North Dakota Medicaid

Drug Utilization Review Board Meeting

September 7th, 2022

Conference Room 210/212

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Meeting Notice

North Dakota Medicaid Drug Use Review Board

Wednesday, September 7, 2022
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: 118 924 403 5 #

Agenda

1. Administrative items
    - DHS announcements

2. Old business
    - Review and approval of June 2022 meeting minutes
    - Budget update
    - Review top 25 drugs for the second quarter of 2022
    - Prior authorization/PDL update
    - Update to Eosinophilic Esophagitis (Dupixent)
    - Update to Bardet-Biedl Syndrome (Imcivree)
    - Update to Heart Failure (Camzyos)
    - Second review of Presbyopia
    - Second review of Cushing's Syndrome
    - Second review of Vernal Keratoconjunctivitis
    - Second review of Wilson's Disease

3. New business
    - Review of Amyloidosis (Vyndaqel, Vyndamax, Tegsedi)
    - Review of Amyotrophic Lateral Sclerosis (Radicava)
    - Review of Chelating Agents (Ferriprox)
    - Discussion of RSV
    - Discussion of RDUR response letter
    - Retrospective DUR profile review update
    - Retrospective DUR criteria recommendations
    - Upcoming meeting date/agenda.
        - Next meeting is December 7th, 2022

Adjourn

Individuals with disabilities who need accommodations, including appropriate auxiliary aids to participate, can contact Stacey Koehly at 701-328-4807, toll-free 800-755-2604, 711 (TTY) or skoehly@nd.gov.

North Dakota Medicaid Drug Use Review (DUR) Board
Meeting Minutes
June 1st, 2022

Members Present: Joshua Askvig, Andrea Honeyman, Kathleen Traylor, Amy Werremeyer, Laura Kroetsch, Tanya Schmidt, Kevin Martian, Kristen Peterson, Jennifer Iverson, Gabrielle Balf, Mary Aaland

Medicaid Pharmacy Department: Alexi Murphy, Brendan Joyce, LeNeika Roehrich

Old Business

Chair T. Schmidt called the meeting to order at 1:01 p.m. Vice Chair election was held during this meeting in which T. Schmidt was nominated and voted again to serve as the Board meeting Chair for the following year. Chair T. Schmidt asked for a motion to approve the minutes of the March 2nd, 2022, meeting. J. Askvig moved that the minutes be approved, and K. Martian seconded the motion. The chair called for a voice vote to approve the minutes. The motion passed with no audible dissent.

Review Top 25 Drugs

B. Joyce presented budget updates and the quarterly review of the top 25 drugs based on total claims cost, the top 25 drugs based on the total number of claims, and the top drug classes based on claims and cost for the 1st quarter of 2022. B. Joyce went on to discuss "per member per month" (PMPM) average cost which is the net of all rebates. Within the last eight quarters, the PMPM average has decreased since managed care is no longer involved in the process. However, the total expenses from 2020 to 2021 increased by 21%. B. Joyce presented the 5 drug classes which account for 75% of the cost increase. These classes include agents used for cystic fibrosis, oncology, immunomodulators, HIV, and eczema. The question was brought up about if there is a way to determine how many members will fall off once Medicaid enrollment redetermination begins again. B. Joyce answered that there is currently no way of knowing how many will fall off.

PDL/PA Criteria Updates

A. Murphy shared with the Board all the changes made to the Preferred Drug List since the last version of the Preferred Drug List was posted. Notable changes include adding Pyrukynd, Ferriprox, and Vijoice to PA for the Over 3000 criteria. A couple notable changes in the Antifungals section and Glucose Rescue Medications section include changing Noxafil and Vfend to preferred and Gvoke to preferred, respectively. All PDL updates are listed in the handout for the June 2022 DUR Board meeting. When a new version of the PDL is published and posted to the website, all updates/changes made since the last version are called out at the top of the document itself. During public comment, Vruti Patel from Xeris thanked the Board for allowing Gvoke to become a preferred agent.

Update to Sedatives/Hypnotics

L. Morgan presented the proposed changes to the Sedatives/Hypnotics section in which Smith-Magenis Syndrome was added with initial and renewal criteria. The preferred agent requiring a clinical PA is Hetlioz. M. Aaland asked how there will be confirmation of a specialist being involved in the member's treatment for this disease state. L. Morgan discussed that the provider submitting the PA must list the specialist involved in the treatment of the member. M. Aaland expressed concerns about the requirement for a sleep-disorder specialist to be involved, as it seemed vague about who is considered a specialist in the field. After discussion amongst the Board members, clarification was made about the requirement for a sleep-disorder specialist.

Update to Lupus Nephritis

L. Morgan presented changes made to the Lupus Nephritis section in the PDL. Initial approval duration for Lupkynis was adjusted from 12 months to 6 months. Additionally, more specific criteria about required documentation to support member clinical benefit and improvement since starting Lupkynis were added for renewal.

Update to Chronic Kidney Disease

L. Morgan presented updates to Kerendia in the Chronic Kidney Disease section. For this agent, the member must have a history of diabetes and meet the parameters listed for estimated glomerular filtration rate (eGFR) and urinary albumin-to-creatinine ratio (UACR). K. Martian asked if the requirement of the labs will be enforced for all facilities, including those that do not possess the ability to produce such labs. A. Murphy responded that if this does come up during review, then exceptions can be made depending on the situation. For now, that concern will be monitored. During public comment, Bashir Kalayah from Bayer Pharmaceuticals gave an overview of Kerendia. He made a request to the Board to allow Kerendia without concurrent use of an ACE-inhibitor, or ARB, and a SGLT-2 inhibitor. During discussion, A. Murphy stated that the requirement for concurrent use of those agents will be waved if the member has a contraindication, allergy, or other extenuating circumstance for why the member cannot take the agent.

Update to Heart Failure

L. Morgan presented updates to the Heart Failure second line agent's section. The prescriber must now be, or be in consult, with a cardiologist for approval of Verquvo and Corlanor. All other criteria remained the same.

Update to Drug Utilization Review Policies

L. Morgan presented an update to the Preferred Drug List (PDL) that discussed the Drug Utilization Review Policies. This policy was already in effect prior to the update; however, the policy was added to the PDL for provider clarity on the topic. A. Werremeyer discussed her concerns of this policy and how it may limit medical care for a member if his or her provider does not advocate for the member's need for the requested treatment. A.Werremeyer explained how many agents are used in practice based on literary support versus FDA-approval. A. Murphy answered that per federal law, clinical literature cannot be used as a basis for approval of agents not compendia supported. B. Joyce also added that Kepro, the contracted prior authorization reviewer, will not be utilized to review non-compendia supported use of agents. Rather, letters and emails may be submitted to ND Medicaid resources to discuss the use of non-compendia supported use of agents. G. Balf added her concerns also of the Drug Utilization Review policy and the restrictions it can pose on members. B. Joyce responded that this policy has always been in place, but it is just now being added to the PDL for reference. L. Kroetsch was also in favor of changing the language in this section to let practitioners know there is a route they can take to advocate for their patients to use non-compendia supported agents.

Synagis Discussion

A Murphy presented data on RSV and the use of Synagis in recent years. A. Murphy presented the seasonal cost of Synagis from 2016 to 2021 for ND Medicaid. She also presented Region 8 reported seasons and how North Dakota matched up to the start and end of those seasons. Overall, ND Medicaid started covering Synagis earlier than other states in Region 8. A. Murphy went on to discuss how to determine "seasonality" and how to measure consistency of RSV detection. This topic will be discussed more at the next meeting.

Second Review of Familial Cholestasis Pruritis

L. Morgan presented initial and renewal criteria for Bylvay and Livmarli. These agents will be approved for 6 months initially and 12 months for renewal. Bylvay and Livmarli both have product specific criteria listed which requires genetic testing to support appropriate diagnosis and medication use. Bylvay and Livmarli are listed as preferred agents that require clinical PA. Standing in for Chair T. Schmidt, A. Honeyman called for a voice vote to approve the updated criteria, which passed with no audible dissent.

<u>New Business</u>

Review of Wilson's Disease

L. Morgan presented a review of the disease state and agents used in the treatment of Wilson's Disease to the Board. A motion was made by A. Werremeyer to manage these medications through prior authorization. The motion was seconded by K. Martian. Prior authorization criteria for these agents will be presented, reviewed, and voted on by the Board at the next meeting.

Review of Cushing's Syndrome
L. Morgan presented a review of the disease state and agents used in the treatment of Cushing's Syndrome to the Board. During public comment, Vruti Patel from Xeris gave an overview of Recorlev and requested it be added to the PDL. K. Martian asked what, if any, clinical benefit would come from using the racemic mixture of ketoconazole (Recorlev) versus ketoconazole. Vruti Patel answered that there is currently no clinical benefit showing superiority of Recorlev over ketoconazole, but rather there is a broader indication and prescriber support for using Recorlev. A motion was made by K. Martian to manage these medications through prior authorization. The motion was seconded by A. Honeyman. Prior authorization criteria for these agents will be presented, reviewed, and voted on by the Board at the next meeting.

Review of Presbyopia
L. Morgan presented a review of the disease state and agents used in the treatment of presbyopia to the Board. During public comment, Nathan Blake from AbbVie made himself available for questions from the Board. A. Murphy then asked the Board if they want to consider this agent for cosmetic use or add it to the PDL for prior authorization. K. Martian and B. Joyce brought up the medical need for some members who may not be able to wear glasses. A motion was made by K. Martian to manage these medications through prior authorization. The motion was seconded by A. Werremeyer. Prior authorization criteria for these agents will be presented, reviewed, and voted on by the Board at the next meeting.

Review of Vernal Keratoconjunctivitis
L. Morgan presented a review of the disease state and agents used in the treatment of vernal keratoconjunctivitis to the Board. A motion was made by A. Werremeyer to manage these medications through prior authorization. The motion was seconded by J. Askvig. Prior authorization criteria for these agents will be presented, reviewed, and voted on by the Board at the next meeting.

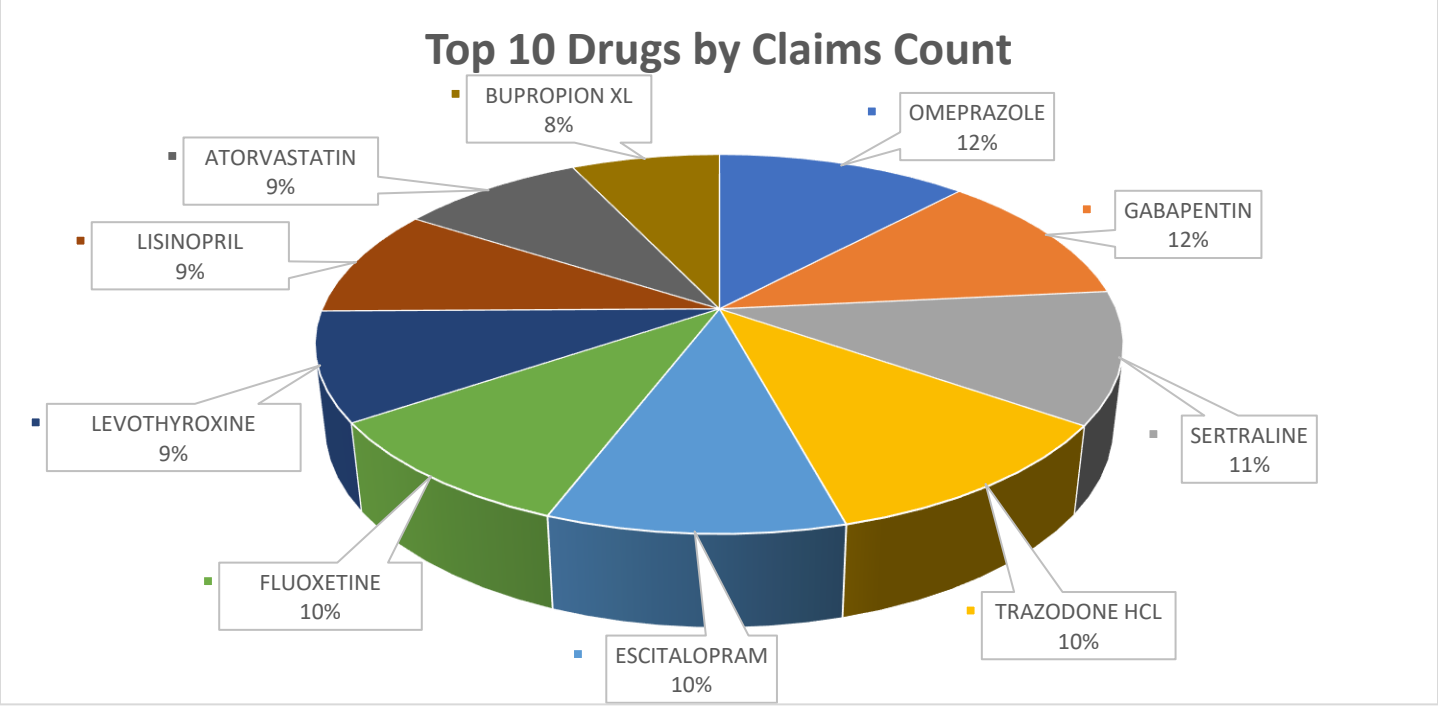
Retrospective Drug Utilization Review (RDUR) Criteria Recommendations
L. Morgan reviewed the RDUR criteria that were selected for review of January and March of Q1 2022. Presented data included number of profiles reviewed, number of cases identified for intervention, and the number of letters sent, as well as an overview of what RDUR interventions were identified as most prevalent for each monthly cycle. There was a special mailing sent in February to providers about neuropsychiatric events reported with the use of Singulair. Additionally, L. Morgan presented Q1 2022 RDUR response rate data from prescribers and pharmacies. M. Aaland discussed her concerns about the low response rate from prescribers and pharmacies, and from there, the Board discussed ways to increase the response rate. Some mentioned making the response form shorter and more direct, choosing more useful RDUR criteria, and narrowing down and communicating with the non-responders. The recommended RDUR criteria enclosed in the packet were developed from product information provided by the manufacturers and are consistent with new indications, new drugs added, and new warnings. These proposed criteria will be added to the current set of criteria and will be used in future DUR cycles. M. Aaland moved to approve the new criteria and K. Martian seconded the motion. Standing in for Chair T. Schmidt, A. Honeyman called for a voice vote to approve the new criteria, which passed with all present members voting to approve.

Adjournment and Upcoming Meeting Date
A. Honeyman adjourned the meeting at 3:25 pm. The next DUR Board meeting will be held September 7th, 2022, at 1:00 pm at the state capitol building.

Top 25 Drugs Based on Number of Claims from 04/01/2022 – 06/30/2022

Drug	Claims	Patients	Claims Cost	Cost / Claim	% Total Claims	Dif.
1. OMEPRAZOLE	4,846	2,403	$62,645.00	$12.93	1.86%	↑1
2. GABAPENTIN	4,688	1,958	$69,536.71	$14.83	1.80%	↓1
3. SERTRALINE HCL	4,368	2,393	$59,893.29	$13.71	1.68%	NC
4. TRAZODONE HCL	4,167	2,035	$56,455.50	$13.55	1.60%	NC
5. ESCITALOPRAM OXALATE	4,082	2,273	$55,106.37	$13.50	1.57%	NC
6. FLUOXETINE HCL	3,919	2,081	$53,495.61	$13.65	1.51%	NC
7. LEVOTHYROXINE SODIUM	3,648	1,860	$60,734.32	$16.65	1.40%	NC
8. LISINOPRIL	3,500	2,004	$44,850.90	$12.81	1.35%	NC
9. ATORVASTATIN CALCIUM	3,431	1,926	$48,339.61	$14.09	1.32%	↑1
10. BUPROPION XL	3,123	1,665	$55,332.02	$17.72	1.20%	↑2
11. VYVANSE	3,011	1,210	$797,616.43	$264.90	1.16%	↑2
12. PANTOPRAZOLE SODIUM	2,918	1,423	$39,148.04	$13.42	1.12%	↑3
13. HYDROCODONE-APAP	2,875	1,805	$41,794.54	$14.54	1.11%	↑1
14. AMOXICILLIN	2,862	2,688	$39,587.54	$13.83	1.10%	↓5
15. DULOXETINE HCL	2,550	1,328	$41,503.61	$16.28	0.98%	↑2
16. PROAIR HFA	2,529	2,496	$201,469.27	$79.66	0.97%	↓5
17. CYCLOBENZAPRINE HCL	2,499	1,582	$29,726.87	$11.90	0.96%	↑3
18. METFORMIN HCL	2,462	1,361	$32,389.07	$13.16	0.95%	↑1
19. HYDROXYZINE HCL	2,459	1,506	$34,088.56	$13.86	0.95%	↑3
20. CLONIDINE HCL	2,458	1,214	$31,087.60	$12.65	0.95%	↑3
21. BUPRENORPHINE-NALOXONE	2,446	594	$105,402.63	$43.09	0.94%	↓3
22. PREDNISONE	2,410	1,883	$28,906.80	$11.99	0.93%	↓6
23. MONTELUKAST SODIUM	2,403	1,405	$33,676.15	$14.01	0.92%	↑4
24. LAMOTRIGINE	2,397	973	$34,753.76	$14.50	0.92%	↓2
25. CLONAZEPAM	2,307	985	$31,363.57	$13.59	0.89%	↑1

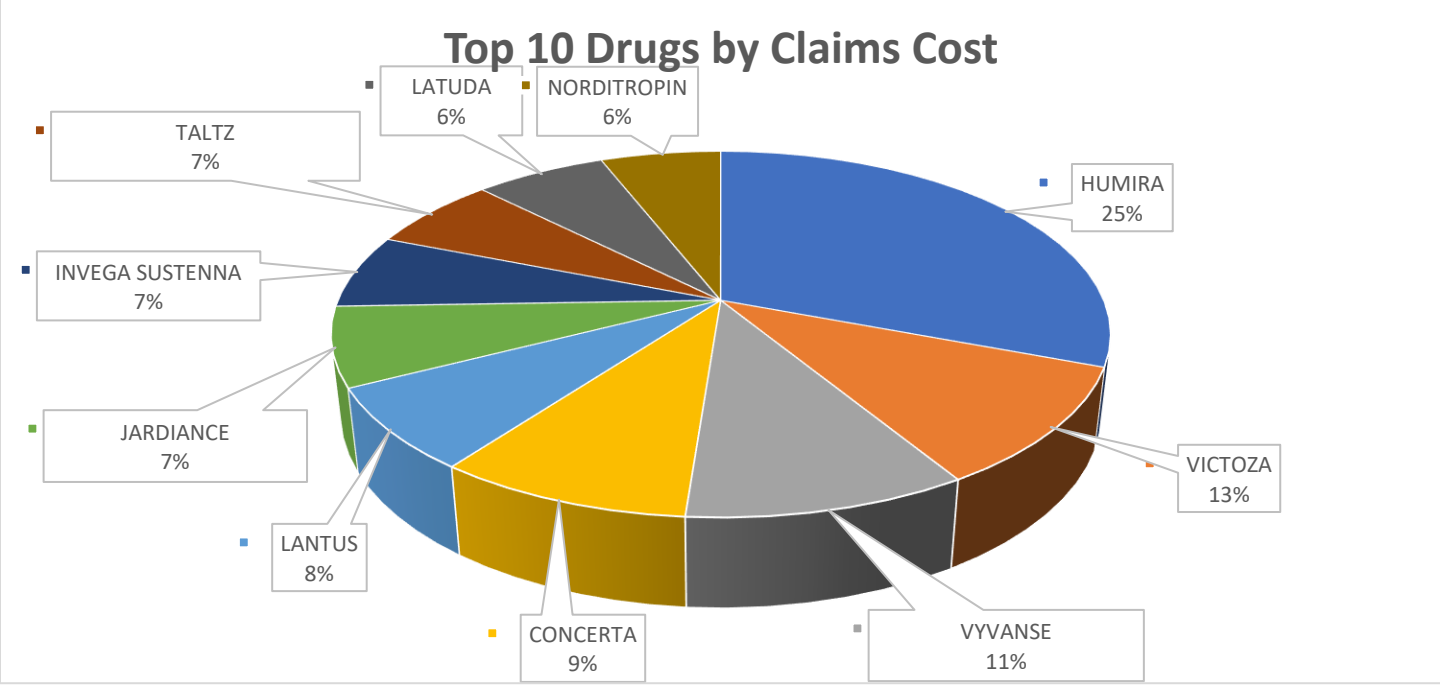
Total Claims	**259,935**



Top 25 Drugs Based on Total Claims Cost from 04/01/2022 – 06/30/2022

Drug	Claims Cost	Claims	Patients	Cost /Claim	% Total Cost	Dif.
1. HUMIRA PEN	$1,908,540.35	256	106	$7,455.24	5.97%	NC
2. VICTOZA	$966,894.90	1157	551	$835.69	3.02%	↑3
3. VYVANSE	$797,616.43	3,011	1,210	$264.90	2.49%	↓1
4. CONCERTA	$677,365.30	1,891	799	$358.20	2.12%	↓1
5. LANTUS SOLOSTAR	$626,924.46	1,246	771	$503.15	1.96%	↓1
6. JARDIANCE	$561,978.00	978	452	$574.62	1.76%	↑5
7. INVEGA SUSTENNA	$522,374.47	210	84	$2,487.50	1.63%	↑1
8. TALTZ AUTOINJECTOR	$521,676.58	83	33	$6,285.26	1.63%	↓2
9. LATUDA	$484,309.49	589	236	$822.26	1.51%	NC
10. NORDITROPIN FLEXPRO	$473,031.57	110	42	$4,300.29	1.48%	↑2
11. STELARA	$418,479.44	17	13	$24,616.44	1.31%	↓4
12. MAVYRET	$396,967.47	32	20	$12,405.23	1.24%	↑6
13. BIKTARVY	$386,920.19	216	98	$1,791.30	1.21%	↓3
14. SYMBICORT	$355,547.64	1,018	595	$349.26	1.11%	↑2
15. ADDERALL XR	$349,293.04	1,969	835	$177.40	1.09%	↑2
16. ADVAIR DISKUS	$340,032.40	922	505	$368.80	1.06%	↑3
17. NOVOLOG FLEXPEN	$335,844.83	486	287	$691.04	1.05%	↓3
18. ELIQUIS	$329,808.12	670	305	$492.25	1.03%	↑2
19. TRIKAFTA	$300,561.80	12	5	$25,046.82	0.94%	↓4
20. VRAYLAR	$292,956.38	317	133	$924.15	0.92%	↑5
21. ABILIFY MAINTENA	$269,404.80	116	47	$2,322.46	0.84%	↑3
22. LEVEMIR FLEXTOUCH	$268,986.86	479	274	$561.56	0.84%	NC
23. GILENYA	$238,174.31	27	10	$8,821.27	0.74%	↑9
24. COSENTYX PEN	$232,660.70	38	14	$6,122.65	0.73%	↑2
25. XIFAXAN	$224,935.00	90	45	$2,499.28	0.70%	↓2

Total Claims Cost	**$31,980,817.33**



Top 15 Therapeutic Classes Based on Number of Claims from 04/01/2022 – 06/30/2022

Therapeutic Class Description	Claims	Patients	Claims Cost	Cost/Claim	% Total Claims	Dif.
1. ANTIDEPRESSANTS	30,158	12,415	$636,897.32	$21.12	11.60%	NC
2. ANTICONVULSANTS	13,669	4,784	$794,503.36	$58.12	5.26%	NC
3. ANTIPSYCHOTIC AGENTS	9,336	3,593	$2,347,175.69	$251.41	3.59%	NC
4. PROTON-PUMP INHIBITORS	8,144	3,949	$145,481.30	$17.86	3.13%	NC
5. SEDATIVES/HYPNOTICS	7,318	3,688	$112,364.11	$15.35	2.82%	NC
6. OPIATE AGONISTS	7,032	3,600	$118,975.08	$16.92	2.71%	NC
7. AMPHETAMINES	6,433	2,656	$1,191,664.83	$185.24	2.47%	NC
8. NSAIDS	6,427	4,221	$96,528.18	$15.02	2.47%	NC
9. STATINS	5,933	3,294	$85,628.06	$14.43	2.28%	↑1
10. BETA BLOCKERS	5,496	2,902	$100,265.46	$18.24	2.11%	↑2
11. PENICILLIN ANTIBIOTICS	5,291	4,739	$82,457.07	$15.58	2.04%	↑2
12. NON-AMPHETAMINE STIMULANTS	5,150	1,982	$1,005,997.10	$195.34	1.98%	↓1
13. ACE-INHIBITORS	4,458	2,525	$70,224.93	$15.75	1.72%	↑2
14. BIGUANIDES	4,110	2,278	$57,055.48	$13.88	1.58%	↑2
15. BETA AGONISTS	4,078	3,662	$311,670.94	$76.43	1.57%	↑2

Top 15 Therapeutic Classes Based on Claims Cost from 04/01/2022 – 06/30/2022

Therapeutic Class Description	Claims Cost	Claims	Patients	Cost/Claim	% Total Cost	Dif.
1. DMARDS	$3,411,238.61	628	255	$5,431.91	10.67%	NC
2. ANTIPSYCHOTIC AGENTS	$2,347,175.69	9,336	3,593	$251.41	7.34%	NC
3. INSULINS	$1,877,264.60	3,635	1,403	$516.44	5.87%	↑1
4. SKIN AND MUCOUS MEMBRANE AGENTS	$1,656,560.21	627	384	$2,642.04	5.18%	↓1
5. AMPHETAMINES	$1,191,664.83	6,433	2,656	$185.24	3.73%	↑2
6. INCRETIN MIMETICS	$1,104,294.55	1,324	593	$834.06	3.45%	↑3
7. ANTINEOPLASTIC AGENTS	$1,079,500.57	573	241	$1,883.95	3.38%	↓2
8. RESPIRATORY CORTICOSTEROIDS	$1,064,547.91	3,643	2,182	$292.22	3.33%	↑2
9. NON-AMPHETAMINE STIMULANTS	$1,005,997.10	5,150	1,982	$195.34	3.15%	↑2
10. ANTIRETROVIRALS	$967,402.05	779	294	$1,241.85	3.02%	↓2
11. ANTICONVULSANTS	$794,503.36	13,669	4,784	$58.12	2.48%	↓5
12. SGLT-2 INHIBITORS	$768,726.22	1,358	627	$566.07	2.40%	↑1
13. IMMUNOMODULATORY AGENTS	$702,514.04	89	34	$7,893.42	2.20%	↓1
14. ANTIDEPRESSANTS	$636,897.32	30,158	12,415	$21.12	1.99%	NC
15. HCV ANTIVIRALS	$615,716.35	60	34	$10,261.94	1.93%	NC

PDL UPDATE

Drug Name	PA	Class
Adlarity	PA	Alzheimer's agents
Aspruzyo Sprinkle	PA	Non-Preferred Dosage Forms
Camzyos	PA	Heart Failure/3000
Lyvispah	PA	muscle relaxants
Mounjaro	PA	Diabetes
Radicava	PA	3000
Tegsedi	PA	3000
Voquenza	PA	anti-infectives resistance prevention
Vtama	PA	Topical plaque psoriasis
deferasirox (Jadenu) tablets	remove PA	Preferred Dosage Forms

Eosinophilic Esophagitis

Prior Authorization Form - Dupixent

Group Criteria:

- **Initial Criteria:** *Approval Duration = 6 months*
  - The prescriber must be, or be in consultation with, a gastroenterologist
  - The member must have ≥15 intraepithelial eosinophils per high-power field (eos/hpf).
  - Member must have failed a 3-month trial of a swallowed inhaled respiratory corticosteroid (budesonide or fluticasone).
- **Renewal Criteria:** *Approval Duration = 12 months*
  - The prescriber must provide documentation showing that the member has achieved a significant reduction in dysphagia symptoms since treatment initiation.
  - The member must have achieved an esophageal intraepithelial eosinophil count of ≤6 eos/hpf.

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

Imcivree

General Prior Authorization Form

- **Initial Criteria:** *Approval Duration = 4 months*
  - The member must have a diagnosis of obesity (BMI > 30 kg/m2 for adults or > 95th percentile using growth chart assessments for pediatric members)
  - The member's obesity must be due to one of the following (A or B):
    A. Variants interpreted as pathogenic, likely pathogenic, or of unknown significance:
      - proopiomelanocortin (POMC)
      - proprotein convertase subtilisin/kexin type 1 (PCSK1)
      - leptin receptor (LEPR) deficiency

    B. A diagnosis of Bardet-Biedl Syndrome (BBS) as evidenced by three or more of the following:
      - Rod-cone dystrophy
      - Polydactyly
      - Genital anomalies
      - Renal anomalies
      - Intellectual impairment
  - The medication is prescribed by, or in consultation with, an endocrinologist or expert in rare genetic disorders of obesity
  - The member's weight and body mass index (BMI) must be provided within the last 60 days
- **Renewal Criteria:** *Approval Duration = 12 months*
  - One of the following must be met since starting treatment with Imcivree, as evidenced by medical documentation (e.g., chart notes) attached to the request:
    - Members ≥ 18 years old:
      - First renewal - a 5% weight reduction has been achieved or maintained
      - Subsequent renewal - a 10% weight reduction has been achieved or maintained
    - Members < 18 years old: a 5% reduction in BMI has been achieved or maintained

PREFERRED AGENTS (CLINICAL PA REQUIRED)
IMCIVREE (setmelanotide)

Heart Failure

Electronic Diagnosis Verification

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

Prior Authorization Criteria

General Prior Authorization Form

First Line Agents:

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
ACE (angiotensin-converting enzyme) inhibitors - *all oral agents preferred*	
ARBs (angiotensin receptor blockers) - *all oral agents preferred*	
Beta blockers - *all oral agents preferred*	
ENTRESTO (sacubitril/valsartan)	
eplerenone	
FARXIGA (dapagliflozin)	
JARDIANCE (empagliflozin)	
spironolactone	

Second Line Agents:

Product Specific Criteria:

- **Verquvo:**
  - The prescriber is, or is in consult with, a cardiologist
  - The member must have left ventricular ejection fraction (LVEF) < 45%
  - Documentation of a recent hospitalization or need for IV diuretics (within the past 6 months) must be submitted with request
  - The member is receiving concurrent Entresto, a beta-blocker, a SGLT-2 Inhibitor, and a mineralocorticoid receptor antagonist.
- **Corlanor:**
  - The prescriber is, or is in consult with, a cardiologist
  - The member must have a resting HR ≥ 70 beats per minute on maximally tolerated or target beta blocker dose in sinus rhythm
- **Camzyos (Initial):** *Approval Duration = 6 months*
  - The prescriber is, or is in consult with, a cardiologist
  - Documentation of an echocardiogram assessment of LVEF ≥55% must be provided.
  - Documentation of a left ventricular outflow tract (LVOT) peak gradient ≥50 mmHg at rest or with provocation must be provided.
  - Documentation of oxygen saturation of ≥90% at rest must be provided.
  - The member is receiving concurrent Entresto, a beta-blocker, a SGLT-2 Inhibitor, and a mineralocorticoid receptor antagonist.

Product Specific Criteria (Renewal):

- **Camzyos:** *Approval Duration = 12 months*
  - Documentation of echocardiogram assessments of LVEF ≥50% must be provided
  - Documentation of mixed peak oxygen consumption (pVO_2) by ≥ 1.5 mL/kg/min plus improvement in NYHA class by at least 1 or improvement of pVO_2 by ≥3 mL/kg/min plus no worsening of NYHA class must be provided.

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

Presbyopia

General Prior Authorization Form

Group Criteria:

- **Initial Criteria:** *Approval Duration = 3 months*
  - The prescriber must be, or be in consultation with, an optometrist
  - Documentation of medical necessity must be provided, including contraindication to the use of corrective lenses and how activities of daily living are adversely impacted due to inability to correct vision with corrective lenses.
- **Renewal Criteria:** *Approval Duration = 12 months*
  - Documentation that activities of daily living are positively impacted by drug therapy.

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
VUITY (pilocarpine hydrochloride)	

Drug	Strength	Package Size	WAC Pkg Price	Cost/day*	Cost/month*	Cost/year*
Vuity	1.25%	2.5 mL	$73.49	$2.94	$88.19	$1,058.26

Cushing's Syndrome

General Prior Authorization Form

Group Criteria:

- The medication is prescribed by, or in consultation with, an endocrinologist or specialist in the treatment of endogenous Cushing's syndrome.
- Member must have failed a 3-month trial of combination treatment with ketoconazole tablets and metyrapone.
- Member is not a candidate for surgery or surgery has not been curative, or is waiting for surgery or effect of pituitary radiation.

Product Specific: Recorlev

- **Initial criteria**: *Approval Duration = 6 months*
  - Member must have a mean (at least two measurements) 24-hour urine free cortisol (UFC) level that is 3x above the normal range per the reporting laboratory reference range.
- **Renewal Criteria:** *Approval Duration 12 months*
  - Member must have experienced and maintained clinical benefit since starting treatment with the requested medication, as evidenced by medical documentation (e.g. chart notes) attached to the request (subject to clinical review).
  - Member has normalization of 24-hour urine free cortisol (UFC) level per the reporting laboratory reference range:

Product Specific: Korlym

- **Initial criteria**: *Approval Duration = 6 months*
  - Member has uncontrolled hyperglycemia (type 2 diabetes or glucose intolerance) as defined by a hemoglobin A1c > 7%, despite adherence to an anti-diabetes regimen.
- **Renewal Criteria:** *Approval Duration 12 months*
  - Member must have experienced and maintained clinical benefit since starting treatment with the requested medication, as evidenced by medical documentation (e.g. chart notes) attached to the request (subject to

clinical review) such as improvement in cushingoid appearance, acne, hirsutism, striae, psychiatric symptoms, and excess total body weight.
- Member has improved hyperglycemia as a hemoglobin A1c decrease of 1% or greater not attributed to an increase in medications, dosages, or adherence to an anti-diabetes regimen.

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
KORLYM (mifepristone)	
RECORLEV (levoketoconazole)	

Drug	Strength	Package Size	WAC Pkg Price	Cost/day*	Cost/month*	Cost/year*
Ketoconazole	200 mg	30 and 100 tabs each	$31.50	$2.10 - $8.40	$63 - $252	$756 - $3,024
Metyrapone	250 mg	18 caps each	$724.64	$80.52 - $966.19	$2,415.60 - $28,985.70	$28,987.20 - $347,828.40
Mitotane	500 mg	100 tabs each	$1,165.40	$11.65 - $186.46	$349.50 - $5,593.80	$4,194 - $67,125.60
Isturisa	1 mg, 5 mg, and 10 mg	20 and 60 tabs each	$2,643.80	$528.76 - $1,057.88	$15,862.80 - $31,736.40	$190,353.60 - $380,836.80
Recorlev	150 mg	50 tabs each	$13,500	$540 – $2,160	$16,200 - $64,800	$194,400 - $777,600
Signifor	0.3 mg/mL, 0.6 mg/mL, and 0.9 mg/mL	1 mL ampule	$244.17	$488.34	$14,650.20	$175,802.40
Signifor LAR	10 mg, 20 mg, 30 mg, 40 mg, and 60 mg	1 vial	$14,602.56	$486.75	$14,602.56	$175,230.72
cabergoline	0.5 mg	8 tabs each	$25.04	$0.42 - $43.82	$12.52 - $1,314.60	$150.24 - $15,775.20
Korlym	300 mg	28 and 280 tabs each	$16,156	$577 - $2,308	$17,310 - $69,240	$207,720 - $830,880

Vernal Keratoconjunctivitis

General Prior Authorization Form

Group Criteria:

- **Initial Criteria:** *Approval Duration = 6 months*
  - The prescriber must be or be in consultation with an allergist or ophthalmologist.
  - Member has failed* a 3-month trial of a combination of each of the following:
    - Topical dual-acting mast cell stabilizers/antihistamines such as olopatadine, azelastine hydrochloride, epinastine, pemirolast potassium, and ketotifen fumarate
    - Second- and third-generation oral antihistamines such as fexofenadine, loratadine, desloratadine, cetirizine, and levocetirizine
    - Cyclosporine ophthalmic emulsion 0.05%

    *Failure is defined as requiring frequent or prolonged courses of topical ophthalmic corticosteroids include prednisone acetate 1% and dexamethasone 0.1% for severe cases and prednisolone acetate 0.12%, fluorometholone, medrysone, loteprednol, etabonate 0.2 or 0.5%, and rimexolone 1% or compromised corneal epithelium
- **Renewal Criteria:** *Approval Duration = 12 months*

- Member must have experienced and maintained clinical benefit since starting treatment with the requested medication, as evidenced by medical documentation (e.g. chart notes) attached to the request (subject to clinical review).

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

Drug	Strength	Package Size	WAC Pkg Price	Cost/day*	Cost/month*	Cost/year*
Verkazia	0.1%	120 each	$1,464.96	$48.83	$1,464.96	$17,579.52

Wilson's Disease

General Prior Authorization Form

Product Specific: Trientine hydrochloride

- **Initial criteria**: *Approval Duration = 6 months*
  - Member must have had a 3-month therapeutic trial of a penicillamine agent.

Non-Preferred Agents Criteria:

- Clinical justification must be provided explaining why the member is unable to use the preferred agents (subject to clinical review).
- The member must have failed* a 30-day trial of each preferred agent (listed in boxes below) within the past 2 years, as evidenced by paid claims or pharmacy printouts.

*Failure is defined as product was not effective at maximum tolerated dose or member has a documented intolerance or adverse reaction to inactive ingredients where the non-preferred product is expected to have a different result and other alternatives (e.g. medications in same class) are not an option for the member

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
DEPEN (penicillamine) TITRATAB – *Brand Required*	CUPRIMINE (penicillamine) CAPSULE
trientine hydrochloride	penicillamine capsule
	penicillamine tablet
	SYPRINE (trientine hydrochloride)

Drug	Strength	Package Size	WAC Pkg Price	Cost/day*	Cost/month*	Cost/year*
Penicillamine tablet	250 mg	100 each	$4,652.90	$372.23	$11,166.96	$134,003.52
Penicillamine capsule	250 mg	100 each	$1,080	$86.40	$2,592.00	$31,104.00
Trientine hydrochloride capsule	250 mg	100 each	$750.00	$60.00	$1,800.00	$21,600.00
Cuvrior	Expected to launch in early 2023					

REVIEW OF AMYLOIDOSIS

Overview

Amyloidosis is caused by the deposition of insoluble protein fibrils in tissues and organs. There are several forms of amyloidosis but three main subtypes. These subtypes are AL Amyloidosis, AA Amyloidosis, and transthyretin-related amyloidosis (ATTR). ATTR can be broken down into two types: hereditary ATTR (hATTR) and wild-type ATTR (ATTRwt). The prevalence of hereditary ATTR is poorly characterized but is estimated to be 50,000 individuals worldwide. Most types of ATTR are associated with a 3-to-5-year life expectancy upon diagnosis. Most patients experience neurologic and cardiac symptoms due to the accumulation of these proteins.

Categories of amyloidosis:

- hATTR - PN
  - Val30Met is the most prevalent mutation found for this type
- hATTR-CM (variant ATTR)
  - Caused by a mutation in the transthyretin (TTR) gene
  - Diagnosed in patients as early as their 50s and 60s
  - One variant of hATTR is caused by the Val122Ile mutation (V122I). It is estimated that 4% of African Americans carry this variant.
- ATTRwt-CM (acquired ATTR)
  - Not associated with mutations
  - Associated with aging
  - Predominantly affects men older than 60
- Organ-specific categorization of ATTR
  - ATTR-CM: amyloid aggregates in the myocardium causing cardiomyopathy
  - ATTR-PN: amyloid deposits in the nervous system causing pain, muscle weakness, and autonomic dysfunction

Uncertainties still exist in screening, the assessment of progression, the management of asymptomatic carriers of ATTRv, the use of TTR silencing agents in ATTR-CM, and the financial impact of disease-modifying therapies.

Place in Therapy/Guidelines

Currently, there are three agents approved for treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR - PN) in adults: Onpattro, Amvuttra**,** and Tegsedi. Additionally, there are two agents approved for treatment of cardiomyopathy caused by transthyretin-mediated amyloidosis (hATTR - CM and ATTRwt - CM) in adults: Vyndaqel and Vyndamax. Unfortunately, there are no agents approved for both polyneuropathy and cardiomyopathy.

FDA Approval
Tegsedi: 505(b) New Drug Application (NDA) pathway, Type 1 - New Molecular Entity, PRIORITY; Orphan
Vyndaqel: 505(b) New Drug Application (NDA) pathway, Type 1 - New Molecular Entity, PRIORITY; Orphan
Vyndamax: 505(b) New Drug Application (NDA) pathway, Type 2 - New Active Ingredient, STANDARD; Orphan

Tegsedi (inotersen)

- Mechanism of action: Antisense oligonucleotide
- ATTR-PN Treatment: Liver transplantation has been utilized for most patients. Onpattro, Tegsedi, and Amvuttra are the only treatment options currently**.**
- Patients with ATTRv and polyneuropathy should be considered for TTR silencing therapy with Onpattro or Tegsedi; currently, neither is indicated for ATTRv-CM without polyneuropathy or in ATTRwt-CM. In patients with ATTRv-CM with polyneuropathy, the choice between therapeutic agents is based on accessibility and side-effect profile.

Vyndaqel (tafamidis meglumine) and Vyndamax (tafamidis)

- Mechanism of action: Transthyretin (TTR) dissociation inhibitor
- ATTR-CM Treatment: Previously, treatment options included symptom management and heart transplant. Vyndaqel and Vyndamax are new medication therapies that stabilize the tetramer protein and slow the formation of amyloid that causes ATTR-CM.

- In patients with predominantly cardiac disease resulting from ATTRv or ATTRwt, tafamidis is indicated in those with NYHA class I to III symptoms, and early initiation appears to slow disease progression. The benefit of tafamidis has not been observed in patients with class IV symptoms, severe aortic stenosis, or impaired renal function (GFR < 25 mL/min)

Place in Therapy
The use of combination therapy with an antisense oligonucleotide and a transthyretin (TTR) dissociation inhibitor is appealing to synergistically target both TTR silencing and stabilization of the remaining synthesized protein, but this approach lacks data and may be cost-prohibitive.

Diflusinal (250 mg orally twice daily) may be considered with caution for off-label therapy for asymptomatic ATTR carriers, for patients with ATTR-CM who are not eligible for TTR silencers, or for patients with ATTR-CM who are intolerant of or cannot afford tafamidis.

Given the lack of consensus on defining disease onset in carriers of TTR mutations and what methods (imaging or biomarkers) should be used to monitor disease progression, the timing of initiation of therapy in ATTRv carriers remains an area of uncertainty.

In contrast, in patients with advanced disease, treatment aimed at TTR stabilization is unlikely to be of significant benefit. Although the package label for tafamidis does not provide restrictions on administration, patients with NYHA class IV symptoms, minimally ambulatory patients (walk <100m on a 6-minute walk test), and those with advanced renal dysfunction.

Therapeutically Important Advantages/Disadvantages

- **Tegsedi:**
  - Weekly subcutaneous injection - only self-injectable product of the three available treatment options.
  - Available only through a restricted distribution program called the Tegsedi REMS Program from Accredo Specialty Pharmacy.
- **Vyndaqel and Vyndamax:**
  - Daily oral administration
  - Available exclusively throughout the state pharmacies because of a limited distribution program.
  - Vyndamax 61 mg is bioequivalent to the Vyndaqel 80 mg dose
    - Vyndaqel is the meglumine salt form of tafamidis and available as a 20mg capsule and therefore takes 4 capsules to make a daily dose.
    - Vyndamax is available as a 61mg capsule and therefore has 1 capsule to make a daily dose.

Clinical Studies

- **Tegsedi (NCT01737398)**
  - Randomized, double-blind, placebo-controlled, multicenter clinical trial in adult patients with polyneuropathy caused by hATTR amyloidosis. Participants were randomized to receive either Tegsedi 284 mg (N=113) or placebo (N=60) as a weekly subcutaneous injection for 65 weeks, with 3 doses administered during the first week of treatment.
  - The co-primary efficacy endpoints were the change from baseline to Week 66 in the modified Neuropathy Impairment Scale+7 (mNIS+7) composite score and the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score.
    - The mNIS+7 is an objective composite score and is a measure of neurologic impairment that evaluates muscle weakness, sensation, reflexes, nerve conduction, and autonomic function. The mNIS+7 Composite Score has a range of -22.32 to 346.32 and a higher mNIS+7 composite score indicates lower function.
      - The Norfolk QoL-DN patient- reported subjective score is a measure of physical function/large fiber neuropathy, symptoms, activities of daily living, small fiber neuropathy, and autonomic neuropathy. The Norfolk QoL-DN total score has a range of -4 to 136, and a higher Norfolk QoL-DN score indicates poorer quality of life. Both endpoints significantly favored Tegsedi.
  - The treatment arm of the pivotal trial had a higher proportion of serious adverse events and an adverse event that led to discontinuation, as well as death (1 drug-related) compared to placebo.
- **Vyndaqel (NCT01994889)**
  - The approval of Vyndaqel and Vyndamax was based on data from a 30-month multicenter, international, randomized, double-blind, placebo-controlled study of 441 patients with ATTR-CM caused by ATTRwt or hATTR-CM (Transthyretin

Amyloidosis Cardiomyopathy Clinical Trial (ATTR-ACT), NCT0199488). The phase 3 trial was done to determine efficacy, safety, and tolerability of Vyndaqel on clinical outcomes (i.e. all-cause mortality and frequency of cardiovascular-related hospitalizations) in subjects with either hATTR or ATTRwt resulting in ATTR-CM. Patients in the study received tafamidis 20 mg daily for 30 months, tafamidis 80 mg daily for 30 months or placebo for 30 months. In addition, patients had New York Heart Association (NYHA) classification I-III. Tafamidis was administered to 264 patients (pooled), and 177 patients received placebo.

- The primary outcome measure was the combination of all-cause mortality and frequency of cardiovascular-related hospitalizations.
  - Both of these endpoints significantly favored Vyndaqel
- Vyndaqel also showed significant improvement compared with placebo in patients' functional capacity and health status at six months and continuing through 30 months.
- Vyndaqel was well tolerated with an observed safety profile comparable to placebo.

Cost

Drug	Strength	Package Size	WAC Pkg Price	Cost/day*	Cost/month*	Cost/year*
Tegsedi	284 mg/1.5 mL	1.5 mL syringe	$6,117.86	$873.98	$26,219.40	$314,632.80
Vyndaqel	20 mg	120 capsules	$19,991.64	$666.39	$19,991.64	$239,899.68
Vyndamax	61 mg	1 blister pack, 30 capsules	$19,991.70	$666.39	$19,991.70	$239,900.40

*Based on lowest per unit WAC cost

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REVIEW OF AMYOTROPHIC LATERAL SCLEROSIS

Overview

Amyotrophic lateral sclerosis (ALS), also referred to as Lou Gehrig's disease, is a neurodegenerative disorder that affects upper and lower motor neurons. Initially, this begins with focal weakness then leads to muscle weakness over time. This disease is progressive and fatal, with most patients dying of respiratory failure within 2 to 5 years of onset. There are approximately 24,800 people with ALS in the United States. The average age of diagnosis is 55 to 65 years of age.

Place in Therapy/Guidelines

Currently, there are only two therapies approved for ALS.

- Rilutek – shown to slightly increase overall survival (2-3 months), but it has not been shown to have an effect on physical functioning
- Radicava – has not been shown to have an effect on overall survival, but it has shown to effect physical functioning. Early onset ALS patients (patients diagnosed with definite or probable ALS) were shown to have a greater magnitude of effect.

There are several agents in the pipeline with different mechanisms of action in late phase development for ALS. Two agents, however, Amylyx's AMXOO35 and Biogen/Ionis' Tofersen are under FDA review with decisions expected in September 2022 and January 2023, respectively.

FDA Approval

Rilutek: 505(b) New Drug Application (NDA) pathway, Type 1 - New Molecular Entity, PRIORITY; Orphan
Exservan: 505(b)(2) New Drug Application (NDA) pathway, Type 3 - New Dosage Form, STANDARD; Orphan
Tiglutik: 505(b)(2) New Drug Application (NDA) pathway, Type 3 - New Dosage Form, STANDARD; Orphan
Radicava: 505(b) New Drug Application (NDA) pathway, Type 1 - New Molecular Entity, STANDARD; Orphan
Radicava ORS: 505(b) New Drug Application (NDA) pathway, Type 3 - New Dosage Form, PRIORITY; Orphan

Place in Therapy

There are no treatments available that stop or significantly slow down the progression of ALS. Riluzole and Radicava are the only agents currently approved. These agents have been shown to only provide modest benefit. Riluzole is the only therapy found to impact survival, however.

Due to the limited agents available, treatment of ALS is focused on symptom management and palliative care.

Therapeutically Important Adverse Effects/Advantages

- **Rilutek, Exservan, and Tiglutik (riluzole):**
  - Mechanism of action: unknown for how it exerts its therapeutic effects in patients with ALS
  - Oral formulations (tablet, film, suspension) available only; tablets may be crushed and given via feeding tube, if necessary
  - Generic option available for tablet
  - Dosing: 50 mg PO BID
- **Radicava and Radicava ORS (edaravone):**
  - Mechanism of action: unknown for how it exerts its therapeutic effects in patients with ALS, but it is thought to work by eliminating oxygen-free radicals, which are responsible for nerve damage.
  - Available as an IV and oral formulation (suspension).
  - Initial dosing: 105 mg (5mL) PO daily for 14 days OR 60mg IV daily for 14 days, followed by 14 days dug free
  - Subsequent dosing: 105 mg (5mL) PO daily for 10 days of a 14-day period OR 60 mg IV daily for 10 days of a 14-day period, followed by 14 days drug free
  - Patients treated with 60 mg IV may be switched to 105 mg (5mL) oral suspension

Clinical Studies

- The global multi-center, open-label study MT-1186-A01, evaluated approximately 185 ALS patients across approximately 50 sites in the U.S., Canada, Europe and Japan over the course of 48 weeks of treatment. After a screening, study participants (18 to 75 years of age) received oral edaravone at a dose designed to deliver the therapeutic equivalent of the IV formulation of Radicava in 28-day cycles- once daily for 10 days in the first 14 days, followed by 14 days without treatment.
- The 24-week safety and tolerability results showed adverse events reported by ≥ 5% of subjects were muscular weakness, fatigue, back pain, constipation, headache, and dyspnea. 5.9% discontinued due to adverse events.
- Changes from baseline in participants' ALS functional rating scale-revised ALSFRS-R score to week 24 were evaluated. At the beginning of the study, patients had an average ALSFRS-R score of 40 (SD 4.5). At Week 24, the average change from baseline in ALSFRS-R score was -5.6 (95% CI -6.5 to -4.8).
- In addition to the current MT-1186-A01 Phase 3 study, an extension study, MT-1186-A03, is ongoing to explore patient safety after 96 weeks of edaravone administration. Changes in participants' ALSFRS-R scores and time until invasive breathing procedures or death also will be assessed.

Cost

Drug	Strength	Package Size	WAC Pkg Price	Cost/day*	Cost/month*	Cost/year*
Rilutek	50 mg tab	60 each	$3,076.80	$102.56	$3,076.80	$36,921.60
Exservan	50mg film	60 each	$3,142.80	$104.76	$3,142.80	$37,713.60
Tiglutik	50 mg/10 mL suspension	600 mL bottle	$3,510.00	$117.00	$3,510.00	$42,120.00
Riluzole (generic)	50 mg tab	60 each	$40.20	$1.34	$40.20	$482.40
Radicava	30 mg/100 mL IV	100 mL bag	$612.00	$421.60	$12,648.00	$151,776.00
Radicava ORS	105 mg/5 mL suspension	50 mL bottle	$12,719.50	$438.12	$13,143.48	$157,721.80

*Based on lowest per unit WAC cost

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REVIEW OF CHELATING AGENTS

Overview

Chelating agents are utilized for reducing the amount of harmful heavy metals found in the blood and tissue. These agents are generally classified by which metal they target. The most common target metals include iron, copper, mercury, and lead. Some chelating agents have a high degree of specificity for a particular target metal, while others may target multiple metals.

Place in Therapy/Guidelines

Management of excessive heavy metal accumulation or poisoning is highly dependent on avoiding or eliminating the source of exposure. Chelating agents are used in conjunction with avoiding the source and have been found to be very effective.

- **Iron chelating agents:** deferoxamine (IV), deferasirox (PO), and deferiprone (PO)
- **Copper chelating agents:** penicillamine (PO), trientine (PO), and dimercaprol (IV)
    - These agents are used in the treatment of Wilson's disease
    - Dimercaprol is also effective in lowering arsenic and mercury levels
- **Lead and other heavy metals:** succimer (dimercaptonol) (PO), dimercaprol (BAL) (IV), and ethylenediaminetetraacetic acid (EDTA) (IV)
    - Succimer appears to be more effective and better tolerated than other agents
    - These agents can also be used for lowering arsenic, mercury, and cadmium levels

FDA Approval

Ferriprox tablet: 505(b) New Drug Application (NDA) pathway, Type 1 - New Molecular Entity, STANDARD; Orphan
Ferriprox solution: 505(b) New Drug Application (NDA) pathway, Type 3 – New Dosage Form, STANDARD; Orphan
Ferriprox BID tablet: 505(b) New Drug Application (NDA) pathway, Type 5 – New Formulation or New Manufacturer, STANDARD; Orphan

Therapeutically Important Adverse Effects/Advantages

- **Ferriprox (deferiprone):**
    - Mechanism of action: binds with ferric ions to form neutral 3:1 (deferiprone:iron) complexes that are stable over a large range of pH values. This binding affinity is lower for other metals (zinc and copper) than for iron.
    - Absolute neutrophil count, ALT, and zinc levels must be tested at baseline and monitored through treatment. Weekly white blood cell counts are recommended.
    - Black box warning: Agranulocytosis and Neutropenia
    - ADULT dosing for transfusion hemosiderosis, With thalassemia syndrome, sickle cell disease or other anemias:
        - (1000-mg tablet, 3-times-daily regimen) Initial, 75 mg/kg/day (actual body weight) orally in 3 divided doses
        - (500-mg tablet, 3-times-daily regimen) Initial, 75 mg/kg/day (actual body weight) orally in 3 divided doses
        - (100 mg/mL oral solution) Initial, 25 mg/kg (actual body weight) orally 3 times per day for a total of 75 mg/kg/day
        - (Ferriprox (R) Twice-a-Day, 1000-mg tablet) Initial, 75 mg/kg/day (actual body weight) orally in 2 divided doses per day, taken approximately 12 hours apart, with food
        - Maintenance, adjust dosage to individual patient response and therapeutic goals (maintenance or reduction of body iron burden); MAX 99 mg/kg/day in divided doses
    - PEDIATRIC dosing for transfusion hemosiderosis, With thalassemia syndrome, sickle cell disease or other anemias:
        - (1000-mg tablet, 3-times-daily regimen; 8 years or older) Initial, 75 mg/kg/day (actual body weight) orally in 3 divided doses
        - (500-mg tablet, 3-times-daily regimen; 8 years or older) Initial, 75 mg/kg/day (actual body weight) orally in 3 divided doses
        - (100 mg/mL oral solution; 3 years or older) Initial, 25 mg/kg (actual body weight) orally 3 times per day for a total of 75 mg/kg/day

- (Ferriprox (R) Twice-a-Day, 1000-mg tablet; 8 years or older) Initial, 75 mg/kg/day (actual body weight) orally in 2 divided doses, taken approximately 12 hours apart, with food
- Maintenance, adjust dosage to individual patient response and therapeutic goals (maintenance or reduction of body iron burden); MAX 99 mg/kg/day in divided doses

Clinical Studies

- Transfusional Iron Overload in Patients with Thalassemia Syndromes
  - A prospective, planned, pooled analysis of patients with thalassemia syndromes from several studies
  - Efficacy of deferiprone was assessed in transfusion-dependent iron overload patients in whom previous iron chelation therapy had failed or was considered inadequate due to poor tolerance
  - Deferiprone therapy (35-99 mg/kg/day) was considered successful in individual patients who experienced a ≥ 20% decline in serum ferritin within one year of starting therapy.
  - Data from a total of 236 patients were analyzed. Of the 224 patients with thalassemia who received deferiprone monotherapy and were eligible for serum ferritin analysis, 105 (47%) were male and 119 (53%) were female. The mean age of these patients was 18.2 years (range 2 to 62; 91 patients were <17).
  - For the patients in the analysis, the endpoint of at least a 20% reduction in serum ferritin was met in 50% (of 236 subjects), with a 95% confidence interval of 43% to 57%.
- Efficacy and Safety of Ferriprox® in Patients With Sickle Cell Disease or Other Anemias (FIRST) NCT02041299
  - An actively-controlled non-inferiority study compared the efficacy of FERRIPROX to that of deferoxamine in patients with sickle cell disease and other transfusion-dependent anemias by evaluating liver iron concentration (LIC)
  - The efficacy of FERRIPROX was established based upon the change in LIC from baseline after 12 months of FERRIPROX (75 or 99 mg/kg/day) compared to deferoxamine (20 or 40 mg/kg (pediatric patients); 40 or 50 mg/kg (adult patients)).
  - Among the 152 FERRIPROX treated patients, the mean age was 16.9; 54.6% were male; 78.9% were White, 15.1% were Black, and 5.9% were Multi-racial
  - Over 12 months, the Least Squares estimate of mean decrease from baseline in LIC was 4.13 ± 0.50 mg/g dw for FERRIPROX and 4.38 ± 0.59 mg/g dw for deferoxamine, and the non-inferiority criterion was met.

Cost

Drug	Strength	Package Size	WAC Pkg Price	Cost/day*	Cost/month*	Cost/year*
Ferriprox	100 mg/mL; 500 mg; 1,000 mg; 1,000 mg BID	500 mL solution; 100 tab; 50 tab	$7,650; $7,649; $7,648.50; $9,741	$1,071; $803.15; $803.10; $1,022.81	$32,130; $24,094.50; $24,093; $30,684.30	$385,560; $289,134; $289,116; $368,211.60
Deferiprone (generic)	500 mg; 1,000 mg	100 tab; 50 tab	$6,148.00; $6,975.50	$645.54; $732.43	$19,366.20; $21,972.90	$232,394.40; $263,674.80

*Based on lowest per unit WAC cost

References:
1. Ferriprox (deferiprone) 500 mg tablets [prescribing information]. Cary, NC: Chiesi USA Inc; November 2021.
2. Ferriprox (deferiprone) oral solution [prescribing information]. Cary, NC: Chiesi USA Inc; November 2021.
3. Ferriprox (deferiprone) 1,000 mg tablets [prescribing information]. Cary, NC: Chiesi USA Inc; November 2021.
4. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Chelating Agents. [Updated 2017 Jan 23]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK548531/

5. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Deferiprone. [Updated 2017 Dec 27]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK548086/
6. Kwiatkowski JL, Hamdy M, El-Beshlawy A, Ebeid FSE, Badr M, Alshehri A, Kanter J, Inusa B, Adly AAM, Williams S, Kilinc Y, Lee D, Tricta F, Elalfy MS. Deferiprone vs deferoxamine for transfusional iron overload in SCD and other anemias: a randomized, open-label noninferiority study. Blood Adv. 2022 Feb 22;6(4):1243-1254. doi: 10.1182/bloodadvances.2021004938. PMID: 34847228; PMCID: PMC8864642.

RSV Discussion

American Academy of Pediatrics Recommendations:

Following the institution of nonpharmacologic interventions (eg, masking, social distancing) for the prevention of COVID-19 in March of 2020, the number of RSV infections in the United States decreased rapidly and dramatically. Interactions between SARS-CoV-2 and other respiratory viruses also may have altered RSV epidemiology. RSV activity in the United States remained very low through the traditional 2020-2021 fall-winter season but increased in the spring of 2021, with numbers of cases rising to a level similar to a fall-winter season throughout the different regions of the United States and continuing over the spring, summer, and fall. This interseasonal activity was a marked deviation from the typical RSV seasonal epidemiology and was not generally followed by a second wave of increased RSV circulation in the winter.

Currently, RSV activity in the United States remains variable by region but is increasing in some parts of the country. The Centers for Disease Control and Prevention (CDC) monitors RSV activity in the United States in collaboration with state and county health departments and commercial and clinical laboratories. These data are available from the National Respiratory and Enteric Virus Surveillance System (NREVSS)

With the shift in seasonality noted in 2021 and the current regional rise in interseason RSV cases, the AAP continues to support the use of palivizumab in eligible infants in any region experiencing rates of RSV activity at any time in 2022 similar to a typical fall-winter season. The AAP recommends initiating the standard administration of palivizumab, which consists of 5 consecutive monthly doses. This regimen provides serum levels associated with protection for 6 months, the length of a typical RSV season.

Reference:

American Academy of Pediatrics. Updated Guidance: Use of Palivizumab Prophylaxis to Prevent Hospitalization From Severe Respiratory Syncytial Virus Infection During the 2022-2023 RSV Season. American Academy of Pediatrics; July 2022. Available at: https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/interim-guidance-for-use-of-palivizumab-prophylaxis-to-prevent-hospitalization/

Category Criteria: *Approval Duration = 5 weight-based doses within 6 months. No further prior authorization approvals will be given following season offset.*

Respiratory Syncytial Virus (RSV) Season defined as onset (1st of 2 consecutive weeks when percentage of PCR tests positive for RSV is > 3% and offset (Last of 2 consecutive weeks when percentage of PCR tests positive for RSV is < 3%) as reported by The National Respiratory and Enteric Virus Surveillance System (NREVSS) Midwest Region
RSV Regional Trends - NREVSS | CDC

The Midwest region contains:
ND, MN, SD, NE, KS, IA, MO, WI, IL, MI, IN, OH

CDC Seasonal Data:
New methodology: Orange - Start Date (6/29/2021) and End Date (12/25/2021)
Old methodology: Green - Start Date (10/19/2021) and End date (04/21/2022)

Week	Date	PCR %	Week	Date	PCR %
38	05/01/21	0.528	72	12/25/21	2.446
39	05/08/21	0.772	73	01/01/22	2.250
40	05/15/21	1.027	74	01/08/22	2.040
41	05/22/21	1.570	75	01/15/22	1.568
42	05/29/21	1.957	76	01/22/22	1.482
43	06/05/21	3.008	77	01/29/22	1.215
44	06/12/21	2.851	78	02/05/22	1.139
45	06/19/21	3.644	79	02/12/22	1.291
46	06/26/21	5.911	80	02/19/22	1.143
47	07/03/21	5.670	81	02/26/22	1.052
48	07/10/21	8.358	82	03/05/22	1.037
49	07/17/21	9.324	83	03/12/22	1.095
50	07/24/21	13.525	84	03/19/22	1.130
51	07/31/21	15.945	85	03/26/22	0.941
52	08/07/21	16.661	86	04/02/22	1.059
53	08/14/21	16.226	87	04/09/22	0.854
54	08/21/21	21.921	88	04/16/22	1.192
55	08/28/21	20.783	89	04/23/22	0.936
56	09/04/21	20.548	90	04/30/22	1.119
57	09/11/21	19.446	91	05/07/22	0.873
58	09/18/21	18.233	92	05/14/22	1.214
59	09/25/21	18.413	93	05/21/22	1.223
60	10/02/21	18.213	94	05/28/22	1.350
61	10/09/21	17.660	95	06/04/22	1.797
62	10/16/21	16.468	96	06/11/22	1.827
63	10/23/21	15.765	97	06/18/22	1.950
64	10/30/21	14.583	98	06/25/22	2.224
65	11/06/21	11.779	99	07/02/22	2.230
66	11/13/21	10.022	100	07/09/22	2.034
67	11/20/21	7.224	101	07/16/22	2.182
68	11/27/21	5.229	102	07/23/22	1.984
69	12/04/21	5.625	103	07/30/22	2.151
70	12/11/21	3.822	104	08/06/22	2.740
71	12/18/21	2.669			

New Template:

PRESCRIBER RESPONSE: *Please fax it to 866-798-4904 when completed.*

All information used to generate the enclosed letter, including Prescriber identification, was obtained from Pharmacy Claims Data. If there appears to be an error in the information provided, please note the discrepancy. Thank you for your cooperation.

Is this patient under your care
_____Yes
_____ No, but has been in the past
_____ No, I provide ER / urgent care services or provided coverage for a colleague
_____ No, never

Did you do anything with this information?

_____Yes, what action did you take? _____

_____No, why not? _____

Did you find this information useful?
_____Yes
_____No

Please explain how this information was useful/not useful or other information that you would consider useful:

Previous Template:

PRESCRIBER RESPONSE: *Please fax it to 866-798-4904 when completed.*

All information used to generate the enclosed letter, including Prescriber identification, was obtained from Pharmacy Claims Data. If there appears to be an error in the information provided, please note the discrepancy. Thank you for your cooperation.

1. This patient **is** under my care:

_____ I have reviewed the information and will continue without change.
_____ however, I did not prescribe the following medication(s)_____.
_____ and has an appointment to discuss drug therapy.
_____ however, has not seen me recently.
_____ however, I was not aware of other prescribers.
_____ I have reviewed the information and modified drug therapy.
_____ I have not modified drug therapy because benefits outweigh the risks.
_____ I have tried to modify therapy, however the patient refuses to change.
_____ I have tried to modify therapy, however symptoms reoccurred.

2. This patient **is not** under my care:

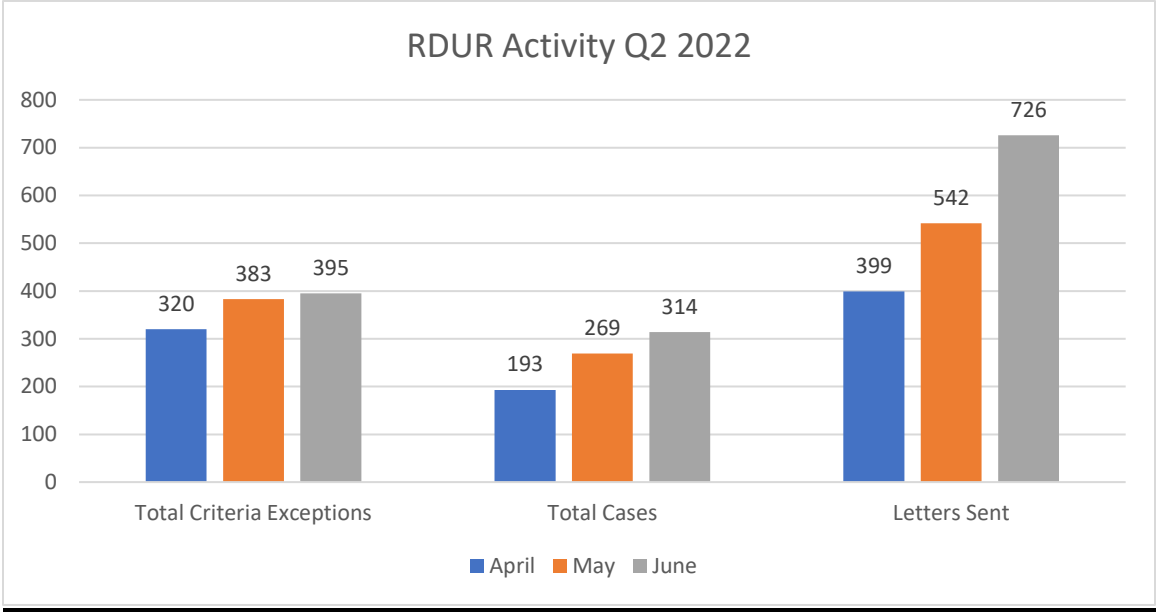
_____ however, I did prescribe medication while covering for other MD or in the ER.
_____ but has previously been a patient of mine.
_____ because the patient recently expired.
_____ and has never been under my care.

3. I have reviewed the enclosed information and found it:
_____ very useful_____ useful_____ neutral_____ somewhat useful_____ not useful.

4. Please check here if you wish to receive reference information on the identified problem___. (Please provide a fax number if available_____-_____-_____.)

Comments: _____
_____
_____
_____
If you would like to receive additional updates about the ND Medicaid pharmacy program by email, please provide your email address: _____

RDUR Activity Overview: Q2 2022



April Cases by Type of Criteria

Criteria Description	# of Cases	% of Cases
DRUG-DRUG INTERACTIONS	2	1.04%
DRUG-DISEASE INTERACTIONS	12	6.22%
INAPPROPRIATE PEDIATRIC THERAPY	27	13.99%
OVERUTILIZATION	40	20.73%
UNDERUTILIZATION	112	58.03%

DRUG-DRUG INTERATIONS: DUAL P-GP & 3A4 INHIBITION
DRUG-DISEASE INTERACTIONS: STATINS/NIACIN/FIBRIC ACID & HEPATIC IMPAIRMENT, NSAIDS & CV PROBLEMS
OVERUTILIZATION: SEDATIVE AGENTS
UNDERUTILIZATION: LONG-TERM ASTHMA CONTROLLERS, PIOGLITAZONE, METFORMIN IR/XR

May Cases by Type of Criteria

Criteria Description	# of Cases	% of Cases
DRUG-DISEASE INTERACTIONS	196	72.86%
DRUG-DRUG INTERACTION	58	21.56%
UNDERUTILIZATION	15	5.58%

DRUG-DISEASE INTERACTIONS: CYCLOBENZAPRINE & ARRHYTHMIAS, ZOPIDEM/SULFONYLUREA & HYPERKALEMIA, OLANZAPINE/MIRTAZAPINE & NARROW ANGLE GLAUCOMA
DRUG-DRUG INTERACTIONS: CETIRIZINE & CHLOROQUINE, ESCITALOPRAM/CITALOPRAM/FLUOXETINE/FLUVOXAMINE/PAROXETINE/SERTRALINE & PIMOZIDE
UNDERUTILIZATION: VENLAFAXINE IR/ER

June Cases by Type of Criteria

Criteria Description	# of Cases	% of Cases
ATYPICAL NEUROLEPTICS AND METABOLIC EFFECTS	10	3.18%
BISPHOSPHONATE ADE	11	3.50%
CONTRACEPTION & NICOTINE DEPENDENCE	4	1.27%
DRUG-DISEASE INTERACTION	4	1.27%
MODAFINIL AND NARCOTIC USE	1	0.32%
OVERUTILIZATION	13	4.14%
SUPPORT ACT CRITERIA	136	43.32%
TIZANIDINE TOXICITY	4	1.27%
UNDERUTILIZATION	131	41.72%

DRUG-DISEASE INTERACTIONS: ROSUVASTATIN & RENAL IMPAIRMENT, OXYBUTYNIN & URINARY RETENTION
OVERUTILIZATION: AFORMOTERAL, PREGABALIN, DESVENLAFAXINE
UNDERUTILIZATION: CLOZAPINE, OLANZAPINE, RISPERIDONE, ZIPRASIDONE, ARIPIPRAZOLE, QUETIAPINE, CHLORPROMAZINE, ARBS, DULOXETINE, DARUNAVIR, TRUVADA, ZIDOVUDINE, DESVENLAFAXINE, TIOTROPIUM/OLODATEROL, EMPAGLIFLOZIN/METFORMIN

NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
3RD QUARTER 2022

Criteria Recommendations ***Approved Rejected***

1. Daridorexant / Overuse _____ _____

Alert Message: Quviviq (daridorexant) may be over-utilized. The recommended dosage range is 25 mg to 50 mg of daridorexant taken orally no more than once per night within 30 minutes of going to bed (with at least 7 hours remaining prior to planned awakening).

Drugs/Diseases

Util A	Util B	Util C (Negating)
Daridorexant		Hepatic Impairment

Max Dose: 50 mg/day

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Quviviq Prescribing Information, April 2022, Idorsia Pharmaceuticals Ltd.

2. Daridorexant / Overuse – Hepatic Impairment _____ _____

Alert Message: Quviviq (daridorexant) may be over-utilized. The maximum recommended dosage in patients with moderate hepatic impairment (Child-Pugh score 7–9) is 25 mg of daridorexant no more than once per night. Moderate hepatic impairment may increase daridorexant systemic exposure to a clinically relevant extent, which may increase the frequency or severity of adverse reactions.

Drugs/Diseases

Util A	Util B	Util C
Daridorexant	Hepatic Impairment	

Max Dose: 25 mg/day

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Quviviq Prescribing Information, April 2022, Idorsia Pharmaceuticals Ltd.

3. Daridorexant / Severe Hepatic Impairment _____ _____

Alert Message: Quviviq (daridorexant) is not recommended in patients with severe hepatic impairment (Child-Pugh score ≥ 10). Daridorexant has not been studied in this patient population.

Drugs/Diseases

Util A	Util B	Util C
Daridorexant	Cirrhosis Liver Failure	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Quviviq Prescribing Information, April 2022, Idorsia Pharmaceuticals Ltd.

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

4. Daridorexant / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of Quviviq (daridorexant) have not been established in pediatric patients.

Drugs/Diseases
Util A Util B Util C
Daridorexant

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Quviviq Prescribing Information, April 2022, Idorsia Pharmaceuticals Ltd.

5. Daridorexant / Narcolepsy _____ _____
Alert Message: Quviviq (daridorexant) is contraindicated in patients with narcolepsy.

Drugs/Diseases
Util A Util B Util C
Daridorexant Narcolepsy

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Quviviq Prescribing Information, April 2022, Idorsia Pharmaceuticals Ltd.

6. Daridorexant / Therapeutic Appropriateness - Duration _____ _____
Alert Message: Because sleep disturbances may be the presenting manifestation of a medical and/or psychiatric disorder, treatment of insomnia should be initiated only after careful evaluation of the patient. The failure of insomnia to remit after 7 to 10 days of treatment may indicate the presence of a primary psychiatric and/or medical illness that should be evaluated. Worsening of insomnia or the emergence of new cognitive or behavioral abnormalities may be the result of an unrecognized underlying psychiatric or medical disorder and can emerge during the course of treatment with sleep-promoting drugs such as Quviviq (daridorexant).

Drugs/Diseases
Util A Util B Util C
Daridorexant

Day Supply: > 10 days

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Quviviq Prescribing Information, April 2022, Idorsia Pharmaceuticals Ltd.

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

7. Daridorexant / Complex Sleep Behavior _____ _____

Alert Message: Complex sleep behaviors, including sleepwalking, sleep-driving, and engaging in other activities while not fully awake (e.g., preparing and eating food, making phone calls, having sex), have been reported to occur with the use of hypnotics, including orexin receptor antagonists such as Quviviq (daridorexant). These events can occur in hypnotic-naïve as well as in hypnotic-experienced persons. Discontinue daridorexant immediately if a patient experiences a complex sleep behavior.

Drugs/Diseases

Util A	Util B	Util C
Daridorexant	Other Sleep Disorders	
	Sleepwalking	
	Parasomnia	

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Quviviq Prescribing Information, April 2022, Idorsia Pharmaceuticals Ltd.

8. Daridorexant / Depression & Suicidality _____ _____

Alert Message: As with other hypnotics, Quviviq (daridorexant) should be administered with caution in patients exhibiting symptoms of depression. Worsening of depression or suicidal ideation may occur. Patients with psychiatric disorders, including insomnia, are at increased risk of suicide. In primarily depressed patients treated with hypnotics, worsening of depression and suicidal thoughts and actions (including completed suicides) have been reported.

Drugs/Diseases

Util A	Util B	Util C
Daridorexant	Depression	
	Suicidal Ideation	

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Quviviq Prescribing Information, April 2022, Idorsia Pharmaceuticals Ltd.

9. Daridorexant / Compromised Respiratory Function _____ _____

Alert Message: The effects of Quviviq (daridorexant) on respiratory function should be considered if prescribed to patients with compromised respiratory function. Daridorexant has not been studied in patients with moderate OSA requiring CPAP or severe OSA. Daridorexant has not been studied in patients with severe COPD.

Drugs/Diseases

Util A	Util B	Util C
Daridorexant	COPD	
	Obstructive Sleep Apnea	

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Quviviq Prescribing Information, April 2022, Idorsia Pharmaceuticals Ltd.

10. Daridorexant / Strong CYP3A4 Inhibitors _____ _____

Alert Message: The concurrent use of Quviviq (daridorexant) with a strong CYP3A4 inhibitor is not recommended. Daridorexant is a CYP3A4 substrate, and concomitant use with a strong 3A4 inhibitor has been shown to significantly increase exposure to daridorexant, increasing the risk of daridorexant-related adverse reactions.

Drugs/Diseases

Util A	Util B		Util C
Daridorexant	Clarithromycin	Nelfinavir	
	Cobicistat	Posaconazole	
	Indinavir	Ritonavir	
	Itraconazole	Saquinavir	
	Ketoconazole	Voriconazole	
	Nefazodone		

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Quviviq Prescribing Information, April 2022, Idorsia Pharmaceuticals Ltd.

11. Daridorexant / Moderate CYP3A4 Inhibitors _____ _____

Alert Message: Concomitant use with Quviviq (daridorexant) with a moderate CYP3A4 inhibitor increases exposure to daridorexant, which may increase the risk of daridorexant-related adverse reactions. The recommended dose of daridorexant is 25 mg when used with a moderate CYP3A4 inhibitor.

Drugs/Diseases

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

Max Dose: 25 mg/day

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Quviviq Prescribing Information, April 2022, Idorsia Pharmaceuticals Ltd.

12. Daridorexant / Strong to Moderate CYP3A4 Inducers _____ _____

Alert Message: Concomitant use of Quviviq (daridorexant) with a strong or moderate CYP3A4 inducer decreases exposure to daridorexant, which may reduce the efficacy of daridorexant. Concomitant use of daridorexant with a strong or moderate inducer of CYP3A4 is not recommended.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Quviviq Prescribing Information, April 2022, Idorsia Pharmaceuticals Ltd.

13. Daridorexant / CNS Depressants _____ _____

Alert Message: Concomitant use of alcohol or other CNS depressants with Quviviq (daridorexant) may lead to additive impairment of psychomotor performance and risk of CNS depression. Use daridorexant with caution in patients receiving CNS depressants. Consider dose adjustment of daridorexant and/or the CNS depressant(s) if used concomitantly. Avoid alcohol consumption with daridorexant.

Drugs/Diseases

Util A	Util B	Util C
Daridorexant	CNS Depressants	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Quviviq Prescribing Information, April 2022, Idorsia Pharmaceuticals Ltd.

14. Daridorexant / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no available data on Quviviq (daridorexant) use in pregnant women to evaluate for drug-associated risks of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. There will be a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to daridorexant during pregnancy. Pregnant women exposed to daridorexant and their healthcare providers are encouraged to call and register with Idorsia Pharmaceuticals Ltd.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Quviviq Prescribing Information, April 2022, Idorsia Pharmaceuticals Ltd.

15. Daridorexant / Therapeutic Appropriateness _____ _____

Alert Message: There are no data on the presence of Quviviq (daridorexant) in human milk, the effects on the breastfed infant, or the effects on milk production. Daridorexant and its metabolites were present in the milk of lactating rats. When a drug is present in animal milk, it is likely that the drug will be present in human milk. Infants exposed to daridorexant through breastmilk should be monitored for excessive sedation. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for daridorexant and any potential adverse effects on the breastfed infant from daridorexant or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Daridorexant	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Quviviq Prescribing Information, April 2022, Idorsia Pharmaceuticals Ltd.

16. Tezepelumab-ekko / Overuse _____ _____
Alert Message: Tezspire (tezepelumab-ekko) may be over-utilized. The recommended dosage of tezepelumab-ekko is 210 mg administered subcutaneously, once every 4 weeks.

Drugs/Diseases

Util A	Util B	Util C
Tezepelumab-ekko		

Max Dose: 210 mg q 4 weeks

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Tezspire Prescribing Information, Dec. 2021, AstraZeneca.

17. Tezepelumab-ekko / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of Tezspire (tezepelumab-ekko) in patients younger than 12 years of age have not been established.

Drugs/Diseases

Util A	Util B	Util C
Tezepelumab-ekko		

Age Range: 0 – 11 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Tezspire Prescribing Information, Dec. 2021, AstraZeneca.

18. Tezepelumab-ekko / Corticosteroids _____ _____
Alert Message: Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy with Tezspire (tezepelumab-ekko). Reductions in corticosteroid dose, if appropriate, should be gradual and performed under the direct supervision of a physician. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

Drugs/Diseases

Util A	Util B	Util C
Tezepelumab-ekko	Corticosteroids	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Tezspire Prescribing Information, Dec. 2021, AstraZeneca.

19. Tezepelumab-ekko / Helminth Infections _____ _____

Alert Message: Treat patients with pre-existing helminth infections before initiating therapy with Tezspire (tezepelumab-ekko). If patients become infected while receiving treatment with tezepelumab-ekko and do not respond to anti-helminth treatment, discontinue treatment with tezepelumab-ekko until the infection resolves.

Drugs/Diseases

Util A	Util B	Util C
Tezepelumab-ekko	Helminth Infection	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Tezspire Prescribing Information, Dec. 2021, AstraZeneca.

20. Tezepelumab-ekko / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no available data on Tezspire (tezepelumab-ekko) use in pregnant women to evaluate for any drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Placental transfer of monoclonal antibodies such as tezepelumab-ekko is greater during the third trimester of pregnancy; therefore, potential effects on a fetus are likely to be greater during the third trimester of pregnancy.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Tezepelumab-ekko	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Tezspire Prescribing Information, Dec. 2021, AstraZeneca.

21. Tezepelumab-ekko / Lactation _____ _____

Alert Message: There is no information regarding the presence of Tezspire (tezepelumab-ekko) in human milk, its effects on the breastfed infant, or its effects on milk production. However, tezepelumab-ekko is a human monoclonal antibody immunoglobulin (IgG2 lambda), and immunoglobulin G (IgG) is present in human milk in small amounts. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for tezepelumab-ekko and any potential adverse effects on the breastfed infant from tezepelumab-ekko or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Tezepelumab-ekko	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Tezspire Prescribing Information, Dec. 2021, AstraZeneca.

22. Tezepelumab-ekko / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be underutilizing Tezspire (tezepelumab-ekko). 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
Tezepelumab-ekko		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Enel J Med 2005; 353:487- 497.
Murphy AC, Proeschal A, Brightling CE, et al. The Relationship Between Clinical Outcomes and Medication Adherence in difficult-to-control Asthma. Thorax. 2012;67:751-753.
Lindsay JT, Heaney LG. Nonadherence in Difficult Asthma - Facts, Myths, and a Time to Act. Patient Prefer Adherence. 2013;7:329-336. Published 2013 Apr 19. doi:10.2147/PPA.S38208

23. Baclofen Oral Solution / Overuse _____ _____

Alert Message: Ozobax (baclofen oral solution) may be over-utilized. The maximum recommended dose of baclofen oral solution is 80 mg daily (20 mg four times a day).

Drugs/Diseases

Util A	Util B	Util C
Baclofen Oral Solution		

Max Dose: 80 mg/day

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Ozobax Prescribing Information, Sept. 2019, Metacel Pharmaceuticals, LLC.

24. Baclofen Oral Solution / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Ozobax (baclofen oral solution) in pediatric patients below the age of 12 years have not been established.

Drugs/Diseases

Util A	Util B	Util C
Baclofen Oral Solution		

Age Range: 0 – 11 yoa

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Ozobax Prescribing Information, Sept. 2019, Metacel Pharmaceuticals, LLC.

25. Baclofen Oral Solution / Renal Impairment _____ _____

Alert Message: Because baclofen is primarily excreted unchanged by the kidneys, Ozobax (baclofen oral solution) should be used with caution in patients with renal impairment. Dosage reduction may be necessary for patients with renal impairment.

Drugs/Diseases

Util A	Util B	Util C
Baclofen Oral Solution	Renal Impairment	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Ozobax Prescribing Information, Sept. 2019, Metacel Pharmaceuticals, LLC.

26. Baclofen Oral Solution / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no adequate data on the risk of major birth defects, miscarriages, or other maternal adverse outcomes associated with the use of Ozobax (baclofen oral solution) in pregnant women. There are adverse effects on fetal outcomes associated with withdrawal from baclofen after delivery.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Baclofen Oral Solution	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Ozobax Prescribing Information, Sept. 2019, Metacel Pharmaceuticals, LLC.

27. Baclofen Oral Solution / Lactation _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Baclofen Oral Solution	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Ozobax Prescribing Information, Sept. 2019, Metacel Pharmaceuticals, LLC.

Criteria Recommendations	*Approved*	*Rejected*

28. Baricitinib / Overutilization _____ _____

Alert Message: The maximum recommended dose of Olumiant (baricitinib) for the treatment of alopecia areata is 4 mg per day.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Baricitinib		Strong OAT3 Inhibitors CKD Stage 3, 4, 5 ESRD Dialysis Rheumatoid Arthritis

Max Dose: 4 mg/day

References:

Olumiant Prescribing Information, June 2022, Eli Lilly and Company.

29. Baricitinib / OAT3 Inhibitors / Alopecia Areata _____ _____

Alert Message: The recommended dose of Olumiant (baricitinib) in patients with alopecia areata taking strong organic anion transporter 3 (OAT3) inhibitors is 2 mg once daily (half the maximum recommended dose of 4 mg). Baricitinib is an OAT3 substrate, and concurrent use with a strong inhibitor of OAT3 inhibitor may result in increased baricitinib exposure.

Drugs/Diseases

Util A	Util B	Util C (Include)
Baricitinib	Probenecid Teriflunomide Leflunomide	Alopecia Areata

Max Dose: 2 mg/day

References:

Olumiant Prescribing Information, June 2022, Eli Lilly and Company.

30. Baricitinib / Renal Impairment / Alopecia Areata _____ _____

Alert Message: Olumiant (baricitinib) may be over-utilized. The recommended maximum dose of baricitinib in patients with alopecia areata with moderate renal impairment (estimated glomerular filtration rate (GFR) between 30 and 60 mL/min/1.73 m2) is 2 mg once daily. Baricitinib is not recommended for use in patients with alopecia areata and severe renal impairment (estimated GFR of less than 30 mL/min/1.73 m2).

Drugs/Diseases

Util A	Util B	Util C (Included)
Baricitinib	CKD 3	Alopecia areata

References:

Olumiant Prescribing Information, June 2022, Eli Lilly and Company.

31. Baricitinib / Myocardial Infarction & Stoke _____ _____

Alert Message: Olumiant (baricitinib), a Janus kinase inhibitor (JAK), should be discontinued in patients that have experienced a myocardial infarction or stroke. In a postmarketing safety study, RA patients ≥50 years of age with ≥1 cardiovascular risk factor treated with another JAK inhibitor, a higher rate of major adverse cardiovascular events (defined as cardiovascular death, myocardial infarction, and stroke) was observed when compared with TNF blockers. Patients who are current or past smokers are at additional increased risk.

Drugs/Diseases

Util A	Util B	Util C
Baricitinib	Myocardial Infarction	
	Stroke	

References:

Olumiant Prescribing Information, June 2022, Eli Lilly and Company.

32. GLP-1 Receptor Agonists / Gallbladder Disease _____ _____

Alert Message: Acute events of gallbladder disease such as cholelithiasis or cholecystitis have been reported in GLP-1 receptor agonist trials and postmarketing. If cholelithiasis is suspected, gallbladder studies and appropriate clinical follow-up are indicated.

Drugs/Diseases

Util A	Util B	Util C
Albiglutide	Cholelithiasis	
Dulaglutide	Biliary Colic	
Exenatide	Cholecystitis	
Liraglutide		
Lixisenatide		
Semaglutide		

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Facts & Comparison, 2022, Wolters Kluwer Health.

33. Metoclopramide Nasal Spray / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Gimoti (metoclopramide) in pediatric patients have not been established. Metoclopramide is not recommended for use in pediatric patients due to the risk of tardive dyskinesia (TD) and other extrapyramidal symptoms, as well as the risk of methemoglobinemia in neonates. Dystonias and other extrapyramidal symptoms associated with metoclopramide are more common in pediatric patients than in adults.

Drugs/Diseases

Util A	Util B	Util C
Metoclopramide Nasal		

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gimoti Prescribing Information, Jan. 2021, Evoke Pharma, Inc.

34. Metoclopramide Nasal Spray / Tardive Dyskinesia (Black Box) _____ _____

Alert Message: Gimoti (metoclopramide) is contraindicated in patients with a history of tardive dyskinesia (TS) or a dystonic reaction to metoclopramide. Metoclopramide can cause tardive dyskinesia (TD), a syndrome of potentially irreversible and disfiguring involuntary movements. The risk of developing TD and the likelihood that TD will become irreversible increases with duration of treatment and total cumulative dosage. Additionally, the risk of developing TD is increased among the elderly, especially elderly women, and in patients with diabetes mellitus. Due to the risk of developing TD, avoid treatment with metoclopramide for longer than 12 weeks. Metoclopramide is not recommended in geriatric patients as initial therapy.

Drugs/Diseases

Util A	Util B	Util C (Include)
Metoclopramide Nasal		Tardive Dyskinesia

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gimoti Prescribing Information, Jan. 2021, Evoke Pharma, Inc.

35. Metoclopramide Nasal Spray / Gastrointestinal Motility Issues _____ _____

Alert Message: Gimoti (metoclopramide) is contraindicated in patients with conditions where stimulation of gastrointestinal motility might be dangerous (e.g., in the presence of gastrointestinal hemorrhage, mechanical obstruction, or perforation).

Drugs/Diseases

Util A	Util B	Util C (Include)
Metoclopramide Nasal		GI Hemorrhage
		GI Obstruction
		GI Perforation

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gimoti Prescribing Information, Jan. 2021, Evoke Pharma, Inc.

36. Metoclopramide Nasal Spray / Pheochromocytoma _____ _____

Alert Message: Gimoti (metoclopramide) is contraindicated In patients with pheochromocytoma or other catecholamine-releasing paragangliomas. Metoclopramide may cause a hypertensive/pheochromocytoma crisis, probably due to the release of catecholamines from the tumor.

Drugs/Diseases

Util A	Util B	Util C (Include)
Metoclopramide Nasal		Pheochromocytoma

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gimoti Prescribing Information, Jan. 2021, Evoke Pharma, Inc.

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

37. Metoclopramide Nasal Spray / Epilepsy _____ _____
Alert Message: Gimoti (metoclopramide) is contraindicated in patients with epilepsy. Metoclopramide may increase the frequency and severity of seizures.

Drugs/Diseases

Util A	Util B	Util C (Include)
Metoclopramide Nasal		Epilepsy

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gimoti Prescribing Information, Jan. 2021, Evoke Pharma, Inc.

38. Metoclopramide Nasal Spray / Depression _____ _____
Alert Message: Avoid Gimoti (metoclopramide) use in patients with a history of depression. Depression has occurred in metoclopramide-treated patients with and without a history of depression. Symptoms have included suicidal ideation and suicide.

Drugs/Diseases.

Util A	Util B	Util C (Include)
Metoclopramide Nasal		Depression

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gimoti Prescribing Information, Jan. 2021, Evoke Pharma, Inc.

39. Metoclopramide Nasal Spray / Hypertension _____ _____
Alert Message: The use of Gimoti (metoclopramide) should be avoided in patients with hypertension. Metoclopramide may elevate blood pressure.

Drugs/Diseases

Util A	Util B	Util C
Metoclopramide Nasal	Hypertension	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gimoti Prescribing Information, Jan. 2021, Evoke Pharma, Inc.

40. Metoclopramide Nasal Spray / Fluid Retention & Volume Overload _____ _____
Alert Message: Because metoclopramide produces a transient increase in plasma aldosterone, patients with cirrhosis or congestive heart failure may be at risk of developing fluid retention and volume overload. Discontinue Gimoti (metoclopramide) if any of these adverse reactions occur.

Drugs/Diseases

Util A	Util B	Util C (Include)
Metoclopramide Nasal	Fluid Retention	Cirrhosis
	Volume Overload	Congestive Heart Failure

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gimoti Prescribing Information, Jan. 2021, Evoke Pharma, Inc.

41. Metoclopramide Nasal Spray / Moderate to Severe Renal Impairment _____ _____

Alert Message: Gimoti (metoclopramide) is not recommended in patients with moderate and severe renal impairment (creatinine clearance less than 60 mL/minute), including those receiving hemodialysis and continuous ambulatory peritoneal dialysis. The clearance of metoclopramide is decreased, and the systemic exposure is increased in patients with moderate to severe renal impairment compared to patients with normal renal function, which may increase the risk of adverse reactions.

Drugs/Diseases

Util A	Util B	Util C (Include)
Metoclopramide Nasal		CKD Stage 3, 4, and 5
		ESRD
		Hemodialysis

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gimoti Prescribing Information, Jan. 2021, Evoke Pharma, Inc.

42. Metoclopramide Nasal Spray / Antipsychotics _____ _____

Alert Message: The concurrent use of Gimoti (metoclopramide) with antipsychotics should be avoided. Both metoclopramide and antipsychotics can cause tardive dyskinesia (TD), other extrapyramidal symptoms (EPS), and neuroleptic malignant syndrome (NMS). Concomitant use of metoclopramide with these drugs may have an additive effect.

Drugs/Diseases

Util A	Util B	Util C
Metoclopramide Nasal	Antipsychotics	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gimoti Prescribing Information, Jan. 2021, Evoke Pharma, Inc.

43. Metoclopramide Nasal Spray / Strong CY2D6 Inhibitors _____ _____

Alert Message: The concurrent use of Gimoti (metoclopramide) with strong CYP2D6 inhibitors (e.g., bupropion, fluoxetine, paroxetine, and quinidine) is not recommended. Metoclopramide is a CYP2D6 substrate, and inhibition of CYP2D6-mediated metabolism may result in increased metoclopramide plasma concentrations and increased risk of adverse effects, including extrapyramidal symptoms.

Drugs/Diseases

Util A	Util B	Util C
Metoclopramide Nasal	Bupropion	
	Fluoxetine	
	Paroxetine	
	Quinidine	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gimoti Prescribing Information, Jan. 2021, Evoke Pharma, Inc.

Recommendations ***Approved Rejected***

44. Metoclopramide Nasal Spray / MAOIs _____ _____

Alert Message: The concurrent use of Gimoti (metoclopramide) with monoamine oxidase inhibitors (MAOIs) should be avoided. Both metoclopramide and MAOIs can elevate blood pressure, and concurrent use of these drugs increase the risk of hypertension.

Drugs/Diseases

Util A	Util B	Util C
Metoclopramide Nasal	Isocarboxazid	
	Phenelzine	
	Tranylcypromine	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gimoti Prescribing Information, Jan. 2021, Evoke Pharma, Inc.

45. Metoclopramide Nasal Spray / Drugs Decreasing Gastric Motility _____ _____

Alert Message: Caution should be exercised when Gimoti (metoclopramide) is coadministered with a drug that impairs gastrointestinal motility. Metoclopramide stimulates gastric motility, and concurrent use with drugs that decrease gastric motility may cause a decrease in metoclopramide efficacy.

Drugs/Diseases

Util A	Util B	Util C
Metoclopramide Nasal	Anticholinergics	
	Opioids	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gimoti Prescribing Information, Jan. 2021, Evoke Pharma, Inc.

46. Metoclopramide Nasal Spray / Dopamine Agonists _____ _____

Alert Message: Gimoti (metoclopramide) is a dopamine antagonist, and concurrent use with a dopamine agonist (e.g., bromocriptine, levodopa, and rotigotine) may decrease the effectiveness of either drug. Avoid concomitant use of these agents if possible.

Drugs/Diseases

Util A	Util B	Util C
Metoclopramide Nasal	Apomorphine	
	Bromocriptine	
	Cabergoline	
	Levodopa	
	Pramipexole	
	Ropinirole	
	Rotigotine	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gimoti Prescribing Information, Jan. 2021, Evoke Pharma, Inc.

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

47. Metoclopramide Nasal Spray / Hepatic Impairment _____ _____

Alert Message: Gimoti (metoclopramide) use is not recommended in patients with moderate or severe (Child-Pugh B or C) hepatic impairment. Patients with severe hepatic impairment (Child-Pugh C) have reduced systemic metoclopramide clearance (by approximately 50%) compared to patients with normal hepatic function. The resulting increase in metoclopramide blood concentrations increases the risk of adverse reactions. There are no pharmacokinetic data evaluating the safety of metoclopramide in patients with moderate hepatic impairment (Child-Pugh B).

Drugs/Diseases

Util A	Util B	Util C
Metoclopramide Nasal	Hepatic Impairment	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gimoti Prescribing Information, Jan. 2021, Evoke Pharma, Inc.

48. Abaloparatide / Overuse _____ _____

Alert Message: Tymlos (abaloparatide) may be over-utilized. The recommended dose is 80 mcg subcutaneously once daily. The cumulative use of abaloparatide for more than 2 years during a patient's lifetime is not recommended.

Drugs/Diseases

Util A	Util B	Util C
Abaloparatide		

Max Dose: 80 mcg/day

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.

Tymlos Prescribing Information, Dec. 2021, Radius Health, Inc.

49. Abaloparatide / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Abaloparatide		

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.

Tymlos Prescribing Information, Dec. 2021, Radius Health, Inc.

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

50. Abaloparatide / Risk of Osteosarcoma _____ _____

Alert Message: In animal studies, Tymlos (abaloparatide) caused a dose-dependent increase in the incidence of osteosarcoma in male and female rats. It is not known if abaloparatide will cause osteosarcoma in humans. The use of abaloparatide is not recommended in patients at increased risk for osteosarcoma, including those with Paget's disease of the bone or unexplained elevations of alkaline phosphatase, open epiphyses, bone metastases or skeletal malignancies, hereditary disorders predisposing to osteosarcoma, or prior external beam or implant radiation therapy involving the skeleton. The cumulative use of abaloparatide and parathyroid hormone analogs (e.g., teriparatide) for more than 2 years during a patient's lifetime is not recommended.

Drugs/Diseases

Util A	Util B	Util C (Include)
Abaloparatide		Paget's Disease
		Malignant Neoplasm of the Bone

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.

Tymlos Prescribing Information, Dec. 2021, Radius Health, Inc.

51. Abaloparatide / Hypercalcemia _____ _____

Alert Message: Tymlos (abaloparatide) may cause hypercalcemia. Abaloparatide use is not recommended in patients with pre-existing hypercalcemia or in patients who have an underlying hypercalcemia disorder, such as primary hyperparathyroidism, because of the possibility of exacerbating hypercalcemia.

Drugs/Diseases

Util A	Util B	Util C (Include)
Abaloparatide		Hypercalcemia
		Primary Hyperparathyroidism

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.

Tymlos Prescribing Information, Dec. 2021, Radius Health, Inc.

52. Abaloparatide / Hypercalciuria & Urolithiasis _____ _____

Alert Message: Tymlos (abaloparatide) may cause hypercalciuria. It is unknown whether abaloparatide may exacerbate urolithiasis in patients with a history of urolithiasis. If active urolithiasis or pre-existing hypercalciuria is suspected, measurement of urinary calcium excretion should be considered.

Drugs/Diseases

Util A	Util B	Util C
Abaloparatide	Hypercalciuria	
	Urolithiasis	

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.

Tymlos Prescribing Information, Dec. 2021, Radius Health, Inc.

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

53. Abaloparatide / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Tymlos (abaloparatide) is not intended for use in females of reproductive potential. There are no human data with abaloparatide use in pregnant women to inform any drug-associated risks. Animal reproduction studies with abaloparatide have not been conducted.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Abaloparatide	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female

Age Range: 11 – 50 yoa

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.

Tymlos Prescribing Information, Dec. 2021, Radius Health, Inc.

54. Abaloparatide / Therapeutic Appropriateness _____ _____ Alert Message:
Tymlos (abaloparatide) is not intended for use in females of reproductive potential.
There is no information on the presence of abaloparatide in human milk, the effects on the breastfed infant, or the effects on milk production.

Drugs/Diseases

Util A	Util B	Util C
Abaloparatide	Lactation	

Gender: Female

Age Range: 11 – 50 yoa

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.

Tymlos Prescribing Information, Dec. 2021, Radius Health, Inc.

55. Abrocitinib / Overuse _____ _____
Alert Message: Cibinqo (abrocitinib) may be over-utilized. The recommended dosage of abrocitinib is 100 mg once daily. If an adequate response is not achieved with abrocitinib 100 mg daily after 12 weeks, consider increasing the dosage to 200 mg once daily. Discontinue abrocitinib therapy if an inadequate response is seen after the dosage increase to 200 mg once daily.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Abrocitinib		Cirrhosis
		Hepatic Failure
		CKD 2, 3, 4, 5, & ESRD

Max Dose: 200 mg/day

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

56. Abrocitinib / Overuse Mild Renal Impairment _____ _____

Alert Message: Cibinqo (abrocitinib) may be over-utilized. The recommended dosage of abrocitinib in patients with mild renal impairment (eGFR 60 – 89 mL/min) is 100 mg once daily. If an adequate response is not achieved after 12 weeks, the dose of abrocitinib can be doubled to 200 mg once daily.

Drugs/Diseases

Util A	Util B	Util C (Include)
Abrocitinib		CKD Stage 2

Max Dose: 200 mg/day

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

57. Abrocitinib / Overuse Moderate Renal Impairment _____ _____

Alert Message: Cibinqo (abrocitinib) may be over-utilized. The recommended dosage of abrocitinib in patients with moderate renal impairment (eGFR 30 – 59 mL/min) is 50 mg once daily. If an adequate response is not achieved after 12 weeks, the dose of abrocitinib can be doubled to a maximum of 100 mg once daily.

Drugs/Diseases

Util A	Util B	Util C (Include)
Abrocitinib		CKD Stage 3

Max Dose: 100 mg/day

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

58. Abrocitinib / Severe Renal Impairment & ESRD _____ _____

Alert Message: Cibinqo (abrocitinib) is not recommended for use in patients with severe renal impairment (eGFR 15 - 29 mL/min) or end-stage renal disease (eGFR < 15 mL/min) hepatic impairment. Abrocitinib has not been studied in this patient population.

Drugs/Diseases

Util A	Util B	Util C (Include)
Abrocitinib		CKD Stage 4
		CKD Stage 5
		ESRD

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

59. Abrocitinib / Severe Hepatic Impairment _____ _____

Alert Message: Cibinqo (abrocitinib) is not recommended for use in patients with severe hepatic impairment. Abrocitinib has not been studied in this patient population.

Drugs/Diseases

Util A	Util B	Util C (Include)
Abrocitinib		Cirrhosis
		Hepatic Failure

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

60. Abrocitinib / Therapeutic Appropriateness _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Abrocitinib		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

61. Abrocitinib / Antiplatelets (minus 81 mg Aspirin) _____ _____

Alert Message: Cibinqo (abrocitinib) is contraindicated in patients taking antiplatelet therapies, except for low-dose aspirin (≤81 mg daily), during the first 3 months of treatment. Coadministration of abrocitinib with antiplatelet therapy drugs may increase the risk of bleeding with thrombocytopenia. Treatment with abrocitinib was associated with an increased incidence of thrombocytopenia and lymphopenia.

Drugs/Diseases

Util A	Util B	Util C
Abrocitinib	Aspirin > 81 mg	
	Anagrelide	
	Cilostazol	
	Clopidogrel	
	Dipyridamole	
	Prasugrel	
	Pentoxifylline	
	Ticagrelor	
	Ticlopidine	
	Vorapaxar	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

62. Abrocitinib / Serious Infections (Black Box) _____ _____

Alert Message: Patients treated with Cibinqo (abrocitinib) may be at increased risk for developing serious infections that may lead to hospitalization or death. The most frequent serious infections reported with abrocitinib were herpes simplex, herpes zoster, and pneumonia. Avoid the use of abrocitinib in patients with an active, serious infection, including localized infections. The risks and benefits of treatment with abrocitinib should be carefully considered prior to initiating therapy in patients with chronic or recurrent infections. If a serious or opportunistic infection develops, discontinue abrocitinib and control the infection.

Drugs/Diseases

Util A	Util B	Util C
Abrocitinib	Serious Infections	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

63. Abrocitinib / Tuberculosis (Black Box) _____ _____

Alert Message: Cibinqo (abrocitinib) is not recommended for use in patients with active tuberculosis (TB). Evaluate and test patients for TB before starting. Abrocitinib therapy and consider yearly screening for patients in highly endemic areas for TB. For patients with a new diagnosis of latent TB or prior untreated latent TB, or patients with a negative test for latent TB but who are at high risk for TB infection, start preventive therapy for latent TB prior to initiation of abrocitinib. Monitor patients for the development of signs and symptoms of TB, including patients who were tested negative for latent TB infection prior to initiating therapy.

Drugs/Diseases

Util A	Util B	Util C
Abrocitinib	Tuberculosis	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

64. Abrocitinib / Rheumatoid Arthritis (Black Box) _____ _____

Alert Message: Cibinqo (abrocitinib) is not approved for use in rheumatoid arthritis (RA). 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 all-cause mortality, including sudden cardiovascular death, was observed in patients treated with the JAK inhibitor compared with TNF blockers. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with abrocitinib.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Abrocitinib	Rheumatoid Arthritis	Atopic Dermatitis

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

Criteria Recommendations ***Approved Rejected***

65. Abrocitinib / Malignancies (Black Box) _____ _____
Alert Message: Malignancies, including non-melanoma skin cancer (NMSC), were observed in clinical studies with Cibinqo (abrocitinib) for atopic dermatitis. Perform periodic skin examinations for patients who are at increased risk for skin cancer. Exposure to sunlight and UV light should be limited by wearing protective clothing and using a broad-spectrum sunscreen. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with abrocitinib, particularly in patients with a known malignancy (other than a successfully treated NMSC), patients who develop a malignancy when on treatment, and patients who are current or past smokers.

Drugs/Diseases

Util A	Util B	Util C
Abrocitinib	Malignant Neoplasms	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

66. Abrocitinib / Myocardial Infarction & Stoke (Black Box) _____ _____
Alert Message: Major adverse cardiovascular events were reported in clinical studies of Cibinqo (abrocitinib) for atopic dermatitis. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with abrocitinib, particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if they occur. Discontinue abrocitinib in patients that have experienced a myocardial infarction or stroke.

Drugs/Diseases

Util A	Util B	Util C
Abrocitinib	Myocardial Infarction Stroke	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

67. Abrocitinib / Thrombosis (Black Box) _____ _____ Alert Message:
Deep venous thrombosis (DVT) and pulmonary embolism (PE) have been reported in patients treated with Cibinqo (abrocitinib). Thrombosis, including PE, DVT, and arterial thrombosis, have been reported in patients receiving JAK inhibitors used to treat inflammatory conditions. Many of these adverse reactions were serious and some resulted in death. In RA patients 50 years of age and older with at least one cardiovascular risk factor treated with another JAK inhibitor, a higher rate of thrombosis was observed when compared with TNF blockers. Avoid abrocitinib in patients at risk. If symptoms of thrombosis occur, discontinue abrocitinib and treat appropriately.

Drugs/Diseases

Util A	Util B	Util C
Abrocitinib	Pulmonary Embolism Deep Vein Thrombosis Arterial Thrombosis	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

68. Abrocitinib / Strong 2C19 Inhibitors _____ _____

Alert Message: Coadministration of Cibinqo (abrocitinib) with strong CYP2C19 inhibitors increases the combined exposure of abrocitinib and its two active metabolites, M1 and M2, which may increase the adverse reactions of abrocitinib. In patients taking strong inhibitors of CYP2C19, reduce the dosage to 50 mg once daily. If an adequate response is not achieved with abrocitinib 50 mg daily after 12 weeks, consider increasing the dosage to 100 mg once daily. Discontinue therapy if an inadequate response is seen after dosage increase to 100 mg once daily.

Drugs/Diseases

Util A	Util B	Util C
Abrocitinib	Fluconazole	
	Fluoxetine	
	Fluvoxamine	
	Ticlopidine	

Max Dose: 100 mg/day

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

69. Abrocitinib / Moderate to Strong Inhibitors of Both 2C19 & 2C9 _____ _____

Alert Message: Coadministration of Cibinqo (abrocitinib) with drugs that are moderate to strong inhibitors of both CYP2C19 and CYP2C9 increases the exposure of abrocitinib and its two active metabolites, M1 and M2, which may increase the adverse reactions of abrocitinib. Avoid concomitant use of abrocitinib with drugs that are moderate to strong inhibitors of both CYP2C19 and CYP2C9.

Drugs/Diseases

Util A	Util B	Util C
Abrocitinib	Efavirenz	
	Etravirine	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

70. Abrocitinib / Strong Inducers of Both 2C19 & 2C9 _____ _____

Alert Message: Coadministration of Cibinqo (abrocitinib) with strong CYP2C19 or CYP2C9 inducers decreases the combined exposure of abrocitinib and its two active metabolites, M1 and M2, which may result in loss of or reduced clinical response. Avoid concomitant use of abrocitinib with strong CYP2C19 or CYP2C9 inducers.

Drugs/Diseases

Util A	Util B	Util C
Abrocitinib	Apalutamide	
	Rifampin	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

71. Abrocitinib / P-gp Substrates _____ _____

Alert Message: Coadministration of Cibinqo (abrocitinib) with P-gp substrate increases plasma concentrations of P-gp substrates and may result in potential adverse reactions of the P-gp substrate where small concentration changes may lead to serious or life-threatening toxicities (e.g., digoxin). Monitor appropriately or dose titrate P-gp substrate where small concentration changes may lead to toxicities when coadministered with abrocitinib.

Drugs/Diseases

Util A	Util B	Util C
Abrocitinib	Atorvastatin	
	Cobimetinib	
	Cyclosporine	
	Dabigatran	
	Digoxin	
	Dolutegravir	
	Everolimus	
	Glecaprevir/Pibrentasvir	
	Lapatinib	
	Lefamulin	
	Loperamide	
	Lovastatin	
	Maraviroc	
	Morphine	
	Naldemedine	
	Ranolazine	
	Simvastatin	
	Sirolimus	
	Tenofovir	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

72. Abrocitinib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Available data from pregnancies reported in clinical trials with Cibinqo (abrocitinib) are not sufficient to establish a drug associated risk for major birth defects, miscarriage, or other adverse maternal or fetal outcomes. In animal reproduction studies, oral administration of abrocitinib to pregnant rats and rabbits during organogenesis at exposure 14 or 5 times the maximum recommended human dose (MRHD) based on AUC comparison, respectively, resulted in maternal dystocia and skeletal variations in rats and no adverse effects in rabbits.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

73. Abrocitinib / Lactation _____ _____

Alert Message: There are no data on the presence of Cibinqo (abrocitinib) in human milk, the effects on the breastfed infant, or the effects on milk production. In animal studies, abrocitinib was secreted in the milk of lactating rats. When a drug is present in animal milk, the drug will likely be present in human milk. Because of the serious adverse findings in adults, including risks of serious infections, malignancy, and thrombosis, advise women not to breastfeed during treatment with abrocitinib and for one day after the last dose (approximately 5-6 elimination half-lives).

Drugs/Diseases

Util A	Util B	Util C
Abrocitinib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Cibinqo Prescribing Information, Jan. 2022, Pfizer, Inc.

74. Abrocitinib / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Cibinqo (abrocitinib). 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
Abrocitinib		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Feldman SR, Cox LS, Strowd LC, Gerber RA, Faulkner S, Sierka D, Smith TW, Cappelleri JC, Levenberg ME. The Challenge of Managing Atopic Dermatitis in the United States. Am Health Drug Benefits. 2019. Apr;12(2):83-93. PMID: 31057694; PMCID: PMC6485648.
Eicher L. Knop M, Aszodi N, et al. A Systemic Review of Factors Influencing Treatment Adherence in Chronic Inflammatory Skin Disease – Strategies for Optimizing Treatment Outcome. JEADV. 2019. (33):2253-2263.

75. Dupilumab / Overutilization _____ _____

Alert Message: The recommended maximum maintenance dose of Dupixent (dupilumab) for the treatment of eosinophilic esophagitis in adults and pediatric patients 12 years of age and older weighing at least 40 kg is 300 mg given every week.

Drugs/Diseases

Util A	Util B	Util C (Include)
Dupilumab		Eosinophilic Esophagitis

Maintenance Max Dose: 300mg every week.

Age Range: 12 - yoa

References:

Clinical Pharmacology, 2017 Elsevier/Gold Standard.

Dupixent Prescribing Information, May 2022, Regeneron Pharmaceuticals, Inc.

76. Dupilumab / Therapeutic Appropriateness _____ _____

Alert Message: The safety and efficacy of Dupixent (dupilumab) for the treatment of eosinophilic esophagitis in pediatric patients less than 12 years of age and weighing less than 40 kg have not been established.

Drugs/Diseases`1 week

Util A	Util B	Util C (Negate**)**
Dupilumab	Eosinophilic Esophagitis	Asthma
		Atopic Dermatitis

Age Range: 0 – 11 yoa

References:

Clinical Pharmacology, 2017 Elsevier/Gold Standard.

Dupixent Prescribing Information, May 2022, Regeneron Pharmaceuticals, Inc.

77. Lurasidone / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Latuda (lurasidone) for the treatment of bipolar depression in pediatric patients less than 10 years of age have not been established.

Drugs/Diseases

Util A	Util B	Util C (Include)
Lurasidone		Bipolar Depression

Age Range: 0 – 9 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Facts & Comparisons, 2022 Updates, Wolters Kluwer Health.

78. Mirtazapine / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of mirtazapine have not been established in pediatric patients.

Drugs/Diseases

Util A	Util B	Util C
Mirtazapine		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Facts & Comparisons, 2022 Updates, Wolters Kluwer Health.

79. Selumetinib / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Koselugo (selumetinib) have not been established in pediatric patients younger than 2 years of age.

Drugs/Diseases

Util A	Util B	Util C
Selumetinib		

Age Range: 0 – 1 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Koselugo Prescribing Information, May 2021, AstraZeneca.

80 Selumetinib / Cardiomyopathy _____ _____

Alert Message: The safety of Koselugo (selumetinib) has not been established in patients with a history of impaired left ventricular ejection fraction (LVEF) or a baseline ejection fraction that is below the institutional lower limit of normal (LLN). Cardiomyopathy, defined as a decrease in LVEF ≥ 10% below baseline, occurred in 23% of 74 pediatric patients who received selumetinib in a clinical trial (SPRINT). Assess ejection fraction by echocardiogram prior to initiating treatment, every 3 months during the first year of treatment, every 6 months thereafter, and as clinically indicated. Withhold, reduce dose, or permanently discontinue selumetinib based on the severity of the adverse reaction.

Drugs/Diseases

Util A	Util B	Util C (Include)
Selumetinib		Heart Failure

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Koselugo Prescribing Information, May 2021, AstraZeneca.

81. Selumetinib / Skin Toxicity _____ _____

Alert Message: Skin toxicities, including severe palmar-plantar erythrodysesthesia syndrome, have occurred in adult patients with multiple tumor types who received Koselugo (selumetinib) as a single agent or in combination with other anti-cancer agents. Monitor patients for severe skin rashes. Withhold, reduce dose, or permanently discontinue selumetinib based on the severity of the adverse reaction.

Drugs/Diseases

Util A	Util B	Util C
Selumetinib	Rash	
	Pruritus	
	Dermatitis	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Koselugo Prescribing Information, May 2021, AstraZeneca.

82. Selumetinib / Ocular Toxicity _____ _____

Alert Message: Koselugo (selumetinib) can cause ocular toxicity (e.g., blurred vision, photophobia, retinal vein occlusion (RVO), and retinal pigment epithelial detachment (RPED)). Conduct comprehensive ophthalmic assessments prior to initiating selumetinib, at regular intervals during treatment, and for new or worsening visual changes. Permanently discontinue selumetinib in patients with RVO. Withhold selumetinib in patients with RPED, follow up with optical coherence tomography assessments every 3 weeks until resolution, and resume selumetinib at a reduced dose. For other ocular toxicities, withhold, reduce dose, or permanently discontinue selumetinib based on the severity of the adverse reaction.

Drugs/Diseases

Util A	Util B	Util C
Selumetinib	Blurred Vision	
	Photophobia	
	Retinal Vein Occlusion	
	Retinal Pigment Epithelia Detachment	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Koselugo Prescribing Information, May 2021, AstraZeneca.

83. Selumetinib / Gastrointestinal Toxicity _____ _____

Alert Message: Serious gastrointestinal toxicities, including perforation, colitis, ileus, and intestinal obstruction, occurred in an unapproved population of adult patients with multiple tumor types who received Koselugo (selumetinib) as a single agent or in combination with other anti-cancer agents. Advise patients to start an anti-diarrheal agent (e.g., loperamide) immediately after the first episode of unformed, loose stool and increase fluid intake during diarrhea episodes. Withhold, reduce dose, or permanently discontinue selumetinib based on the severity of the adverse reaction.

Drugs/Diseases

Util A	Util B	Util C
Selumetinib	Colitis	
	Diarrhea	
	Intestinal Perforation	
	Intestinal Obstruction	
	Ileus	

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Koselugo Prescribing Information, May 2021, AstraZeneca.

84. Selumetinib / Moderate or Strong CYP3A4 Inhibitors _____ _____

Alert Message: The co-administration of Koselugo (selumetinib) with moderate or strong CYP3A4 inhibitors should be avoided. Selumetinib is a CYP3A4 substrate, and concomitant use of selumetinib with a moderate or strong CYP3A4 inhibitor increases selumetinib plasma concentrations, which may increase the risk of adverse reactions. If coadministration with strong or moderate CYP3A4 inhibitors cannot be avoided, reduce the selumetinib dosage as recommended in the official prescribing information. After discontinuation of a strong or moderate CYP3A4 inhibitor for 3 elimination half-lives, resume the selumetinib dose that was taken prior to initiating the inhibitor or fluconazole.

Drugs/Diseases

Util A	Util B		Util C
Selumetinib	Atazanavir	Fosamprenavir	
	Aprepitant	Idelalisib	
	Cimetidine	Indinavir	
	Ciprofloxacin	Itraconazole	
	Clarithromycin	Ketoconazole	
	Clotrimazole	Nefazodone	
	Cobicistat	Nelfinavir	
	Crizotinib	Posaconazole	
	Cyclosporine	Ritonavir	
	Diltiazem	Saquinavir	
	Dronedarone	Tipranavir	
	Erythromycin	Verapamil	
	Fluconazole	Voriconazole	
	Fluvoxamine		

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Koselugo Prescribing Information, May 2021, AstraZeneca.

85. Selumetinib / Moderate or Strong CYP3A4 Inducers _____ _____

Alert Message: The co-administration of Koselugo (selumetinib) with moderate or strong CYP3A4 inducers should be avoided. Selumetinib is a CYP3A4 substrate, and concomitant use of selumetinib with a moderate or strong CYP3A4 inducer decreases selumetinib plasma concentrations, which may reduce selumetinib efficacy.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Koselugo Prescribing Information, May 2021, AstraZeneca.

86. Selumetinib / Vitamin E Supplements _____ _____

Alert Message: Koselugo (selumetinib) capsules contain vitamin E, and daily intake of vitamin E that exceeds the recommended or safe limits may increase the risk of bleeding. Supplemental vitamin E is not recommended if daily vitamin E intake exceeds the recommended or safe limits. An increased risk of bleeding may occur in patients who are co-administered selumetinib with vitamin K antagonists or anti-platelet agents.

Drugs/Diseases

Util A	Util B	Util C
Selumetinib	Vitamin E	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Koselugo Prescribing Information, May 2021, AstraZeneca.

87. Selumetinib / Vitamin K Antagonist & Antiplatelet agents _____ _____

Alert Message: Koselugo (selumetinib) capsules contain vitamin E, and coadministration with vitamin K antagonist or antiplatelet agents may increase the risk of bleeding. Monitor for bleeding in these patients. Increase international normalized ratio (INR) monitoring, as appropriate, in patients taking a vitamin-K antagonist. Perform anticoagulant assessments, including INR or prothrombin time, more frequently and adjust the dose of vitamin K antagonists or anti-platelet agents as appropriate.

Drugs/Diseases

Util A	Util B		Util C
Selumetinib	Anagrelide	Ticagrelor	
	Cilostazol	Ticlopidine	
	Clopidogrel	Vorapaxar	
	Dipyridamole	Warfarin	
	Prasugrel		

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Koselugo Prescribing Information, May 2021, AstraZeneca.

88. Selumetinib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on findings from animal studies and its mechanism of action, Koselugo (selumetinib) can cause fetal harm when administered to a pregnant patient. There are no available data on the use of selumetinib in pregnant patients to evaluate drug-associated risk. In animal reproduction studies, administration of selumetinib to mice during organogenesis caused reduced fetal weight, adverse structural defects, and effects on embryo-fetal survival at approximate exposures > 5-times the human exposure at the clinical dose of 25 mg/m2 twice daily. Advise pregnant patients of the potential risk to the fetus.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Selumetinib	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Koselugo Prescribing Information, May 2021, AstraZeneca.

89. Selumetinib / Lactation _____ _____

Alert Message: There are no data on the presence of Koselugo (selumetinib) and its active metabolite in human milk or their effects on the breastfed child or milk production. Selumetinib and its active metabolite were present in the milk of lactating mice. Due to the potential for adverse reactions in a breastfed child, advise patients not to breastfeed during treatment with selumetinib and for 1 week after the last dose.

Drugs/Diseases

Util A	Util B	Util C
Selumetinib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Koselugo Prescribing Information, May 2021, AstraZeneca.

90. Selumetinib / Therapeutic Appropriateness _____ _____

Alert Message: Advise patients of reproductive potential to use effective contraception during treatment and for 1 week after the last dose of Koselugo (selumetinib). Selumetinib can cause fetal harm when administered to a pregnant patient.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Selumetinib		Contraceptives

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Koselugo Prescribing Information, May 2021, AstraZeneca.

Criteria Recommendations ***Approved Rejected***

91. Selumetinib / Therapeutic Appropriateness _____ _____
Alert Message: Advise male patients with partners of reproductive potential to use effective contraception during treatment with Koselugo (selumetinib) and for 1 week after the last dose.

Drugs/Diseases
Util A Util B Util C
Selumetinib

Gender: Male

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Koselugo Prescribing Information, May 2021, AstraZeneca.

92. Selumetinib / Non-adherence _____ _____
Alert Message: Based on refill history, your patient may be under-utilizing Koselugo (selumetinib). Nonadherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased outcomes and additional healthcare costs.

Drugs/Diseases
Util A Util B Util C
Selumetinib

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med. 2005;353:487-97.
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.