indicate PFIC Type 2 with ABCB11 variants that predict complete absence of BSEP-3 protein.
- Livmarli Only:
  - Genetic testing confirms pathogenic variant of JAG1 or NOTCH1

Renewal Criteria - Approval Duration: 12 months

- The member has experienced an improvement in pruritis, as evidenced by clinical documentation.
- The member must have experienced a reduction in ~~serum bile acid as defined as a bile acid reduction ≥ 70% or reaching a bile acid level ≤ 70 micromol/L~~ bilirubin < 6.5mg/dL and bile acids < 200 micromol/L.

References

1. Sokol RJ, Gonzales EM, Kamath BM, et al. Predictors of 6-year event-free survival in Alagille syndrome patients treated with maralixibat, an ileal bile acid transporter inhibitor. Hepatology 2023; 78:1698.
2. Shneider BL, Spino CA, Kamath BM, Magee JC, Ignacio RV, Huang S, Horslen SP, Molleston JP, Miethke AG, Kohli R, Leung DH, Jensen MK, Loomes KM, Karpen SJ, Mack C, Rosenthal P, Squires RH, Baker A, Rajwal S, Kelly D, Sokol RJ, Thompson RJ; for ChiLDReN and UK IMAGO/IMAGINE Investigators. Impact of long-term administration of maralixibat on children with cholestasis secondary to Alagille syndrome. Hepatol Commun. 2022 Aug;6(8):1922-1933. doi: 10.1002/hep4.1992. Epub 2022 Jun 7. PMID: 35672955; PMCID: PMC9315125.

New Business:

FIRST REVIEW OF ACID BLOCKERS (VOQUEZNA)

Acid blockers are used in various disease states such as ulcer treatment, H. pylori, hypersecretory conditions, and gastroesophageal reflux disease (GERD). GERD can be classified as nonerosive reflux disease (NERD), erosive esophagitis (EE), and Barrett's esophagus (BE). Voquezna is a first-in-class potassium competitive acid blocker (PCAB) that has been FDA approved for the treatment of H. pylori and EE. Proton pump inhibitors (PPIs) are first line agents for EE.

	Histamine H_2 Receptor Antagonist (H_2RA)	**PPIs**	**PCAB**
Drugs within the category	• Cimetidine • Famotidine • Nizatidine	• dexlansoprazole (Dexilant) • esomeprazole (Nexium) • lansoprazole (Prevacid) • omeprazole (Prilosec) • omeprazole-sodium bicarb (Zegerid) • pantoprazole (Protonix) • rabeprazole (Aciphex)	Voquezna (vonoprazan)
Difference in Mechanism	Inhibits H_2 receptors	Inhibits H+, K+-ATPase enzyme system	inhibits H+, K+-ATPase enzyme system by reversibly binding to K+
Prodrug	No	Yes: must be taken 30-60 minutes prior to food to create an acidic environment	No
Onset	1 hour	1-3 hours	2-3 hours
Maximal acid suppression after dosing	10-12 hours	3-5 days	1 day
Duration of treatment	Twice daily up to 12 weeks	• Healing: daily for 8 weeks, an additional 8 weeks of treatment may be considered • Maintenance: various durations	• Healing: daily for 8 weeks • Maintenance: daily for 6 months
Warnings	Risk of delirium	Carry similar warnings such as C difficile infection, bone fractures, hypomagnesemia, vitamin B12 deficiency, gastric malignancy, etc.	
Cost per **year**	~$36	~$20±	$7,800

Based on adult dosing for EE maintenance at lowest per unit WAC cost. ± omeprazole or pantoprazole, comparing solid dosage forms.

FDA Approval

Voquezna (vonoprazan): 505(b) New Drug Application (NDA) pathway

- Triple Pak (vonoprazan tablets; amoxicillin capsules; clarithromycin tablets): Type 1 New Molecular Entity and Type 4 New Combination, PRIORITY
- Dual Pak (vonoprazan tablets; amoxicillin capsules): Type 5 New formulation (Dual Pack) – New Molecular Entity, PRIORITY
- Voquezna (vonoprazan): STANDARD

**Initial approval 5/3/22 for H. pylori, amendment 5/19/23 due to response from 2/7/23 action letter (impurities); new indication approval 11/1/23 for EE*

Clinical Trials

Approval was based on results from Phase 3 PHALCON-EE study (NCT04124926). The trial was a randomized, double-blind, multicenter study that enrolled 1,024 patients with EE in U.S. and Europe. The study compared Voquezna to lansoprazole.

Primary Endpoint:

- Healing phase:
  - Results showed that Voquezna 20 mg was non-inferior with healing rate of all grades of EE of 93% compared to 85% for lansoprazole 30 mg by week 8 (P<0.0001)
- Maintenance phase
  - Results showed that Voquezna 20 mg was non-inferior to lansoprazole for maintaining healing of EE through week 24 (79.2% for Voquezna vs 72% for lansoprazole) (P<0.0001)

Secondary Endpoints:

- Healing phase:
  - Demonstrated superior rates of healing in patients with moderate-to-severe disease (LA Grade C/D) at Week 2 with Voquezna 20 mg (70%) compared to lansoprazole 30 mg (53%) (P=0.0008)
  - Voquezna 20 mg also demonstrated non-inferiority to lansoprazole 30 mg in mean percentage of 24-hour heartburn free days over the healing period
- Maintenance phase:
  - Voquezna 10 mg (79%) was superior to lansoprazole 15 mg (72%) in all randomized patients as well as a subset of patients with moderate to severe EE (75% for Voquezna 10 mg compared to 61% for lansoprazole 15 mg) (P=0.0490)
  - Voquezna 10 mg demonstrated non-inferiority to lansoprazole 15 mg for relief of heartburn

Safety: Adverse advents were comparable to lansoprazole in the trial.

Place in Therapy

Voquezna is a potential option in patients with severe erosive esophagitis (LA Class C/D) and PPI-refractory patients.

Advantages	Disadvantages
• Alternative for patients who do not respond to first line agents or with severe EE • Voquezna does not depend on gastric acid activation to inhibit acid secretion and binds to active and inactive proton pumps while PPIs only inhibit active proton pumps. • Does not require formulation to protect from gastric acid. • Can be administered without regard to meals.	• Cost • Non-inferiority designed trials compared use of Voquezna to lansoprazole only; one study did not compare to compendia supported lansoprazole dosing • Long term safety is unknown • Does not have alternative dosage forms, cannot be crushed/chewed

Current Utilization

	Quarter 1 2023			Quarter 2 2023		
Medication	**Rx Count**	**% of Rx**	**Reimb Amount**	**Rx Count**	**% of Rx**	**Reimb Amount**
cimetidine	26	0.3%	$844.33	29	0.3%	$890.57
cimetidine HCl	5	0.0%	$210.95	1	0.0%	$22.54
dexlansoprazole	108	1.1%	$31,107.28	108	1.1%	$31,308.80
esomeprazole	129	1.3%	$7,383.80	125	1.2%	$7,691.18
famotidine	1,087	10.9%	$19,313.87	1,122	11.1%	$19,908.84
lansoprazole	129	1.3%	$2,519.34	148	1.5%	$4,112.76
nizatidine	0	0.0%	$ -	1	0.0%	$24.47
omeprazole	5,177	51.8%	$67,175.16	5,131	50.8%	$65,739.63
omeprazole/Na bicarbonate	0	0.0%	$ -	26	0.3%	$8,260.43
pantoprazole	3,327	33.3%	$49,760.50	3,402	33.7%	$50,794.56
rabeprazole	15	0.1%	$272.85	14	0.1%	$254.51
Voquezna	0	0.0%	$ -	0	0.0%	$ -
TOTALS	10,003		$178,588.08	10,107		$189,008.29
	Quarter 3 2023			**Quarter 4 2023**		
Medication	**Rx Count**	**% of Rx**	**Reimb Amount**	**Rx Count**	**% of Rx**	**Reimb Amount**
cimetidine	28	0.3%	$904.72	20	0.2%	$691.40
cimetidine HCl	0	0.0%	$ -	113	0.0%	$34,313.91
dexlansoprazole	111	1.2%	$32,559.51	113	1.3%	$34,313.91
esomeprazole	110	1.2%	$6,286.60	101	1.2%	$6,062.66
famotidine	1,043	11.1%	$17,959.25	1,044	12.1%	$18,414.72
lansoprazole	122	1.3%	$3,134.73	136	1.6%	$3,616.81
nizatidine	0	0.0%	$ -	0	0.0%	$ -
omeprazole	4,759	50.9%	$60,845.25	4,316	49.9%	$55,390.54
omeprazole/Na bicarbonate	33	0.4%	$9,902.83	71	0.8%	$22,157.53
pantoprazole	3,123	33.4%	$45,733.56	2,835	32.8%	$42,169.08
rabeprazole	28	0.3%	$509.32	16	0.2%	$301.77
Voquezna	0	0.0%	$ -	0	0.0%	$ -
TOTALS	9,357		$177,835.77	8,765		$217,432.33

References:

1. *Vonoprazan. In-Depth Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. January 11, 2024. https://www.micromedexsolutions.com*
2. *Vonoprazan. Drug Facts and Comparisons. Wolters Kluwer Health, Inc. Riverwoods, IL. January 25, 2024. http://online.factsandcomparisons.com*
3. *Voquezna (vonoprazan oral tablets). [prescribing information]. Buffalo Grove, IL: Phathom Pharmaceuticals Inc; 2023.*
4. *U.S. Food and Drug Administration, Center for Drug Evaluation and Research. Voquezna NDA 215151 approval letter, November 1, 2023. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2023/215151Orig1s000ltr.pdf*
5. *Voquezna: A New Treatment for Erosive GERD. IPD Analytics. Aventura, FL. November 2023. https://www.ipdanalytics.com*
6. *Proton Pump Inhibitors. Drug Facts and Comparisons. Wolters Kluwer Health, Inc. Riverwoods, IL. January 31, 2024. http://online.factsandcomparisons.com*
7. *Histamine H2 Antagonists. Drug Facts and Comparisons. Wolters Kluwer Health, Inc. Riverwoods, IL. January 31, 2024. http://online.factsandcomparisons.com*
8. *Cimetidine. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. January 24, 2024. https://www.micromedexsolutions.com*

9. *Famotidine. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. January 24, 2024. https://www.micromedexsolutions.com*
10. *Nizatidine. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. December 28, 2023. https://www.micromedexsolutions.com*
11. *Dexlansoprazole. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. January 25, 2024. https://www.micromedexsolutions.com*
12. *Esomeprazole. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. January 25, 2024. https://www.micromedexsolutions.com*
13. *Lansoprazole. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. January 25, 2024. https://www.micromedexsolutions.com*
14. *Omeprazole. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. January 25, 2024. https://www.micromedexsolutions.com*
15. *Omeprazole/sodium bicarbonate. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. February 5, 2024. https://www.micromedexsolutions.com*
16. *Pantoprazole. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. January 25, 2024. https://www.micromedexsolutions.com*
17. *Rabeprazole. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. January 25, 2024. https://www.micromedexsolutions.com*
18. *Laine L, Sharma P, Mulford DJ, et al. Pharmacodynamics and pharmacokinetics of the potassium-competitive acid blocker vonoprazan and the proton pump inhibitor lansoprazole in US subjects. Am J Gastroenterol 2022;117:1158-1161.*
19. *Lundell L, Vieth M, Gibson F, et al. Systematic review: The effects of long-term proton pump inhibitor use on serum gastrin levels and gastric histology. Aliment Pharmacol Ther 2015;42:649-663.*

FIRST REVIEW OF SEBORRHEIC DERMATITIS (ZORYVE)

Seborrheic dermatitis is a chronic relapsing condition involving sebaceous glands; although the cause is unknown, *Malassezie* species is oftentimes associated with the condition. Symptoms range from mild, such as dandruff, to severe involving widespread yellowish scales.

Treatment is dependent on the severity and location of the condition, but may consist of topical antifungals, anti-inflammatories, Lobrox (crisaborole), or Zoryve (roflumilast); refractory seborrheic dermatitis may require oral antifungal treatment. Topical corticosteroids (TCS) are considered first or second line agents depending on the severity.

General key notes for treatment options:

- Some agents are used off-label for seborrheic dermatitis
- Most products share similar dermatologic side effects: erythema, pruritis, burning
- Age limitations on various products from ingredients that are not safe for certain ages (e.g., propylene glycol)
- Most products have various formulations

Topical Antifungals:	
Rationale for use	• Decrease *Malassezie* and mild anti-inflammatory activity • **Place in therapy:** Considered first line for mild severity
Agents per guidelines	Azoles: • Ketoconazole 2% cream, 2% gel, 2% shampoo • Miconazole 2 % cream • Terbinafine 1% solution/cream
	Ciclopirox 0.77% gel, 1% shampoo
Mechanism	• Azoles: inhibits cytochrome P450 and alters cell wall permeability • Ciclopirox: exact mechanism of action is unknown, inhibits transport of substrates to fungal cells
Frequency	• Shampoos are often used twice weekly for treatment and once weekly for maintenance • Topical skin agents are used once to twice daily
Key notes	• Multiple formulations • Slower onset than TCS • Some agents have limited data: miconazole, terbinafine
Cost per **gram**	$~1.00
Topical Anti-Inflammatory Agents:	
Rationale for use	• TCS and calcineurin inhibitors are used due to their anti-inflammatory effects • **Place in therapy:** o TCS considered first line for moderate to severe cases and second line for no improvement after antifungal use in mild cases o Calcineurin inhibitors used in cases with frequent relapse
Mechanism	• TCS: induce phospholipase A2 inhibitory proteins and inhibit release of arachidonic acid • Calcineurin inhibitors (tacrolimus, pimecrolimus): inhibits transport of agents required for synthesis of DNA, RNA, and protein
Key Points	• TCS: limitations of use due to side effects (e.g., adrenal suppression, Cushing syndrome, hyperglycemia, skin atrophy, etc.) • Relapse occurs more often with TCS • Calcineurin inhibitor with the most data: pimecrolimus 1% cream
Cost per **gram**	• Topical corticosteroid: $~1 • Tacrolimus: $2.33 • Pimecrolimus: $8.13

Topical Phosphodiesterase-4 (PDE4) Inhibitors	
Drugs within the class	• Eucrisa (crisaborole) • Zoryve (roflumilast): foam is FDA approved for seborrheic dermatitis
Rationale for use	• Mechanism for therapeutic effect is not well defined • **Place in therapy:** considered after frequent use of steroids
Mechanism	Phosphodiesterase-4 (PDE4) inhibitor, increases intracellular cyclic adenosine monophosphate (cAMP) levels
Key Points	• High cost
Cost per **gram**	• Eucrisa: $10.73 • Zoryve: $14.30

Based on lowest per unit WAC cost; cost per gram provided since cost of therapy will depend on extent/location of dermatitis
**Other agents are available such as over-the-counter products (i.e., selenium sulfide, zinc pryithione, tar shampoo) and steroidal device Promiseb*

FDA Approval

Zoryve (roflumilast): December 15, 2023; 505(b) New Drug Application (NDA) pathway Type 3 New Dosage Form and Type 4 New Combination, STANDARD

Clinical Trials

Approval was based on two randomized, double blind, vehicle-controlled trials STRATUM (NCT04973228) and Trial 203 (NCT04091646). Enrolled total was 683 adult and pediatric patients with seborrheic dermatitis involving the scalp, face, and/or body with Investigator Global Assessment (IGA) of moderate or severe (IGA of 3 or 4 on a 5-point scale from 0 to 4) were randomized to receive Zoryve foam or vehicle once daily for 8 weeks.

Primary Endpoints: Proportion of subjects who achieved IGA treatment success at week 8. Success was defined as score of clear (0) or almost clear (1), plus a 2-grade improvement from baseline.

- In STRATUM, patients randomized to Zoryve foam achieved a 79.5% IGA success compared to 58% IGA success with vehicle foam. There was a higher percentage of subjects who achieved a reduction of at least 4 points on the Worst Itch-Numeric Rating Scale (WI-NRS), among subjects with at least 4 from baseline, at week 8 in the group who received Zoryve foam (62.8%) vs vehicle foam (40.6%).
- In Trial 203, patients randomized to Zoryve foam achieved 73.1% IGA success compared to 40.5% IGA success with vehicle foam.

Safety: Adverse effects reported were similar among groups

Place in Therapy

May be considered after frequent use of steroids and non-response to other treatment options.

Advantages	Disadvantages
• Option for patients who do not response to other agents • Avoid TCS side effects	• High cost • Age limitations (9 years and older) • One formulation (foam) option is FDA approved for seborrheic dermatitis • Clinical trial did not have an active comparator

Current Utilization

	Quarter 1 2023			Quarter 2 2023		
Medication	**Rx Count**	**% of Rx**	**Reimb Amount**	**Rx Count**	**% of Rx**	**Reimb Amount**
alclometasone dipropionate	8	0.2%	$373.96	1	0.0%	$40.68
betamethasone dipropionate	90	2.8%	$4,801.74	99	3.0%	$3,238.19
betamethasone valerate	35	1.1%	$2,314.77	27	0.8%	$959.05
betamethasone/prop glyc	15	0.5%	$513.32	21	0.6%	$634.10
ciclopirox	6	0.2%	$148.42	10	0.3%	$327.89
clobetasol propionate	222	6.8%	$5,702.73	226	6.9%	$4,963.06
clobetasol propionate/emoll	3	0.1%	$124.09	2	0.1%	$54.83
desonide	92	2.8%	$3,651.94	91	2.8%	$2,929.72
desoximetasone	1	0.0%	$32.79	2	0.1%	$58.49
Eucrisa (crisaborole)	3	0.1%	$2,129.88	1	0.0%	$356.18
fluocinolone acetonide	69	2.1%	$2,273.74	57	1.7%	$1,929.94
fluocinolone/shower cap	23	0.7%	$791.44	13	0.4%	$372.24
fluocinonide	137	4.2%	$3,522.99	131	4.0%	$3,762.04
fluocinonide/emollient base	1	0.0%	$61.38	1	0.0%	$70.08
fluticasone propionate	3	0.1%	$75.78	9	0.3%	$198.21
halobetasol propionate	3	0.1%	$75.58	1	0.0%	$24.10
hydrocortisone	512	15.6%	$14,179.23	490	14.9%	$7,877.91
hydrocortisone acetate	0	0.0%	$-	0	0.0%	$ -
hydrocortisone butyrate	1	0.0%	$68.78	1	0.0%	$79.06
hydrocortisone valerate	3	0.1%	$ 109.85	5	0.2%	$180.15
hydrocortisone/pramoxine	7	0.2%	$1,100.85	8	0.2%	$1,240.55
ketoconazole	505	15.4%	$12,987.18	511	15.5%	$10,370.62
miconazole nitrate	1	0.0%	$-	2	0.1%	$ -
mometasone furoate	65	2.0%	$1,862.16	43	1.3%	$825.69
pimecrolimus	34	1.0%	$14,564.44	28	0.8%	$14,086.65
tacrolimus	119	3.6%	$9,888.15	106	3.2%	$8,542.11
terbinafine	0	0.0%	$-	0	0.0%	$ -
triamcinolone acetonide	1314	40.2%	$30,445.29	1411	42.8%	$21,938.97
Zoryve (roflumilast)	0	0.0%	$-	0	0.0%	$ -
TOTALS	3272		$111,800.48	3297		$85,060.51
	Quarter 3 2023			**Quarter 4 2023**		
Medication	**Rx Count**	**% of Rx**	**Reimb Amount**	**Rx Count**	**% of Rx**	**Reimb Amount**
alclometasone dipropionate	3	0.1%	$91.36	4	0.1%	$120.44
betamethasone dipropionate	94	3.1%	$3,240.90	67	2.4%	$2,214.46
betamethasone valerate	26	0.8%	$737.24	25	0.9%	$914.76
betamethasone/prop glyc	18	0.6%	$496.94	20	0.7%	$580.76
ciclopirox	7	0.2%	$258.27	11	0.4%	$439.97
clobetasol propionate	202	6.6%	$4,511.46	194	7.0%	$4,204.26
clobetasol propionate/emoll	0	0.0%	$ -	2	0.1%	$62.39

desonide	80	2.6%	$2,221.88	69	2.5%	$1,965.07
desoximetasone	4	0.1%	$299.31	2	0.1%	$123.26
Eucrisa (crisaborole)	0	0.0%	$ -	0	0.0%	$ -
fluocinolone acetonide	61	2.0%	$1,888.10	55	2.0%	$1,797.77
fluocinolone/shower cap	19	0.6%	$615.10	21	0.8%	$735.79
fluocinonide	118	3.8%	$3,019.66	116	4.2%	$2,970.08
fluocinonide/emollient base	0	0.0%	$ -	0	0.0%	$ -
fluticasone propionate	6	0.2%	$132.49	5	0.2%	$110.12
halobetasol propionate	3	0.1%	$121.35	4	0.1%	$124.90
hydrocortisone	424	13.8%	$6,706.38	425	15.2%	$6,807.32
hydrocortisone acetate	0	0.0%	$ -	0	0.0%	$ -
hydrocortisone butyrate	0	0.0%	$ -	0	0.0%	$ -
hydrocortisone valerate	1	0.0%	$22.94	2	0.1%	$42.17
hydrocortisone/pramoxine	6	0.2%	$949.93	5	0.2%	$435.68
ketoconazole	512	16.6%	$10,152.77	458	16.4%	$9,300.72
miconazole nitrate	0	0.0%	$ -	0	0.0%	$ -
mometasone furoate	45	1.5%	$867.32	36	1.3%	$731.42
pimecrolimus	26	0.8%	$12,806.03	27	1.0%	$9,615.48
tacrolimus	112	3.6%	$7,967.57	116	4.2%	$8,096.75
terbinafine	0	0.0%	$ -	0	0.0%	$ -
triamcinolone acetonide	1311	42.6%	$20,741.75	1124	40.3%	$17,496.10
Zoryve (roflumilast)	0	0.0%	$ -	0	0.0%	$ -
TOTALS	3078		$77,848.75	2788		$68,889.67

References:

1. *Zoryve (roflumilast topical foam, 0.3%). [prescribing information]. Westlake Village, CA: Arcutis Biotherapeutics Inc; December 2023.*
2. *U.S. Food and Drug Administration, Center for Drug Evaluation and Research. Zoryve NDA 217242 approval letter, December 15, 2023. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2023/217242Orig1s000ltr.pdf*
3. *Del Rosso JQ. Adult seborrheic dermatitis: a status report on practical topical management. J Clin Aesthet Dermatol. 2011 May;4(5):32-8. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3100109/pdf/jcad_4_5_32.pdf.*
4. *Sasseville D. Seborrheic dermatitis in adolescents and adults. UpToDate, Fowler J, Corona R (Ed) [Internet]. Waltham, MA: UptoDate; January 12, 2024. Available from: www.uptodate.com*
5. *Roflumilast. Drug Facts and Comparisons. Wolters Kluwer Health, Inc. Riverwoods, IL. January 9, 2024. http://online.factsandcomparisons.com*
6. *Roflumilast. In-Depth Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. January 11, 2024. https://www.micromedexsolutions.com*
7. *Identifier NCT04973228, Trial of PDE4 Inhibition With Roflumilast for the Management of Seborrheic Dermatitis (STRATUM). ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). March 10, 2023. Available from: http://clinicaltrials.gov*
8. *Identifier NCT04091646, Safety and Efficacy of ARQ-154 Foam in Subjects With Seborrheic Dermatitis. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). July 3, 2023. Available from: http://clinicaltrials.gov*
9. *Corticosteroids, topical. Drug Facts and Comparisons. Wolters Kluwer Health, Inc. Riverwoods, IL. January 31, 2024. http://online.factsandcomparisons.com*
10. *Tacrolimus. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. February 1, 2024. https://www.micromedexsolutions.com*
11. *Pimecrolimus. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. December 13, 2023. https://www.micromedexsolutions.com*
12. *Crisaborole. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. April 14, 2023. https://www.micromedexsolutions.com*

FIRST REVIEW OF PRIMARY HYPEROXALURIA TYPE 1 (RIVFLOZA)

Primary hyperoxaluria Type 1 (PH1) is a rare disease that can lead to kidney damage and failure. Patients with PH1 have an excess production of oxalate causing kidney and urinary stones; over time as kidney function decreases, stones can be deposited elsewhere.

Management of PH1 includes increasing fluid intake, urinary alkalization, and high-dose vitamin B6 (pyridoxine). Patients are evaluated for the need of dialysis and transplant as well. There are two FDA approved ribonucleic acid interference (RNAi) medications (Rivloza and Oxlumo) for the treatment of PH1 that work by targeting various stages of oxalate production; there is no evidence to support using these agents together. Both Rivfloza and Oxlumo's most reported side effects are injection site reactions.

	Rivfloza (nedosiran)	Oxlumo (lumasiran)
Mechanism	• Inhibits expression of hepatic lactate dehydrogenase (LDH) • LDH is the enzyme for the last step of oxalate production	• Targets hydroxyacid oxidase 1 (HAO1) which decreases glycolate oxidate (GO) enzyme • This leads to a decrease in glyoxylate, a substrate for oxalate production
Administration	• Subcutaneous by a healthcare professional (HCP), caregiver, or patient • Once monthly	• Subcutaneous by a HCP • Three monthly loading doses, then every 3 months
Labeled indication	• PH1, 9 years of age and older, adults • Relatively preserved kidney function (e.g., eGFR ≥30 mL/minute/1.73 m^2)	• PH1, pediatric and adults
Cost per **dose**	$62,880.00	$104,698.00
Cost per **year**	$754,560.00	$628,188.00

Based on dosing for adult weighing 60 kg at lowest per unit WAC cost. Does not include cost of administration by healthcare provider.

FDA Approval

Rivfloza (nedosiran sodium): September 29, 2023; 505(b) New Drug Application (NDA) pathway; Type 1 New Molecular Entity, STANDARD; orphan

Clinical Trials

Rivfloza was approved based on the randomized, double-blind phase 2 PHYOX2 trial (NCT03847909) which compared Rivfloza (N=23) and placebo (N=12) in patients aged 6 years or older with PH1 or PH2 and relatively preserved kidney function. Efficacy was not evaluated for PH2 population due to low enrollment in the trial, so Rivfloza is only indicated for PH1.

After 6 months of treatment in PHY0X2, patients could enroll in the single-arm extension study, PHY0X3 (NCT04042402). All patients were treated with Rivfloza and the reduction in urinary oxalate was maintained in the 13 patients with PH1 for an additional 6 months of treatment.

Primary Endpoint:
Area under the curve, from days 90 to 180, of the % change from baseline in 24-hour urinary oxalate excretion: least-squared (LS) mean $AUC_{24\text{-hour Uox}}$ was -3486 (95% CI: -5025, -1947) in the Rivfloza group compared to 1490 (95% CI: 781, 3761) in the placebo group (P<0.0001). Among patients with PH1, the between group difference was 56% (95% CI: 33%, 80%) corrected for BSA in patients < 18 years of age averaged over days 90, 120, 150, and 180.

Secondary Endpoint: Percent of patients to achieve normal or near-normal 24-hour UOx excretion at two consecutive visits (50% vs 0%, P=0.002)

Safety: Injection site reactions most reported

Place in Therapy

Unknown: Long term studies needed to assess efficacy and safety; patients still may require transplant and/or dialysis

Advantages	Disadvantages
• Second approved medication for PH1 with a slightly different mechanism of action • Can be self-administered	• High cost • No head-to-head studies comparing approved products • Smaller population for labeled indication • More frequent dosing • Small enrollment in studies

Current Utilization

	Quarter 1-4 2023		
Medication	**Rx Count**	**% of Rx**	**Reimb Amount**
Oxlumo	0	0	0
Rivfloza	0	0	0

Rivfloza billed with unspecified diagnosis code, not reportable for PH1 use

References:

1. *Rivfloza (nedosiran injection, for subcutaneous use). [prescribing information]. Costa Mesa, CA: Pyramid Laboratories; September 2023.*
2. *U.S. Food and Drug Administration, Center for Drug Evaluation and Research. Rivfloza NDA 215842 approval letter, September 29, 2023. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2023/215842Orig1s000ltr.pdf*
3. *Rivfloza (nedosiran): New Drug Review. IPD Analytics. Aventura, FL. October 2023. https://www.ipdanalytics.com*
4. *Nedosiran injection. Drug Facts and Comparisons. Wolters Kluwer Health, Inc. Riverwoods, IL. January 26, 2024. http://online.factsandcomparisons.com*
5. *Nedosiran. In-Depth Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. October 17, 2023. https://www.micromedexsolutions.com*
6. *Lumasiran. In-Depth Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. October 14, 2022. https://www.micromedexsolutions.com*

FIRST REVIEW OF MYASTHENIA GRAVIS (ZILBRYSQ)

Myasthenia gravis (MG) is an autoimmune disorder that occurs when antibodies attack proteins in the neuromuscular junction membrane; most patients have anti-acetylcholine receptor antibody positive disease (AChR Ab+).

Treatment goals are to improve muscle strength, limit symptoms, and prevent crises. Cholinesterase inhibitors are used in mild to moderate MG for symptom management. Patients oftentimes need immunosuppressive therapy as well; biologics are usually reserved for refractory disease and guidelines do not give preference to certain agents. Rapid immunotherapy agents are used to treat crises.

ORAL AGENTS			
Cholinesterase Inhibitors: Pyridostigmine			
Indication	• Can cause significant cholinergic, cardiac, respiratory, and gastric side effects • Overdosage may cause cholinergic crisis: rare, muscle weakness • Inconsistent response from patient to patient		
Cost per **year**	$1,836		
Immunosuppressive Agents:			
Agents	• Glucocorticoids: typically used initially, have a warning that they can worsen MG within the first 2 weeks of treatment Other agents are used for maintenance and to limit long term steroid use; have warnings for risk of malignancy • Azathioprine • Mycophenolate mofetil • Cyclosporine • Tacrolimus		
Cost per **year**	$192 (azathioprine) - $540 (tacrolimus)		
INJECTABLE AGENTS			
Complement Inhibitors:			
Indication	AChR Ab+		
Agents	**Zilbrysq (zilucoplan)** • Subcutaneous (SC) • Self-administered • Once daily • Can be administered with IVIG and plasma exchange (PE) without requiring dose adjustments	Soliris (eculizumab) • Intravenous (IV) • HCP administered • Once every 2 weeks	Ultomiris (ravulizumab) • IV • HCP administered • Once every 8 weeks
Warnings	• Black box warning (BBW) and risk evaluation mitigation strategy (REMS) due to risk of meningococcal infections • Risk for other infections, including Neisseria meningitis • Pancreatitis and pancreatic cysts		
Cost per **year**	• Zilbrysq: $381,108 • Soliris: $730,576 • Ultomiris: $550,743.93		
FcRn Antagonists:			
Indication	AChR Ab+ *Rystiggo also approved for muscle-specific tyrosine kinase (MuSK) Ab+		
Agents	• Vyvgart (ergartigimod alfa) • Vyvgart Hytrulo (efgartigimod alfa/hyaluronidase) • Rystiggo (rozanolixizumab-noli)		

Key notes	• All are administered by a HCP (Vyvgart IV, others SC) • Frequency is weekly and cyclic • Do not have BBW and REMS requirements but do carry risk of infections
Cost per **cycle**	• Vyvgart: $48,552 • Vyvgart Hytrulo: $63,092 • Rystiggo: $72,600
Anti-B-cell Therapy	
Indication	Refractory MG and/or MuSK antibody-positive disease
Agents	Rituximab (Riabni, Rituxan, Ruxience, Truxima)
Key notes	• IV weekly or biweekly • Labeled warnings for bowel obstruction/perforation, cytopenia, renal toxicity, and tumor lysis syndrome
Cost per **year**	$22,548.48-73,282.56 (depending on dosing frequency)
Rapid Immunotherapy: plasmapheresis and IVIG	
Indication	• MG crisis • Severe or rapidly worsening disease • Can be used to bridge therapy when starting agents with a slower onset

Based on dosing for adult weighing 60 kg (body surface area 1.6 m2) at lowest per unit WAC cost.

FDA Approval

Zilbrysq (zilucoplan): October 17, 2023; 505(b) New Drug Application (NDA) pathway Type 1 New Molecular Entity, STANDARD; orphan

Clinical Trials

Zilbrysq was approved based on a 12-week, multicenter, randomized, double-blind placebo-controlled phase 3 RAISE trial (NCT04115293). 174 patients were randomized to receive either Zilbrysq or placebo.

Primary Endpoint: Patients assigned to Zilbrysq achieved a -4.39 (-5.28, -3.50) change from baseline in the Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) total score vs. -2.30 (-5.28, -3.50) in the placebo group ($P < 0.001$) after twelve weeks of treatment.

Secondary Endpoint:

- Zilbrysq achieved a -6.19 (-7.29, -5.08) change from baseline in the quantitative Myasthenia Gravis (QMG) total score vs. placebo -3.25 (-4.32, -2.17) ($P<0.001$).
- The proportion of MG-ADL responders with at least a 3-point improvement at week 12 was greater for Zilbrysq (73.1%) compared to placebo (46.1%) ($P<0.001$).
- The proportion of QMG responders with at least a 5-point improvement was also greater for Zilbrysq (58%) compared to placebo (33%) at week 12 ($P= 0.0012$)

Safety: Most reported adverse effects were injection site reactions, upper respiratory tract infections, diarrhea but were similar among groups

**In both MG-ADL and QMG scales, higher scores indicate more severe impairment.*

Place in Therapy

Unknown: may be used as early therapy in place of glucocorticoids, as bridge therapy until immunotherapy takes effect, or as chronic maintenance therapy for refractory disease. Clinical experience for refractory MG is limited compared to other biologic agents.

Advantages	Disadvantages
• First approved complement inhibitor that can be given SC and self-administered • Do not have to stop IVIG or PE	• High cost • No head-to-head studies vs other agents • BBW and REMS requirements • Require daily administration

Current Utilization

	Quarter 1 2023			Quarter 2 2023		
Medication	**Rx Count**	**% of Rx**	**Reimb Amount**	**Rx Count**	**% of Rx**	**Reimb Amount**
azathioprine	86	2.3%	$2,296.57	77	2.0%	$1,990.53
cyclosporine	0	0.0%	$ -	0	0.0%	$ -
methylprednisolone	557	14.6%	$8,403.52	602	15.9%	$8,814.20
mycophenolate mofetil	97	2.5%	$8,006.95	93	2.5%	$7,451.39
prednisone	2856	74.8%	$32,761.11	2799	73.9%	$34,111.48
tacrolimus	168	4.4%	$8,590.11	159	4.2%	$6,877.02
Zilbrysq	0	0.0%	$ -	0	0.0%	$-
Soliris	1	0.0%	$7,940.78	7	0.2%	$71,467.02
Ultomiris	1	0.0%	$47,932.66	2	0.1%	$95,864.44
Vyvgart, Vyvgart Hytrulo	0	0.0%	$ -	7	0.2%	$63,117.61
Rystiggo	0	0.0%	$ -	0	0.0%	$-
Rituxan and biosimilars	51	1.3%	$70,953.89	39	1.0%	$43,662.49
TOTALS	3817		$186,885.59	3785		$274,111.56
	Quarter 3 2023			**Quarter 4 2023**		
Medication	**Rx Count**	**% of Rx**	**Reimb Amount**	**Rx Count**	**% of Rx**	**Reimb Amount**
azathioprine	72	2.0%	$2,047.95	64	1.7%	$1,774.88
cyclosporine	0	0.0%	$ -	0	0.0%	$ -
methylprednisolone	517	14.5%	$7,606.84	584	15.6%	$8,574.50
mycophenolate mofetil	107	3.0%	$8,553.27	98	2.6%	$7,575.38
prednisone	2646	74.3%	$30,577.61	2808	75.2%	$32,937.00
tacrolimus	174	4.9%	$12,660.89	168	4.5%	$14,309.80
Zilbrysq	0	0.0%	$ -	0	0.0%	$ -
Soliris	7	0.2%	$83,378.19	0	0.0%	$ -
Ultomiris	2	0.1%	$95,705.28	1	0.0%	$47,932.66
Vyvgart, Vyvgart Hytrulo	0	0.0%	$ -	2	0.1%	$18,207.00
Rystiggo	0	0.0%	$ -	0	0.0%	$ -
Rituxan and biosimilars	37	1.0%	$70,040.51	10	0.3%	$13,871.70
TOTALS	3562		$310,570.54	3735		$145,182.92

References:

1. *Bird SJ. Overview of the treatment of myasthenia gravis. In: Shefner JM, Goddeau RP, editor. UpToDate. [Internet]. Waltham, Mass.: UpToDate; August 17, 2023. Available from: www.uptodate.com*
2. *U.S. Food and Drug Administration, Center for Drug Evaluation and Research. Zilbrysq NDA 216834 approval letter, October 17, 2023.* https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2023/216834Orig1s000ltr.pdf

3. *Zilbrysq (zilocuplan injection, for subcutaneous use). [prescribing information]. Smyrna, GA: UCB, Inc; October 2023.*
4. *Zilbrysq: New Drug Review. IPD Analytics. Aventura, FL. November 2023. https://www.ipdanalytics.com*
5. *Zilucoplan Injection. Drug Facts and Comparisons. Wolters Kluwer Health, Inc. Riverwoods, IL. February 5, 2024. http://online.factsandcomparisons.com*
6. *Zilucoplan. In-Depth Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. November 18, 2023. https://www.micromedexsolutions.com*
7. *Glucocorticoids. Drug Facts and Comparisons. Wolters Kluwer Health, Inc. Riverwoods, IL. January 31, 2024. http://online.factsandcomparisons.com*
8. *Pyridostigmine. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. January 30, 2024. https://www.micromedexsolutions.com*
9. *Azathioprine. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. December 7, 2023. https://www.micromedexsolutions.com*
10. *Mycophenolate mofetil. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. January 23, 2024. https://www.micromedexsolutions.com*
11. *Cyclosporine. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. February 1, 2024. https://www.micromedexsolutions.com*
12. *Tacrolimus. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. February 1, 2024. https://www.micromedexsolutions.com*
13. *Eculizumab. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. June 28, 2023. https://www.micromedexsolutions.com*
14. *Ravulizumab-cwvz. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. December 13, 2023. https://www.micromedexsolutions.com*
15. *Efgartigimod alfa-fcab. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. December 26, 2023. https://www.micromedexsolutions.com*
16. *Efgartigimod alfa/hyaluronidase-qvfc. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. December 26, 2023. https://www.micromedexsolutions.com*
17. *Rozanolixizumab-noli. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. July 18, 2023. https://www.micromedexsolutions.com*
18. *Rituximab. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. January 3, 2024. https://www.micromedexsolutions.com*

FIRST REVIEW OF DUCHENNE MUSCULAR DYSTROPHY (EMFLAZA, AGAMREE)

Duchenne Muscular Dystrophy (DMD) is a rare X-linked disease caused by mutations in the DMD gene which encodes for dystrophin, a protein required for proper muscular function. Patients with DMD experience muscle weakness leading to loss of ambulation, respiratory failure, and cardiac failure. Treatment of DMD targets improving muscle function with the use of corticosteroids and/or improving dystrophin function with exon skipping or gene therapies.

CORTICOSTEROIDS: IMPROVE MUSCULAR FUNCTION		
• Rationale for use: decrease inflammation, improve motor and pulmonary function, postpone loss of ambulation and cardiomyopathy, increase survival • Side effects: weight gain, decreased growth, delayed puberty, bone fractures, behavioral effects, adrenal suppression, immunosuppression, hyperglycemia		
Corticosteroids		
Agents per guidelines	Prednisone or prednisolone	
Cost per **year**	$75.60 (tablets) - $3,720 (suspension)	
Emflaza (deflazacort) and Agamree (vamorolone)		
Similarities	• 2 years and up • Similar efficacy to prednisone • Derivatives of prednisone with more favorable side effects	
	Emflaza (deflazacort)	**Agamree (vamorolone)**
Formulation	Suspension and tablets	Suspension
Compared to prednisone	Less weight gain and behavioral effects; more likely to delay growth	Less growth delay, bone fractures, and behavioral effects
Cost per **year**	$54,620.64 (tablets) – $79,961.76 (suspension)	$114,000
IMPROVE DYSTROPHIN FUNCTION		
• Used in addition to corticosteroid treatment • Have not shown clinically significant benefit but may slow progression		
Exon Skipping Therapy:		
Key notes	• Binds to mRNA to omit exon during processing • Agents: Exondys 51, Vyondys 53, Amondys 45, Viltepso	
Cost per **year**	$460,800 (Exondys, Vyondys 53, Amondys 45) - $473,760 (Viltepso)	
Gene Therapy: Elevidys		
Indication	Introduces shortened version of DMD gene to muscle tissue, one time infusion	
Cost per **infusion**	$3,200,000.00	

Based on pediatric dosing for a 5-year-old patient weighing 20 kg at the lowest per unit WAC cost.

FDA Approval

Emflaza (deflazacort): February 9, 2017; 505(b)(2) New Drug Application (NDA) pathway Type 1 New Molecular Entity, PRIORITY; orphan

Agamree (vamorolone): October 26, 2023; 505(b) New Drug Application (NDA) pathway Type 1 New Molecular Entity, STANDARD; orphan

Clinical Trials

Emflaza

Approval of Emflaza for DMD was based on a multicenter, randomized, double-blind, placebo-controlled, 52-week study (MP-104-NM-001). 196 male patients aged 5 to 15 years of age were enrolled in the study. Patients were randomized to Emflaza, prednisone, or placebo. After 12 weeks, placebo patients were re-randomized to either Emflaza or the active comparator for an additional 40 weeks. Emflaza 1.2mg/kg/day was also analyzed but not included in the results as it is not a recommended dosage due to a higher side effect rate vs. 0.9mg/kg/day.

Primary Endpoint: All groups showed statistically significant improvements in muscle strength score vs placebo from baseline to week 12. Change was greater compared to placebo but not greater than prednisone.

- Emflaza 0.9 mg/kg/day (n = 48): 0.15 (0.01, 0.28); p = 0.0173
- Prednisone 0.75 mg/kg/day (n = 45): 0.27 (0.13, 0.41); p = 0.0002
- Placebo (n = 50): -0.10 (-0.23, 0.03)

Secondary Endpoints: Emflaza maintained greater muscular strength improvement from baseline to week 52.

- Emflaza 0.9 mg/kg/day (n = 41): 0.39 (0.25, 0.54)
- Prednisone 0.75 mg/kg/day (n = 37): 0.23 (0.07, 0.38)

Safety: More adverse events, including serious adverse events and discontinuations, for prednisone

Agamree

Approval of Agamree for the treatment of DMD was based on a multicenter, randomized, double-blind, parallel-group, placebo- and active-controlled, multinational 24-week study (VISION-DMD; NCT03439670). The study enrolled 121 male patients to Agamree, prednisone, or placebo for 24 weeks. After 24 weeks, patients on prednisone or placebo received Agamree at either 2 mg/kg/day or 6 mg/kg/day for an additional 20 weeks.

Primary Endpoint: Change from baseline to Week 24 in Time to Stand Test (TTSTAND) for Agamree compared to placebo.

- TTSTAND velocity (rises/sec) mean change from baseline was -0.012 in the placebo group, 0.033 in the Agamree 2 mg/kg/day group (P=0.017), and 0.048 in the Agamree 6 mg/kg/day group (P=0.002).

Secondary Endpoints: Change from baseline to Week 24 in TTSTAND velocity, 6 Minute Walk Test (6MWT) distance, and Time to Run/Walk 10 meters (TTRW) velocity.

- 6MWT distance (meters) mean change from baseline was -14 in the placebo group, 27 in the Agamree 2 mg/kg/d group (P=0.004), and 29 in the Agamree 6 mg/kg/day group (P=0.002).
- TTRW velocity (meter/second) mean change from baseline was 0.014 in the placebo group, 0.141 in the Agamree 2 mg/kg/d group (P=0.103), and 0.258 in the Agamree 6 mg/kg/day group (P=0.002).

**The primary endpoint and key secondary endpoints were met for the Agamree 6 mg/kg/day treatment group. The Agamree 2 mg/kg/day treatment group was statistically significant vs. placebo for TTSTAND and 6MWT but was not statistically significant vs. placebo for TTRW.*

Safety: Changes in height percentile and decline of serum biomarkers of bone formation were seen in prednisone treated patients but not Agamree

Place in Therapy

Glucocorticoids should be started for children with DMD whose motor skills have plateaued or have started to decline, prior to substantial decline. Glucocorticoid treatment is beneficial for improving motor function, strength, and pulmonary function, delaying the loss of ambulation, and reducing the risk of scoliosis.

Advantages	Disadvantages
• Improved side effect profile compared to prednisone • Offer an option for patients who are unable to tolerate prednisone • Agamree is a novel steroid acting as a potent mineralocorticoid antagonist, which prevents negative mineralocorticoid effects and glucocorticoid receptor binding elements which may contribute to prednisone's side effects.	• High cost • Similar efficacy to low-cost prednisone • No head-to-head trials comparing Agamree and Emflaza

Current Utilization

	Quarter 1 2023			Quarter 2 2023		
Medication	**Rx Count**	**% of Rx**	**Reimb Amount**	**Rx Count**	**% of Rx**	**Reimb Amount**
prednisolone	17	14.5%	$ -	7	5.7%	$1,962.00
prednisone	100	85.5%	$26,786.00	115	94.3%	$24,198.00
Emflaza	0	0.0%	$ -	0	0.0%	$ -
Agamree	0	0.0%	$ -	0	0.0%	$ -
Exondys 51	0	0.0%	$ -	0	0.0%	$ -
Vyondys 53	0	0.0%	$ -	0	0.0%	$ -
Amondys 45	0	0.0%	$ -	0	0.0%	$ -
Viltepso	0	0.0%	$ -	0	0.0%	$ -
Elevidys	0	0.0%	$ -	0	0.0%	$ -
TOTALS	117		$26,786.00	122		$26,160.00
	Quarter 3 2023			**Quarter 4 2023**		
Medication	**Rx Count**	**% of Rx**	**Reimb Amount**	**Rx Count**	**% of Rx**	**Reimb Amount**
prednisolone	0	0.0%	$ -	0	0.0%	$-
prednisone	166	100.0%	$39,894.00	141	100.0%	$28,122.00
Emflaza	0	0.0%	$-	0	0.0%	$-
Agamree	0	0.0%	$-	0	0.0%	$-
Exondys 51	0	0.0%	$-	0	0.0%	$-
Vyondys 53	0	0.0%	$-	0	0.0%	$-
Amondys 45	0	0.0%	$-	0	0.0%	$-
Viltepso	0	0.0%	$-	0	0.0%	$-
Elevidys	0	0.0%	$-	0	0.0%	$-
TOTALS	166		$39,894.00	141		$28,122.00

References:

1. *Darras BT. Duchenne and Becker muscular dystrophy: management and prognosis. UpToDate, Patterson MC, Dashe JF (Ed) [Internet]. Waltham, MA: UpToDate; October 12, 2023. Available from: www.uptodate.com*
2. *Emflaza (deflazacort tablets and oral suspension). [prescribing information]. Northbrook, IL: Marathon Pharmaceuticals; February 2017.*
3. *U.S. Food and Drug Administration, Center for Drug Evaluation and Research. Emflaza NDA 208684 and 208685 approval letter, February 9, 2017. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2017/208684Orig1s000,208685Orig1s000ltr.pdf*
4. *U.S. Food and Drug Administration, Center for Drug Evaluation and Research. Application Number: 208684Orig1s000 Medical Review(s). January 17, 2017. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/208684,208685Orig1s000MedR.pdf*

5. *Emflaza (deflazacort)/Marathon: summary of issues and management in patients with DMD. IPD Analytics. Aventura, FL. February 2017. https://www.ipdanalytics.com*
6. *Deflazacort. Drug Facts and Comparisons. Wolters Kluwer Health, Inc. Riverwoods, IL. February 5, 2024.* http://online.factsandcomparisons.com
7. *Deflazacort. In-Depth Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI.December 5, 2024. https://www.micromedexsolutions.com*
8. *Agamree (vamorolone oral suspension). [prescribing information]. Burlington, MA: Santhera Pharmaceuticals (USA), Inc; October 2023.*
9. *U.S. Food and Drug Administration, Center for Drug Evaluation and Research. Agamree NDA 215239 approval letter, October 26, 2023. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2023/215239Orig1s000ltr.pdf*
10. *Agamree (vamorolone): New Drug Review. IPD Analytics. Aventura, FL. November 2023. https://www.ipdanalytics.com*
11. *Vamorolone. Drug Facts and Comparisons. Wolters Kluwer Health, Inc. Riverwoods, IL. October 27, 2023.*http://online.factsandcomparisons.com
12. *Vamorolone. In-Depth Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI.December 8, 2023. https://www.micromedexsolutions.com*
13. *Glucocorticoids. Drug Facts and Comparisons. Wolters Kluwer Health, Inc. Riverwoods, IL. January 31, 2024. http://online.factsandcomparisons.com*
14. *Eteplirsen. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. August 11, 2023. https://www.micromedexsolutions.com*
15. *Golodirsen. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. December 12, 2023. https://www.micromedexsolutions.com*
16. *Casimersen. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. April 12, 2023. https://www.micromedexsolutions.com*
17. *Viltolarsen. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. August 12, 2023. https://www.micromedexsolutions.com*
18. *Delandistrogene Moxeparvovec-rokl. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. November 14, 2023. https://www.micromedexsolutions.com*
19. *Griggs, Robert C., et al. "Efficacy and safety of deflazacort vs prednisone and placebo for Duchenne muscular dystrophy." Neurology 87.20 (2016): 2123-2131.*

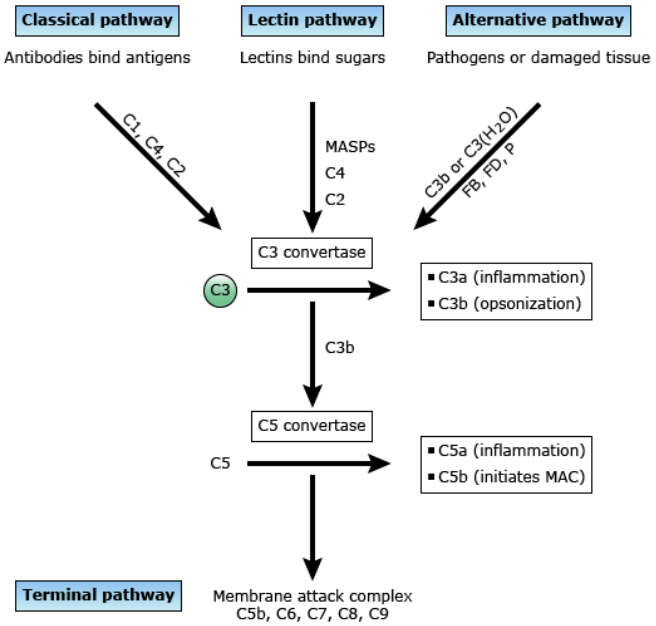
FIRST REVIEW OF PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (EMPAVELI, FABHALTA)

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare hematopoietic stem cell disorder where cells lack surface complementary inhibitor proteins. These cells undergo hemolysis by the complement system, leading to hemolytic anemia. Hemolysis can occur inside (intravascular hemolysis, IVH) or outside of blood vessels (extravascular hemolysis, EVH). Patients with PNH can experience thrombosis, pain, fatigue, dyspnea, and bone marrow suppression.

Treatment of PNH is guided by severity of symptoms, bone marrow suppression, and hemolysis to limit thrombosis. C5 complement inhibitors are the mainstay of treatment; patients who experience breakthrough hemolysis are treated with Empaveli or Fabhalta.

Similarities among all treatment options:

- Agents inhibit various stages of the complement activation system
- BBW for meningococcal infections: require participation in REMS program and vaccination prior to use, may consider antibiotic prophylaxis
  - Empaveli and Fabhalta also require vaccination for all encapsulated bacteria



https://www.uptodate.com/contents/complement-pathways#topicGraphics

C5 Inhibitors		
• Mainstay of treatment • **Hemolysis:** affects IVH only (1/3 of patients will require transfusions) • Can cause infusion reactions **Made by the same company, 80% of patients have been switched over from Soliris to Ultomiris*		
Medication	**Soliris (eculizumab)**	**Ultomiris (ravulizumab)**
Key notes	• IV infusion weekly for 5 weeks then every 2 weeks thereafter, fixed dose	• IV infusion every 8 weeks starting 2 weeks after loading dose, weight based • Adult and pediatric patients ≥1 month of age • Less breakthrough hemolysis
Cost per **year**	$541,409	$550,743.93

C3 Inhibitor	
Empaveli (pegcetacoplan)	
Administration	• Self-administered, subcutaneous twice weekly infusion • Given via commercially available pump or on-body injector
Hemolysis	Affects IVH and EVH
Clinical studies	Superiority evidenced vs Soliris in improvement of hemoglobin levels and decreased need of transfusions
Warnings	Infections, infusion reaction, can interfere with aPTT tests
Cost per **year**	$488,250.88

Factor B Inhibitor	
Fabhalta (iptacopan)	
Administration	• Oral, twice daily • Concerns of hemolysis from nonadherence due to the agent's short half-life
Hemolysis	Affects IVH and EVH
Clinical Studies	Superiority evidenced vs C5 inhibitors in improvement of hemoglobin levels and decreased need of transfusions
Warning	Hyperlipidemia, some patients have required cholesterol lowering medications
Cost per year	$542,465.76

Based on dosing for adult weighing 60 kg at lowest per unit WAC cost.

FDA Approval

Empaveli (pegcetacoplan): May 14, 2021; 505(b) New Drug Application (NDA) pathway Type 1 New Molecular Entity, PRIORITY; orphan

Fabhalta (iptacopan): December 5, 2023; 505(b) New Drug Application (NDA) pathway Type 1 New Molecular Entity, PRIORITY; orphan

Clinical Trials

Empaveli

Approval based on Phase 3 PEGASUS study (NCT03500549). The trial was a randomized, head-to-head, multicenter, open-label study of 80 patients with PNH and hemoglobin levels <10.5 g/dL after Soliris treatment.

Interventions:

- Run-in (4 weeks): continued current Soliris dose alongside self-administered Empaveli
- Randomized, controlled (16 weeks): Empaveli or Soliris
- Open-label (32 weeks): all who completed randomized control period received open-label Empaveli

Primary Endpoint: Results of hemoglobin change from baseline at week 16 showed superiority to Soliris (P<0.001) with an adjusted mean change on 2.37 g/dL for Empaveli vs –1.47 g/dL for Soliris.

Secondary Endpoints: Results showed non-inferiority for transfusion avoidance (85% Empaveli, 15% Soliris, P<0.001) and change in reticulocyte count. Non-inferiority was not evidenced in the change of LDH levels and was not assessed for the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scores.

Safety: Injection-site reactions, infections, diarrhea, fatigue, breakthrough hemolysis

Fabhalta

Approval based on Phase 3 APPLY-PNH study (NCT04558918) and Phase 3 APPOINT-PNH study (NCT04820530).

APPLY-PNH (NCT04558918): The trial was a randomized, multicenter study of 97 patients with PNH and anemia after prior complement C5 inhibitor treatment (Soliris or Ultomiris).

Co-Primary Endpoints: Superiority was shown by an increase in hemoglobin ≥2 g/dL (Fabhalta 82.3%, C5 inhibitors 2.0%, P<0.0001) and ≥12 g/dL (Fabhalta 68.8%, C5 inhibitors 1.8%, P<0.0001) without need for transfusions

Secondary Endpoints: Results showed superiority of transfusion avoidance, change of hemoglobin from baseline, FACIT-F score, change of absolute reticulocyte count, and rate of hemolysis.

Safety: Fabhalta had more reports of headache and diarrhea. C5 inhibitors had more reports of infections and hemolysis.

APPOINT-PNH (NCT04820530): The trial was open-label, single arm, multicenter study of 40 patients with complement inhibitor naïve PNH.

Primary Endpoints: 92.2% of patients experienced an increase in hemoglobin ≥2 g/dL without need for transfusions

Secondary Endpoints: 62.8% of patients experienced an increase in hemoglobin ≥12 without need for transfusions, and 97.6% of patients avoided transfusions. No patients experienced hemolysis or major adverse vascular events.

Safety: Most reported were infections, headache, and rash; serious adverse events reported were COVID-19 and bacterial pneumonia; no discontinuations

Place in Therapy

Potential option for patients experiencing breakthrough hemolysis on treatment with C5 inhibitors.

Advantages	Disadvantages
• First oral agent • Another treatment option for patients who require transfusions despite C5 inhibitor therapy	• No head-to-head trials comparing Empaveli and Fabhalta

Current Utilization

	Quarter 1 2023			Quarter 2 2023		
Medication	**Rx Count**	**% of Rx**	**Reimb Amount**	**Rx Count**	**% of Rx**	**Reimb Amount**
Soliris	1	50.00%	$7,940.78	7	77.78%	$71,467.02
Ultomiris	1	50.00%	$7,940.78	2	22.22%	$95,864.44
Empaveli	0	0.00%	$ -	0	0.00%	$ -
Fabhalta	0	0.00%	$ -	0	0.00%	$-
TOTALS	2		$15,881.56	9		$167,331.46
	Quarter 3 2023			**Quarter 4 2023**		
Medication	**Rx Count**	**% of Rx**	**Reimb Amount**	**Rx Count**	**% of Rx**	**Reimb Amount**
Soliris	7	77.78%	$83,378.19	0	0.00%	$ -
Ultomiris	2	22.22%	$95,705.28	1	100.00%	$47,932.66
Empaveli	0	0.00%	$ -	0	0.00%	$ -
Fabhalta	0	0.00%	$ -	0	0.00%	$ -
TOTALS	9		$179,083.47	1		$47,932.66

References:

1. *Brodsky RA. Treatment and prognosis of paroxysmal nocturnal hemoglobinuria. UpToDate, Larson RA, Rosmarin AG (Ed) [Internet]. Waltham, MA: UptoDate; November 27, 2023. Available from: www.uptodate.com*
2. *Hillmen P, Szer J, Weitz I, Röth A, Höchsmann B, Panse J, Usuki K, Griffin M, Kiladjian JJ, de Castro C, Nishimori H, Tan L, Hamdani M, Deschatelets P, Francois C, Grossi F, Ajayi T, Risitano A, Peffault de la Tour R. Pegcetacoplan versus Eculizumab in Paroxysmal Nocturnal Hemoglobinuria. N Engl J Med. 2021 Mar 18;384(11):1028-1037. doi: 10.1056/NEJMoa2029073. PMID: 33730455.*

3. *Empaveli (pegcetacoplan injection, for subcutaneous use). [prescribing information]. Waltham, MA: Apellis Pharmaceuticals, Inc. May 2021.*
4. *U.S. Food and Drug Administration, Center for Drug Evaluation and Research. Empaveli NDA 215014 approval letter, May 14, 2021. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2021/215014Orig1s000ltr.pdf*
5. *Empaveli (pegcetacoplan): New Drug Review. IPD Analytics. Aventura, FL. May 2021. https://www.ipdanalytics.com*
6. *Pegcetacoplan injection. Drug Facts and Comparisons. Wolters Kluwer Health, Inc. Riverwoods, IL. January 2, 2024. http://online.factsandcomparisons.com*
7. *Pegcetacoplan. In-Depth Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. October 4, 2023. https://www.micromedexsolutions.com*
8. *Fabhalta (iptacopan, oral capsules). [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation. December 2023.*
9. *U.S. Food and Drug Administration, Center for Drug Evaluation and Research. Fabhalta NDA 218276 approval letter, December 5, 2023. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2023/218276Orig1s000ltr.pdf*
10. *Fabhalta (iptacopan): New Drug Review. IPD Analytics. Aventura, FL. January 2024. https://www.ipdanalytics.com*
11. *Iptacopan. Drug Facts and Comparisons. Wolters Kluwer Health, Inc. Riverwoods, IL. December 28, 2023. http://online.factsandcomparisons.com*
12. *Latour RP, Roeth A, Kulasekararaj A, Scheinberg P, Ueda Y, Castro CM, Bona ED, Schrezenmeier H, Langemeijer SM, Barcellini W, Tavitian S, Panse J, Schafhausen P, Mauad VA, Kerloeguen C, Levitch R, RKumar R, Thorburn C, Maitra S, Dahlke M, Risitano AM; Oral Monotherapy with Iptacopan, a Proximal Complement Inhibitor of Factor B, Has Superior Efficacy to Intravenous Terminal Complement Inhibition with Standard of Care Eculizumab or Ravulizumab and Favorable Safety in Patients with Paroxysmal Nocturnal Hemoglobinuria and Residual Anemia: Results from the Randomized, Active-Comparator-Controlled, Open-Label, Multicenter, Phase III Apply-PNH Study. Blood 2022; 140 (Supplement 2): LBA–2. doi: https://doi.org/10.1182/blood-2022-171469*
13. *Iptacopan. In-Depth Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. December 21, 2023. https://www.micromedexsolutions.com*
14. *Eculizumab. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. June 28, 2023. https://www.micromedexsolutions.com*
15. *Ravulizumab-cwvz. Quick Answers and Red Book. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. December 13, 2023. https://www.micromedexsolutions.com*
16. *Liszewski MK, Atkinson JP. Complement pathways. UpToDate, Schur PH, Orange JS, Feldweg AM (Ed) [Internet]. Waltham, MA: UpToDate; November 11, 2022. Available from:* www.uptodate.com

NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
1st QUARTER 2024

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

1. Sotagliflozin / Overuse _____ _____

Alert Message: Inpefa (sotagliflozin) may be over-utilized. The recommended maintenance dose of sotagliflozin is 400 mg once daily.

Drugs/Diseases

Util A	Util B	Util C
Sotagliflozin		

Max Dose: 400 mg/day

References:
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Inpefa Prescribing Information, May 2023, Lexicon Pharmaceuticals, Inc.

2. Sotagliflozin / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Inpefa (sotagliflozin) in pediatric patients under 18 years of age have not been established.

Drugs/Diseases

Util A	Util B	Util C
Sotagliflozin		

Age Range: 0 – 17 yoa

References:
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Inpefa Prescribing Information, May 2023, Lexicon Pharmaceuticals, Inc.

3. Sotagliflozin / Therapeutic Appropriateness _____ _____

Alert Message: Inpefa (sotagliflozin) can cause intravascular volume depletion, which may sometimes manifest as symptomatic hypotension or acute transient changes in creatinine. Patients with impaired renal function (eGFR < 60 mL/min/1.73 m2), elderly patients, or patients on loop diuretics may be at increased risk for volume depletion or hypotension. Before initiating sotagliflozin in patients with one or more of these characteristics, assess volume status and renal function. Monitor for signs and symptoms of hypotension and renal function after initiating therapy.

Drugs/Diseases

Util A	Util B	Util C
Sotagliflozin	CKD Stage 3	
	CKD Stage 4	
	CKD Stage 5	

References:
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Inpefa Prescribing Information, May 2023, Lexicon Pharmaceuticals, Inc.

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

4. Sotagliflozin / Loop Diuretics _____ _____

Alert Message: Inpefa (sotagliflozin) can cause intravascular volume depletion, which may sometimes manifest as symptomatic hypotension or acute transient changes in creatinine. Patients with impaired renal function (eGFR < 60 mL/min/1.73 m2), elderly patients, or patients on loop diuretics may be at increased risk for volume depletion or hypotension. Before initiating sotagliflozin in patients with one or more of these characteristics, assess volume status and renal function. Monitor for signs and symptoms of hypotension and renal function after initiating therapy.

Drugs/Diseases

Util A	Util B	Util C
Sotagliflozin	Bumetanide	
	Ethacrynic Acid	
	Furosemide	
	Torsemide	

References:

Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Inpefa Prescribing Information, May 2023, Lexicon Pharmaceuticals, Inc.

5. Sotagliflozin / Urinary Tract Infection _____ _____

Alert Message: Treatment with SGLT2 inhibitors, including Inpefa (sotagliflozin), increases the risk for urinary tract infections. Serious urinary tract infections, including urosepsis and pyelonephritis, requiring hospitalization have been reported. Evaluate patients for signs and symptoms of urinary tract infections, and promptly treat if indicated.

Drugs/Diseases

Util A	Util B	Util C
Sotagliflozin	Pyelonephritis	
	Urinary Tract Infection	

References:

Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Inpefa Prescribing Information, May 2023, Lexicon Pharmaceuticals, Inc.

6. Sotagliflozin / Genital Mycotic Infections _____ _____

Alert Message: Inpefa (sotagliflozin) use increases the risk of genital mycotic infections. Patients with a history of genital mycotic infections were more likely to develop genital mycotic infections. Monitor and treat appropriately.

Drugs/Diseases

Util A	Util B	Util C
Sotagliflozin	Candida Balanitis	
	Candidiasis of vulva and vagina	
	Urogenital Candidiasis	

References:

Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Inpefa Prescribing Information, May 2023, Lexicon Pharmaceuticals, Inc.

7. Sotagliflozin / Insulin and Insulin Secretagogues _____ _____

Alert Message: Insulin and insulin secretagogues are known to cause hypoglycemia. Inpefa (sotagliflozin) may increase the risk of hypoglycemia when combined with insulin or an insulin secretagogue. A lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when these agents are used in combination with sotagliflozin.

Drugs/Diseases

Util A	Util B	Util C
Sotagliflozin	Insulin	
	Insulin Secretagogues	

References:

Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Inpefa Prescribing Information, May 2023, Lexicon Pharmaceuticals, Inc.

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

8. Sotagliflozin / Digoxin _____ _____

Alert Message: The concurrent use of Inpefa (sotagliflozin) with digoxin may increase digoxin serum concentrations and the risk of digoxin-related adverse effects. Patients taking sotagliflozin with digoxin should be monitored appropriately. Sotagliflozin is a P-gp efflux transport inhibitor, and digoxin is a P-gp substrate.

Drugs/Diseases

Util A	Util B	Util C
Sotagliflozin	Digoxin	

References:
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Inpefa Prescribing Information, May 2023, Lexicon Pharmaceuticals, Inc.

9. Sotagliflozin / Rifampin _____ _____

Alert Message: The concurrent use of Inpefa (sotagliflozin) with rifampin may decrease sotagliflozin serum concentrations and result in decreased sotagliflozin efficacy. Rifampin is a UGT1A9 inducer, and sotagliflozin is a UGT1A9 substrate. Patients taking sotagliflozin with rifampin should be monitored appropriately.

Drugs/Diseases

Util A	Util B	Util C
Sotagliflozin	Rifampin	

References:
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Inpefa Prescribing Information, May 2023, Lexicon Pharmaceuticals, Inc.

10. Sotagliflozin / Lithium _____ _____

Alert Message: The concurrent use of Inpefa (sotagliflozin) with lithium may decrease lithium serum concentrations and result in decreased lithium efficacy. Monitor serum lithium concentration more frequently during sotagliflozin initiation and dosage changes.

Drugs/Diseases

Util A	Util B	Util C
Sotagliflozin	Lithium	

References:
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Inpefa Prescribing Information, May 2023, Lexicon Pharmaceuticals, Inc.

11. Sotagliflozin / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on animal data showing renal effects, Inpefa (sotagliflozin) is not recommended during the second and third trimesters of pregnancy. In rats, renal changes were observed when sotagliflozin was administered during a period of renal development corresponding to the late second and third trimesters of human pregnancy.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Inpefa Prescribing Information, May 2023, Lexicon Pharmaceuticals, Inc.

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

12. Sotagliflozin / Lactation _____ _____

Alert Message: There are no data on the presence of Inpefa (sotagliflozin) in human milk, the effects on the breastfed infant, or the effects on milk production. Sotagliflozin is present in rat milk. When a drug is present in animal milk, it is likely to be present in human milk. Since human kidney maturation occurs in utero and during the first 2 years of life when lactational exposure may occur, there may be risk to the developing human kidney. Because of the potential for serious adverse reactions in a breastfed infant, advise women that breastfeeding is not recommended while taking sotagliflozin.

Drugs/Diseases

Util A	Util B	Util C
Sotagliflozin	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Inpefa Prescribing Information, May 2023, Lexicon Pharmaceuticals, Inc.

13. Sotagliflozin / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Inpefa (sotagliflozin). 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
Sotagliflozin		

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.

14. Tafamidis Meglumine / Overuse _____ _____

Alert Message: Vyndaqel (tafamidis meglumine) may be over-utilized. The recommended dosage of tafamidis meglumine is 80 mg (four 20 mg tafamidis meglumine capsules) once daily.

Drugs/Diseases

Util A	Util B	Util C
Tafamidis Meglumine		

Max Dose: 80 mg/day

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.

Vyndaqel and Vyndamax Prescribing Information, Oct. 2023, Pfizer Inc.

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

15. Tafamidis Meglumine / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Vyndaqel (tafamidis meglumine) have not been established in pediatric patients.

Drugs/Diseases

Util A	Util B	Util C
Tafamidis Meglumine		

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.

Vyndaqel and Vyndamax Prescribing Information, Oct. 2023, Pfizer Inc.

16. Tafamidis Meglumine / BCRP Substrates _____ _____

Alert Message: Vyndaqel (tafamidis meglumine) inhibits breast cancer resistant protein (BCRP) in humans. Coadministration of tafamidis and drugs that are BCRP substrates may increase the exposure of the BCRP substrates (e.g., methotrexate, rosuvastatin, and imatinib) and the risk of substrate-related toxicities. Monitor for signs of BCRP substrate-related toxicities and modify the dosage of the substrate if appropriate.

Drugs/Diseases

Util A	Util B		Util C
Tafamidis Meglumine	Alpelisib	Prazosin	
	Berotralstat	Rosuvastatin	
	Dolutegravir	Talazoparib	
	Glyburide	Tenofovir	
	Methotrexate	Topotecan	
	Pazopanib	Ubrogepant	
	Pibrentasvir	Vemurafenib	

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.

Vyndaqel and Vyndamax Prescribing Information, Oct. 2023, Pfizer Inc.

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

17. Tafamidis Meglumine / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on findings from animal studies, Vyndaqel (tafamidis meglumine) may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Report pregnancies to the Pfizer reporting line at 1-800-438-1985.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Tafamidis Meglumine	Pregnancy	Abortion
	Delivery	
	Miscarriage	

Gender: Female

Age Range: 11 – 50 yoa

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.

Vyndaqel and Vyndamax Prescribing Information, Oct. 2023, Pfizer Inc.

18. Tafamidis Meglumine / Therapeutic Appropriateness _____ _____

Alert Message: There are no available data on the presence of Vyndaqel (tafamidis meglumine) in human milk, the effect on the breastfed infant, or the effect on milk production. Tafamidis is present in rat milk. When a drug is present in animal milk, it is likely the drug will be present in human milk. Based on findings from animal studies that suggest the potential for serious adverse reactions in the breastfed infant, advise patients that breastfeeding is not recommended during treatment with tafamidis meglumine.

Drugs/Diseases

Util A	Util B	Util C
Tafamidis Meglumine	Lactation	

Gender: Female

Age Range: 11 – 50 yoa

References:

Clinical Pharmacology, 2024 Elsevier/Gold Standard.

Vyndaqel and Vyndamax Prescribing Information, Oct. 2023, Pfizer Inc.

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

19. Tafamidis Meglumine / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Vyndaqel (tafamidis meglumine). 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
Tafamidis Meglumine		

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.

20. Lacosamide XR / Overuse _____ _____

Alert Message: Motpoly XR (lacosamide extended-release) may be over-utilized. The maximum recommended maintenance dose of extended-release lacosamide is 400 mg once daily.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Lacosamide XR		CKD Stage 5 ESRD Hepatic Impairment

Max Dose: 400 mg/day

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Motpoly XR Prescribing Information, May 2023, Aucta Pharmaceuticals, Inc.

21. Lacosamide XR / Overuse – Severe Renal Impairment _____ _____

Alert Message: Motpoly XR (lacosamide extended-release) may be over-utilized. For patients with severe renal impairment [creatinine clearance (CLcr) less than 30 mL/min as estimated by the Cockcroft-Gault equation for adults; CLcr less than 30 mL/min/1.73m2 as estimated by the Schwartz equation for pediatric patients] or end-stage renal disease, the maximum recommended dosage is 300 mg. For patients with mild or moderate renal impairment, no dosage is necessary.

Drugs/Diseases

Util A	Util B	Util C (Include)
Lacosamide XR		CKD Stage 5 ESRD

Max Dose: 300 mg/day

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Motpoly XR Prescribing Information, May 2023, Aucta Pharmaceuticals, Inc.

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

22. Lacosamide XR / Overuse – Hepatic Impairment _____ _____

Alert Message: Motpoly XR (lacosamide extended-release) may be over-utilized. For patients with mild or moderate hepatic impairment, the maximum recommended dosage is 300 mg. The dose initiation and titration should be based on clinical response and tolerability in patients with hepatic impairment. Extended-release lacosamide use is not recommended in patients with severe hepatic impairment.

Drugs/Diseases

Util A	Util B	Util C (Include)
Lacosamide XR		Hepatic Impairment

Max Dose: 300 mg/day

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Motpoly XR Prescribing Information, May 2023, Aucta Pharmaceuticals, Inc.

23. Lacosamide / Drugs Effecting Cardiac Conduction _____ _____

Alert Message: Motpoly XR (lacosamide extended-release) should be used with caution in patients on concomitant medications that affect cardiac conduction (sodium channel blockers, beta-blockers, calcium channel blockers, potassium channel blockers), including those that prolong PR interval (including sodium channel blocking AEDs), because of a risk of AV block, bradycardia, or ventricular tachyarrhythmia. In such patients, obtaining an ECG before beginning lacosamide and after lacosamide is titrated to steady-state is recommended.

Drugs/Diseases

Util A	Util B	Util C
Lacosamide XR	Beta-Blockers	
	Calcium Channel Blockers	
	Potassium Channel Blockers	
	Sodium Channel Blockers	

References:

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

24. Lacosamide XR / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Motpoly XR (lacosamide extended-release). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs.

Drugs/Diseases

Util A	Util B	Util C
Lacosamide XR		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Faught E, Duh MS, Weiner JR, et al. Nonadherence to Antiepileptic Drugs and Increased Mortality, Findings from the RANSOM Study. Neurology 2008;71(20): 1572-1578.
Faught RE, Weiner JR, Guerin A, et al. Impact of Nonadherence to Antiepileptic Drugs on Health Care Utilization and Costs: Findings from the RANSOM Study. Epilepsia 2009;50(3):501-509.

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

25. Risperidone ER Suspension / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of Rykindo (risperidone extended-release suspension) in pediatric patients have been established.

Drugs/Diseases

Util A	Util B	Util C
Risperidone ER Suspension		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Rykindo Prescribing Information, Jan. 2023, Shandong Luye Pharmaceutical Co., Ltd.

26. Risperidone ER Suspension / Strong CYP2D6 Inhibitor _____ _____
Alert Message: Concomitant use of Rykindo (risperidone extended-release suspension) with strong CYP2D6 inhibitors may increase the plasma concentration of risperidone and lower the concentration of 9-hydroxyrisperidone, a major active metabolite of risperidone. Refer to the official prescribing information for dosage adjustment for risperidone when initiating or discontinuing concurrent use of a strong CYP2D6.

Drugs/Diseases

Util A	Util B		Util C
Risperidone ER Suspension	Bupropion	Paroxetine	
	Fluoxetine	Quinidine	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Rykindo Prescribing Information, Jan. 2023, Shandong Luye Pharmaceutical Co., Ltd.

27. Risperidone ER Suspension / Strong CYP3A3 Inducers _____ _____
Alert Message: Concomitant use of Rykindo (risperidone extended-release suspension) with strong CYP3A4 inducers may decrease the combined plasma concentrations of risperidone and 9-hydroxyrisperidone, which could lead to decreased efficacy of risperidone treatment. Refer to the official prescribing information for dosage adjustment for risperidone when initiating or discontinuing concurrent CYP3A4 inducers.

Drugs/Diseases

Util A	Util B		Util C
Risperidone ER Suspension	Apalutamide	Phenobarbital	
	Carbamazepine	Phenytoin	
	Enzalutamide	Primidone	
	Mitotane		

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Rykindo Prescribing Information, Jan. 2023, Shandong Luye Pharmaceutical Co., Ltd.

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

28. Etrasimod / Overuse _____ _____

Alert Message: Velsipity (etrasimod) may be over-utilized. The recommended dosage of etrasimod is 2 mg once daily.

Drugs/Diseases

Util A	Util B	Util C
Etrasimod		

Max Dose: 2 mg/day

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Velsipity Prescribing Information, Oct. 2023, Pfizer Inc.

29. Etrasimod / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Etrasimod		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Velsipity Prescribing Information, Oct. 2023, Pfizer Inc.

30. Etrasimod / Contraindication _____ _____

Alert Message: Velsipity (etrasimod) is contraindicated in patients who, in the last 6 months, have experienced a myocardial infarction, unstable angina pectoris, stroke, transient ischemic attack (TIA), decompensated heart failure requiring hospitalization, or Class III or IV heart failure.

Drugs/Diseases

Util A	Util B	Util C
Etrasimod	Class III or IV Heart Failure	
	Decompensated Heart Failure	
	Myocardial Infarction	
	Stroke	
	Transient Ischemic Attack	
	Unstable Angina	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Velsipity Prescribing Information, Oct. 2023, Pfizer Inc.

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

31. Etrasimod / Contraindication _____ _____

Alert Message: Velsipity (etrasimod) is contraindicated in patients who have a history or presence of Mobitz type II second-degree or third-degree AV block, sick sinus syndrome, or sino-atrial block unless the patient has a functioning pacemaker.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Etrasimod	Mobitz type II 2nd Degree	Pacemaker
	Mobitz type II 3rd Degree	
	Sick Sinus Syndrome	
	Sino-atrial Block	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Velsipity Prescribing Information, Oct. 2023, Pfizer Inc.

32. Etrasimod / Infection _____ _____

Alert Message: Velsipity (etrasimod) may increase the risk of infections. Obtain a complete blood count (CBC) before initiation of etrasimod treatment. Monitor for infection during treatment and for 5 weeks after discontinuation. Consider interruption of etrasimod treatment if a serious infection develops. Avoid the use of live attenuated vaccines during and for up to 5 weeks after treatment.

Drugs/Diseases

Util A	Util B	Util C
Etrasimod	Serious Infections	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Velsipity Prescribing Information, Oct. 2023, Pfizer Inc.

33. Etrasimod / Decreased Heart Rate _____ _____

Alert Message: Initiation of Velsipity (etrasimod) may result in a transient decrease in heart rate and AV conduction delays. Obtain an electrocardiogram (ECG) to assess for preexisting cardiac conduction abnormalities before starting treatment. Consider cardiology consultation for conduction abnormalities or concomitant use with other drugs that decrease heart rate.

Drugs/Diseases

Util A	Util B	Util C
Etrasimod	Bradycardia	
	QT Prolongation	
	Atrioventricular Block 1st Degree	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Velsipity Prescribing Information, Oct. 2023, Pfizer Inc.

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

34. Etrasimod / Liver Injury _____ _____

Alert Message: Elevations of aminotransferases may occur in patients receiving Velsipity (etrasimod). Obtain transaminase and bilirubin levels, if not recently available (i.e., within last 6 months), before initiation of etrasimod. Obtain transaminases and bilirubin in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. Discontinue etrasimod if significant liver injury is confirmed.

Drugs/Diseases

Util A	Util B	Util C
Etrasimod	Elevated Serum Enzyme Levels	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Velsipity Prescribing Information, Oct. 2023, Pfizer Inc.

35. Etrasimod / Macular Edema _____ _____

Alert Message: Sphingosine 1-phosphate (S1P) receptor modulators, including Velsipity (etrasimod), have been associated with an increased risk of macular edema. Obtain a baseline evaluation of the fundus, including the macula, near the start of treatment with etrasimod. Periodically conduct an evaluation of the fundus, including the macula, while on therapy and any time there is a change in vision. Macular edema over an extended period of time (i.e., 6 months) can lead to permanent visual loss. Consider discontinuing etrasimod if macular edema develops.

Drugs/Diseases

Util A	Util B	Util C
Etrasimod	Macular Edema	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Velsipity Prescribing Information, Oct. 2023, Pfizer Inc.

36. Etrasimod / Malignancies _____ _____

Alert Message: Cases of malignancies (including skin malignancies) have been reported in patients treated with S1P receptor modulators. Skin examinations are recommended prior to or shortly after the start of treatment and periodically thereafter for all patients, particularly those with risk factors for skin cancer. Providers and patients are advised to monitor for suspicious skin lesions. If a suspicious skin lesion is observed, it should be promptly evaluated.

Drugs/Diseases

Util A	Util B	Util C
Etrasimod	Malignancies	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Velsipity Prescribing Information, Oct. 2023, Pfizer Inc.

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

37. Etrasimod / Moderate to Strong CYP2C9 & Moderate 3A4 Inhibitor _____ _____

Alert Message: Concomitant use of Velsipity (etrasimod) with a drug that is a moderate to strong inhibitor of CYP2C9 and a moderate to strong inhibitor of CYP3A4 is not recommended. In pharmacokinetic studies, increased exposure of etrasimod was observed with concomitant use with a drug that is a moderate inhibitor of CYP2C9 and a moderate inhibitor of CYP3A4 (i.e., fluconazole).

Drugs/Diseases

Util A	Util B	Util C
Etrasimod	Adagrasib	
	Fluconazole	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Velsipity Prescribing Information, Oct. 2023, Pfizer Inc.

38. Etrasimod / Drugs Causing Decreased HR or QT Prolongation _____ _____

Alert Message: A transient decrease in heart rate and AV conduction delays may occur when initiating Velsipity (etrasimod). Because of the potential additive effect on heart rate, etrasimod may increase the risk of QT prolongation and Torsades de Pointes with concomitant use of Class Ia and Class III anti-arrhythmic drugs and QT-prolonging drugs. Seek the advice of a cardiologist before initiating etrasimod treatment with Class Ia (e.g., quinidine, procainamide), Class III anti-arrhythmic drugs (e.g., amiodarone, sotalol), or other drugs that prolong the QT interval.

Drugs/Diseases

Util A	Util B	Util C
Etrasimod	Class 1A Antiarrhythmics	
	Class III Antiarrhythmics	
	Agents Causing QT Prolongation	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Velsipity Prescribing Information, Oct. 2023, Pfizer Inc.

39. Etrasimod / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on animal studies, Velsipity (etrasimod) may cause fetal harm when administered to a pregnant woman. In animal reproduction studies conducted in rats and rabbits, embryofetal toxicity was observed with administration of etrasimod at clinically relevant doses. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception to avoid pregnancy during and for one week after stopping etrasimod.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Velsipity Prescribing Information, Oct. 2023, Pfizer Inc.

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

40. Etrasimod / Lactation _____ _____

Alert Message: There are no data on the presence of Velsipity (etrasimod) in human milk, the effects on the breastfed infant, or the effects of the drug on milk production. When etrasimod was orally administered to female rats during pregnancy and lactation, etrasimod was detected in the plasma of the offspring, suggesting excretion of etrasimod in milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for etrasimod and any potential adverse effects on the breastfed infant from etrasimod or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Etrasimod	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Velsipity Prescribing Information, Oct. 2023, Pfizer Inc.

41. Etrasimod / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Velsipity (etrasimod). 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
Etrasimod		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Kleinsinger, Fred. The Unmet Challenge of Medication Nonadherence. The Permanente Journal. Vol. 22 (2018): 18-033. doi:10.7812/TPP/18-033.

Martin LR, Williams SL, Haskard KB, DiMatteo MR. The Challenge of Patient Adherence. Ther Clin Risk Manag. 2005 Sep.1(3):189-199.

42. Colchicine / Overuse _____ _____

Alert Message: Lodoco (colchicine) may be over-utilized. The recommended dosage of colchicine in adult patients is 0.5 mg.

Drugs/Diseases

Util A	Util B	Util C
Colchicine		

Max Dose: 0.5 mg/day

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lodoco Prescribing Information, June 2023, Agepha Pharma FZ LLC.

Criteria Recommendations	*Approved*	*Rejected*

43. Colchicine / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Colchicine		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lodoco Prescribing Information, June 2023, Agepha Pharma FZ LLC.

44. Colchicine / Strong CYP3A4 Inhibitors & P-gp Inhibitors _____ _____

Alert Message: Concurrent use of strong CYP3A4 inhibitors or P-glycoprotein inhibitors with Lodoco (colchicine) is contraindicated because life-threatening and fatal colchicine toxicity has been reported in these patients with colchicine taken in therapeutic doses.

Drugs/Diseases

Util A	Util B		Util C
Colchicine	Amiodarone	Nefazodone	
	Clarithromycin	Nelfinavir	
	Cobicistat	Posaconazole	
	Cyclosporine	Quinidine	
	Dronedarone	Ranolazine	
	Erythromycin	Ritonavir	
	Itraconazole	Verapamil	
	Ketoconazole	Voriconazole	
	Lapatinib		

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lodoco Prescribing Information, June 2023, Agepha Pharma FZ LLC.

45. Colchicine / Severe Renal Failure _____ _____

Alert Message: Lodoco (colchicine) use is contraindicated in patients with renal failure (creatinine clearance < 15 mL/minute).

Drugs/Diseases

Util A	Util B	Util C
Colchicine	CKD Stage 5	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lodoco Prescribing Information, June 2023, Agepha Pharma FZ LLC.

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

46. Colchicine / Severe Hepatic Impairment _____ _____

Alert Message: Lodoco (colchicine) use is contraindicated in patients with severe hepatic impairment.

Drugs/Diseases

Util A	Util B	Util C
Colchicine	Cirrhosis	
	Hepatic Failure	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lodoco Prescribing Information, June 2023, Agepha Pharma FZ LLC.

47. Colchicine / Blood Dyscrasias _____ _____

Alert Message: Lodoco (colchicine) use is contraindicated in patients with blood dyscrasias. Colchicine can cause myelosuppression, leukopenia, granulocytopenia, thrombocytopenia, pancytopenia, and aplastic anemia, which can be life-threatening or fatal. Gastrointestinal symptoms often are the first sign of colchicine toxicity, so new symptoms should prompt an evaluation for toxicity. Concomitant use of drugs that reduce the metabolism of colchicine or the presence of hepatic or renal impairment increases the risk of developing blood dyscrasias.

Drugs/Diseases

Util A	Util B	Util C
Colchicine	Myelosuppression	
	Leukopenia	
	Granulocytopenia	
	Aplastic anemia	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lodoco Prescribing Information, June 2023, Agepha Pharma FZ LLC.

48. Colchicine / Moderate CYP3A4 Inhibitors _____ _____

Alert Message: The concurrent use of Lodoco (colchicine) with a moderate CYP3A4 inhibitor may result in significant increases in colchicine plasma concentrations and should be avoided. If concurrent use is warranted, monitor patients receiving moderate CYP3A4 inhibitors for signs of colchicine toxicity. Avoid the use of colchicine with a moderate CYP3A4 inhibitor in patients with existing renal or hepatic impairment.

Drugs/Diseases

Util A	Util B		Util C
Colchicine	Aprepitant	Fluconazole	
	Ciprofloxacin	Fluvoxamine	
	Crizotinib	Imatinib	
	Diltiazem		

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lodoco Prescribing Information, June 2023, Agepha Pharma FZ LLC.

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

49. Colchicine / Drugs Causing Myotoxicity _____ _____

Alert Message: Concomitant use of a colchicine-containing product and agents that are associated with myotoxicity (e.g., atorvastatin, simvastatin, pravastatin, fluvastatin, gemfibrozil, and fenofibrate) may potentiate the development of myopathy and rhabdomyolysis. Patients on concurrent therapy should be monitored for signs and symptoms of myotoxicity.

Drugs/Diseases

Util A	Util B		Util C
Colchicine	Atorvastatin	Simvastatin	
	Fluvastatin	Gemfibrozil	
	Lovastatin	Fenofibrate	
	Pravastatin		
	Pitavastatin		

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lodoco Prescribing Information, June 2023, Agepha Pharma FZ LLC.

50. Colchicine / Digoxin _____ _____

Alert Message: Concurrent use of a colchicine-containing product and digoxin may result in myopathy and/or rhabdomyolysis. If concomitant use of these two drugs is necessary, the patient should be monitored for signs and symptoms of rhabdomyolysis (dark-colored urine and/or muscle pain, tenderness, or weakness).

Drugs/Diseases

Util A	Util B	Util C
Colchicine	Digoxin	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lodoco Prescribing Information, June 2023, Agepha Pharma FZ LLC.

51. Colchicine / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Although animal reproduction and developmental studies were not conducted with Lodoco (colchicine), published animal reproduction and development studies indicate that colchicine causes embryofetal toxicity and altered postnatal development at exposures within or above the clinical therapeutic range. Colchicine crosses the human placenta. Colchicine should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:

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

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

52. Colchicine / Lactation _____ _____

Alert Message: Lodoco (colchicine) is present in human milk. Adverse events in breastfed infants have not been reported in the published literature after administration of colchicine to lactating women. There are no data on the effects of colchicine on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for colchicine and any potential adverse effects on the breastfed infant from colchicine or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Colchicine	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

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

53. Colchicine / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Lodoco (colchicine). 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
Colchicine		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Kleinsinger, Fred. The Unmet Challenge of Medication Nonadherence. The Permanente Journal. Vol. 22 (2018): 18-033. doi:10.7812/TPP/18-033.

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

Kim J, Combs K, Downs J, Tillman F., Medication Adherence: The Elephant in the Room. US Pharm. 2018;43(1)30-34.

54. Pexidartinib / Overuse Hepatic Impairment _____ _____

Alert Message: Turalio (pexidartinib) may be over-utilized. The recommended dosage of pexidartinib for patients with moderate hepatic impairment (total bilirubin greater than 1.5 and up to 3 times upper limit of normal (ULN), not due to Gilbert's syndrome, with any AST) is 125 mg twice daily with a low-fat meal. Pexidartinib has not been studied in patients with severe hepatic impairment (total bilirubin >3 to 10 × ULN and any AST).

Drugs/Diseases

Util A	Util B	Util C (Include)
Pexidartinib		Hepatic Impairment

Max Dose: 250 mg/day

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Turalio Prescribing Information, Nov. 2023, Daiichi Sankyo, Inc.

Criteria Recommendations	*Approved*	*Rejected*

55. Tepotinib / Overuse _____ _____

Alert Message: Tepmetko (tepotinib) may be over-utilized. The recommended dosage of tepotinib is 450 mg orally once daily with food until disease progression or unacceptable toxicity.

Drugs/Diseases

Util A	Util B	Util C
Tepotinib		

Max Dose: 450 mg/day

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Tepmetko Prescribing Information, March 2023, EMD Serono.

56. Tepotinib / Therapeutic Appropriateness _____ _____

Alert Message: The safety and efficacy of Tepmetko (tepotinib) in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C
Tepotinib		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Tepmetko Prescribing Information, March 2023, EMD Serono.

57. Tepotinib / Interstitial Lung Disease (ILD)/Pneumonitis _____ _____

Alert Message: ILD/pneumonitis, which can be fatal, occurred in patients treated with Tepmetko (tepotinib). ILD/pneumonitis occurred in 2.2% of patients treated with tepotinib, with one patient experiencing a Grade 3 or higher event; this event resulted in death. Four patients (0.9%) discontinued tepotinib due to ILD/pneumonitis. Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, fever). Immediately withhold tepotinib in patients with suspected ILD/pneumonitis and permanently discontinue if no other potential causes of ILD/pneumonitis are identified.

Drugs/Diseases

Util A	Util B	Util C
Tepotinib	ILD	
	Pneumonitis	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Tepmetko Prescribing Information, March 2023, EMD Serono.

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

58. Tepotinib / Hepatotoxicity _____ _____

Alert Message: Hepatotoxicity occurred in patients treated with Tepmetko (tepotinib). Increased alanine aminotransferase (ALT)/increased aspartate aminotransferase (AST) occurred in 13% of patients treated with tepotinib. Grade 3 or 4 increased ALT/AST occurred in 4.2% of patients. A fatal adverse reaction of hepatic failure occurred in one patient (0.2%). Monitor liver function tests (including ALT, AST, and total bilirubin) prior to the start of tepotinib, every 2 weeks during the first 3 months of treatment, then once a month or as clinically indicated, with more frequent testing in patients who develop increased transaminases or bilirubin. Based on the severity of the adverse reaction, withhold, dose reduce, or permanently discontinue tepotinib.

Drugs/Diseases

Util A	Util B	Util C
Tepotinib	Abnormal Liver Studies	
	Abnormal Liver Transaminase Levels	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Tepmetko Prescribing Information, March 2023, EMD Serono.

59. Tepotinib / Certain P-gp Substrates _____ _____

Alert Message: Tepmetko (tepotinib) is a P-gp inhibitor. Concomitant use of tepotinib with a P-gp substrate increases the concentration of P-gp substrates, which may increase the incidence and severity of adverse reactions of these substrates. Avoid concomitant use of tepotinib with certain P-gp substrates where minimal concentration changes may lead to serious or life-threatening toxicities. If concomitant use is unavoidable, reduce the P-gp substrate dosage if recommended in its approved product labeling.

Drugs/Diseases

Util A	Util B	Util C
Tepotinib	Dabigatran	
	Digoxin	
	Edoxaban	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Tepmetko Prescribing Information, March 2023, EMD Serono.

60. Tepotinib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on findings in animal studies and its mechanism of action Tepmetko (tepotinib) can cause fetal harm when administered to a pregnant woman. Oral administration of tepotinib to pregnant rabbits during the period of organogenesis resulted in malformations (teratogenicity) and anomalies at exposures less than the human exposure based on area under the curve (AUC) at the 450 mg daily clinical dose. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential or males with female partners of reproductive potential to use effective contraception during treatment with tepotinib and for one week after the final dose.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Tepmetko Prescribing Information, March 2023, EMD Serono.

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

61. Tepotinib / Lactation _____ _____
Alert Message: There are no data regarding the secretion of Tepmetko (tepotinib) or its metabolites in human milk or its effects on the breastfed infant or milk production. Advise women not to breastfeed during treatment with (tepotinib and for one week after the final dose.

Drugs/Diseases

Util A	Util B	Util C
Tepotinib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Tepmetko Prescribing Information, March 2023, EMD Serono.

62. Tepotinib / Therapeutic Appropriateness _____ _____
Alert Message: Advise females of reproductive potential to use effective contraception during Tepmetko (tepotinib) treatment and for one week after the final dose. Based on findings in animal studies and its mechanism of action, tepotinib can cause fetal harm when administered to a pregnant woman.

Drugs/Diseases

Util A	Util B	Util C
Tepotinib		

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Tepmetko Prescribing Information, March 2023, EMD Serono.

63. Tepotinib / Therapeutic Appropriateness _____ _____
Alert Message: Advise male patients with female partners of reproductive potential to use effective contraception during Tepmetko (tepotinib) treatment and for one week after the final dose. Based on findings in animal studies and its mechanism of action, tepotinib can cause fetal harm when administered to a pregnant woman.

Drugs/Diseases

Util A	Util B	Util C
Tepotinib		

Gender: Male

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Tepmetko Prescribing Information, March 2023, EMD Serono.

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

64. Tepotinib / Non-adherence _____ _____
Alert Message: Based on refill history, your patient may be under-utilizing Tepmetko (tepotinib). 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
Tepotinib

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.

65. Ritlecitinib / Overuse _____ _____
Alert Message: Litfulo (ritlecitinib) may be over-utilized. The recommended dosage of ritlecitinib is 50 mg orally once daily, with or without food.

Drugs/Diseases
Util A Util B Util C
Ritlecitinib

Max Dose: 50 mg/da

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Litfulo Prescribing Information, June 2023, Pfizer, Inc.

66. Ritlecitinib / Therapeutic Appropriateness _____ _____
Alert Message: The safety and efficacy of Litfulo (ritlecitinib) have not been established in pediatric patients under 12 years of age.

Drugs/Diseases
Util A Util B Util C
Ritlecitinib

Age Range: 0 – 12 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Litfulo Prescribing Information, June 2023, Pfizer, Inc.

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

67. Ritlecitinib / Serious Infections (Box Warning) _____ _____

Alert Message: Serious infections have been reported in patients receiving Litfulo (ritlecitinib). The most frequent serious infections have been appendicitis, COVID-19 infection (including pneumonia), and sepsis. Avoid use of ritlecitinib in patients with an active, serious infection. Closely monitor patients for the development of signs and symptoms of infection during and after treatment with ritlecitinib. Interrupt ritlecitinib if a patient develops a serious or opportunistic infection.

Drugs/Diseases

Util A	Util B	Util C
Ritlecitinib	Serious Infections	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Litfulo Prescribing Information, June 2023, Pfizer, Inc.

68. Ritlecitinib / Tuberculosis (Box Warning) _____ _____

Alert Message: Serious infections have been reported in patients receiving Litfulo (ritlecitinib), including tuberculosis (TB). Ritlecitinib should not be given to patients with active TB. Test for latent TB before and during therapy; treat latent TB prior to use. Monitor all patients for active TB during treatment, even patients with initial negative, latent TB test.

Drugs/Diseases

Util A	Util B	Util C
Ritlecitinib	Tuberculosis Infection	
	Personal History of Tuberculosis	
	Personal History of Latent Tuberculosis	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Litfulo Prescribing Information, June 2023, Pfizer, Inc.

69. Ritlecitinib / Malignancies (Black Box) _____ _____

Alert Message: Malignancies, including non-melanoma skin cancer (NMSC), were observed in clinical trials of Litfulo (ritlecitinib). The risks and benefits of ritlecitinib treatment should be considered prior to initiating or continuing therapy in patients with a known malignancy other than a successfully treated NMSC or cervical cancer.

Drugs/Diseases

Util A	Util B	Util C
Ritlecitinib	Active Diagnosis of Malignant Neoplasm	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Litfulo Prescribing Information, June 2023, Pfizer, Inc.

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

70. Ritlecitinib / Thrombosis & Embolism (Black Warning) _____ _____

Alert Message: Thrombosis has occurred in patients treated with Litfulo (ritlecitinib). Avoid ritlecitinib in patients who may be at increased risk of thrombosis. If symptoms of thrombosis or embolism occur, patients should interrupt ritlecitinib and be evaluated promptly and treated appropriately.

Drugs/Diseases

Util A	Util B	Util C
Ritlecitinib	Arterial Thrombosis & Embolism	
	Venous Thrombosis & Embolism	
	Pulmonary Thrombosis & Embolism	

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

71. Ritlecitinib / Major Cardiovascular Events (Black Warning) _____ _____

Alert Message: Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Litfulo (ritlecitinib), particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. In a large, randomized, postmarketing safety study of another JAK inhibitor in RA patients 50 years of age and older with at least one cardiovascular risk factor, a higher rate of major adverse cardiovascular events (MACE) defined as cardiovascular death, non-fatal myocardial infarction (MI), and non-fatal stroke was observed with the JAK inhibitor compared to those treated with TNF blockers. Patients who are current or past smokers are at additional increased risk. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if they occur. Discontinue ritlecitinib in patients who have experienced a myocardial infarction or stroke.

Drugs/Diseases

Util A	Util B	Util C
Ritlecitinib	Myocardial Infarction	
	Stroke	
	Nicotine Dependence, Cigarette Use	
	Tobacco Use	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Litfulo Prescribing Information, June 2023, Pfizer, Inc.

72. Ritlecitinib / Cirrhosis and Hepatic Failure _____ _____

Alert Message: Litfulo (ritlecitinib) use is not recommended in patients with severe (Child-Pugh C) hepatic impairment.

Drugs/Diseases

Util A	Util B	Util C
Ritlecitinib	Cirrhosis	
	Hepatic Failure	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Litfulo Prescribing Information, June 2023, Pfizer, Inc.

Criteria Recommendations	*Approved*	*Rejected*

73. Ritlecitinib / Sensitive CYP3A Substrates _____ _____

Alert Message: Litfulo (ritlecitinib) is a CYP3A inhibitor. Concomitant use of ritlecitinib increases the AUC and Cmax of CYP3A substrates, which may increase the risk of adverse reactions of the CYP3A substrates. Consider additional monitoring and dosage adjustment in accordance with approved product labeling of CYP3A substrates where small concentration changes may lead to serious adverse reactions when used with ritlecitinib.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Litfulo Prescribing Information, June 2023, Pfizer, Inc.

74. Ritlecitinib / Sensitive CYP1A2 Substrates _____ _____

Alert Message: Litfulo (ritlecitinib) is a CYP1A2 inhibitor. Concomitant use of ritlecitinib increases AUC and Cmax of CYP1A2 substrates, which may increase the risk of adverse reactions of CYP1A2 substrates. Consider additional monitoring and dosage adjustment in accordance with the approved product labeling of CYP1A2 substrates where small concentration changes may lead to serious adverse reactions when used concomitantly with ritlecitinib.

Drugs/Diseases

Util A	Util B		Util C
Ritlecitinib	Alosetron	Theophylline	
	Duloxetine	Tizanidine	
	Ramelteon		
	Tasimelteon		

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Litfulo Prescribing Information, June 2023, Pfizer, Inc.
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

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

75. Ritlecitinib / Strong CYP3A Inducers _____ _____

Alert Message: Coadministration of Litfulo (ritlecitinib) with strong inducers of CYP3A is not recommended. Concomitant use with a strong CYP3A inducer may decrease the AUC and Cmax of ritlecitinib, which may result in loss of or reduced clinical response.

Drugs/Diseases

Util A	Util B		Util C
Ritlecitinib	Apalutamide	Phenobarbital	
	Carbamazepine	Phenytoin	
	Enzalutamide	Primidone	
	Mitotane	Rifampin	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Litfulo Prescribing Information, June 2023, Pfizer, Inc.

76. Ritlecitinib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Available data from clinical trials with Litfulo (ritlecitinib) use in pregnant women are insufficient to identify a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. In animal reproduction studies, oral administration of ritlecitinib to pregnant rats and rabbits during organogenesis caused fetotoxicity and fetal malformations. If a patient becomes pregnant while receiving ritlecitinib, healthcare providers should report ritlecitinib exposure by calling 1-877-390-2940.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Litfulo Prescribing Information, June 2023, Pfizer, Inc.

77. Ritlecitinib / Lactation _____ _____

Alert Message: There are no data on the presence of Litfulo (ritlecitinib) in human milk, the effects on the breastfed infant, or the effects on milk production. Ritlecitinib is present in the milk of lactating rats. When a drug is present in animal milk, it is likely that it will be present in human milk. Because of the serious adverse effects in adults, including risks of serious infection and malignancy, advise women not to breastfeed during treatment with ritlecitinib and for approximately 14 hours after the last dose (approximately 6 elimination half-lives).

Drugs/Diseases

Util A	Util B	Util C
Ritlecitinib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Litfulo Prescribing Information, June 2023, Pfizer, Inc.

78. Ritlecitinib / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Litfulo (ritlecitinib). 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
Ritlecitinib		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Kleinsinger, Fred. The Unmet Challenge of Medication Nonadherence. The Permanente Journal. Vol. 22 (2018): 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.

79. Fluticasone/Vilanterol / Overuse _____ _____

Alert Message: Breo Ellipta (fluticasone/vilanterol) may be over-utilized. The recommended maintenance dose of fluticasone/vilanterol for the treatment of asthma in adults is one 200 mcg fluticasone/25 mcg vilanterol inhalation once daily.

Drugs/Diseases

Util A	Util B	Util C (Include)
Fluticasone/Vilanterol		Asthma

Max Dose: 200mcg/25mcg per day
Age Range: 18 – 999 yoa

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Breo Ellipta Prescribing Information, May 2023, GlaxoSmithKline.

80. Fluticasone/Vilanterol / Overuse _____ _____

Alert Message: Breo Ellipta (fluticasone/vilanterol) may be over-utilized. The recommended maintenance dose of fluticasone/vilanterol for the treatment of asthma in patients 12 to 17 years of age is one 100 mcg fluticasone/25 mcg vilanterol inhalation once daily.

Drugs/Diseases

Util A	Util B	Util C (Include)
Fluticasone/Vilanterol		Asthma

Max Dose: 100mcg/25mcg per day
Age Range: 12 – 17 yoa

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Breo Ellipta Prescribing Information, May 2023, GlaxoSmithKline.

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

81. Fluticasone/Vilanterol / Overuse _____ _____

Alert Message: Breo Ellipta (fluticasone/vilanterol) may be over-utilized. The recommended maintenance dose of fluticasone/vilanterol for the treatment of asthma in patients 5 to 11 years of age is one 50 mcg fluticasone/25 mcg vilanterol inhalation once daily.

Drugs/Diseases

Util A	Util B	Util C (Include)
Fluticasone/Vilanterol		Asthma

Max Dose: 50mcg/25mcg per day
Age Range: 5 – 11 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Breo Ellipta Prescribing Information, May 2023, GlaxoSmithKline.

82. Tirzepatide / Oral Contraceptives _____ _____

Alert Message: The use of Mounjaro (tirzepatide) may reduce the efficacy of oral hormonal contraceptives due to delayed gastric emptying. This delay is largest after the first dose and diminishes over time. Advise patients using oral hormonal contraceptives to switch to a non-oral contraceptive method or add a barrier method of contraception for 4 weeks after initiation and for 4 weeks after each dose escalation with tirzepatide.

Drugs/Diseases

Util A	Util B	Util C
Tirzepatide	Oral Contraceptives	

Gender: Female

Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Mounjaro Prescribing Information, July 2023, Eli Lilly and Company