North Dakota Medicaid
Drug Utilization Review Board Meeting
June 7, 2023
Conference Room 210/212

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Meeting Notice

North Dakota Medicaid Drug Use Review Board

Wednesday, June 7th, 2023
1 to 4 p.m. Central Time

In-Person Information

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

Virtual Information

Join virtually: Click here to join the meeting
Join by phone: 701-328-0950, Conference ID: 731 715 069#

Agenda

1. Call to Order
2. Roll Call
3. Review and Approval of Minutes
4. Reports from Department
    - Administrative Report: Member update, Legislative update, Robert's Rules of Order
    - Financial Report: Budget, Top drugs
    - Clinical Report: Prior authorization update, Criteria update
        - Update to Hepatitis C
        - Update to Chronic Kidney Disease (Filspari)
    - Retrospective DUR report
5. Special Orders
    - Presiding Officer and Vice-Presiding Officer Elections
6. New business
    - Second Review of Hyperparathyroidism
    - Second Review of Influenza
    - Second Review of Neuromyelitis Optica Spectrum Disorder
    - Second Review of Urea Cycle Agents
    - Review of retrospective DUR criteria recommendations
7. Announcements
    - Next Meeting (September 6th, 2023)
8. Adjourn

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

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

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

Others Present:
Medicaid Pharmacy Department: Brendan Joyce, LeNeika Roehrich, Jeff Hostetter

Meeting was called to order: A regular quarterly meeting of the North Dakota Medicaid Drug Use Review (DUR) Board meeting was convened at 1:09 pm CST with Presiding Officer T. Schmidt presiding, and DUR Board Coordinator, L. Morgan recording minutes.

Administrative Items: There were no DHHS announcements at this meeting.

Approval of Meeting Minutes: Motion was made by J. Askvig, and seconded to approve the minutes of the December 7, 2022, meeting as distributed. **Motion carried.**

Reports:
Budget Update provided by B. Joyce
B. Joyce reported on hyper-cost drugs (i.e., Stelara, Dupixent, Humira, Hepatitis C agents), 30 drugs making up 47% of the Medicaid drug budget, and 6 drug classes (i.e., immunomodulators, oncology, cystic fibrosis, HIV) which account for 93% of increase in spend. The increase in drug spend is not attributable to the increase in members, but rather, it is from the increased use of hyper-cost drugs.

Review Top 25 Drugs provided by B. Joyce
B. Joyce presented the quarterly review of the top 25 drugs based on total cost of claims, the top 25 drugs based on the total number of claims, and the top drug classes based on claims and cost for the 4th quarter of 2022. This report can be found in the handout.

PDL/PA Criteria Updates provided by L.Roehrich
L. Roehrich shared with the Board all changes made to the Preferred Drug List (PDL) since the last update. This report can be found in the handout.

Update to C. difficile Associated Diarrhea (CDAD) provided by L. Morgan
L. Morgan discussed the addition of a CDAD prevention section to the PDL which listed criteria for Rebyota. This report can be found in the handout.

Update to Vaginal Infections provided by L. Morgan
L. Morgan discussed the "Fungal Infections" category to the "Vaginal Infections" section of the PDL along with updated criteria. There are now two categories (Bacterial and Fungal) which separate treatment options for either infection. This report can be found in the handout.

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

Hyperparathyroidism:
Motion: Moved by A. Werremeyer for the Department to develop criteria for hyperparathyroidism, motion was seconded.

Influenza:
Motion: Moved by J. Askvig for the Department to develop criteria for influenza, motion was seconded.

Neuromyelitis Optica Spectrum Disorder:
Motion: Moved by J. Askvig for the Department to develop criteria for neuromyelitis optica spectrum disorder, motion was seconded.

Urea Cycle Agents:
Motion: Moved by L. Kroetsch for the Department to develop criteria for urea cycle agents, motion was seconded.

Discussion of Respiratory Syncytial Virus (RSV): L. Roehrich presented data from the Midwest region and, more specifically, North Dakota for the 2022 – 2023 RSV season. The data set for North Dakota from start-to-finish matched the Midwest Region of the RSV season, which was presented in a bell-shaped curve. This presentation confirms that following the CDC RSV positivity data allows for better representation and coverage for members during the RSV season. The presented material can be found in the handout.

Retrospective Drug Utilization Review (RDUR) Criteria Recommendations: L. Morgan reviewed the RDUR criteria that were selected for review of each month of the last quarter. October consisted of a special mailing to prescribers of the buprenorphine monoproduct. The presented material can be found in the handout.
Motion: Moved by K. Martian to approve the RDUR criteria, motion was seconded. **Motion carried.**

Remicade Biosimilar Update: L. Roehrich presented a fax sent to providers discussing the preferred Remicade biosimilars effective January 1st, 2023. Biosimilars Avsola and Renflexis will not require prior authorization (PA). All other agents, Remicade, Inflectra, and infliximab will require PA. The presented material can be found in the handout.

Adjournment:
Motion: Moved by L. Kroetsch to adjourn the meeting, motion was seconded. **Motion carried.**

Meeting was adjourned at 2:15 pm CST.

Date of Minutes Approval:

Minutes submitted by: Lauren Morgan, Kepro

Legislative Update: Highlighted changes affecting DUR Board

Senate Bill 2156: Effective August 1, 2023

Quorum:

- Definition: One-half or more of nonvacant voting board member positions

Residency Requirements:

- Pharmacist and physician members do not have to be residents of the state of ND if they provide telehealth services to residents of ND. In-state members should continue to be recruited to fill positions and replace out-of-state members.
- Pharmaceutical representative members do not need to be in-state residents

Restricted Classes:

- Stimulant medications is no longer a restricted class; immunosuppressants for prophylaxis of organ transplant rejection has been added as a restricted class.
- Restricted classes may have prior authorization requirements if they are meet one of the following exceptions:
    - Multisource brands of the identical molecular structure
    - Extended-release products when the immediate-release product is available without prior authorization
    - Products that have the same active ingredient or moiety
    - Dosage forms that do not provide a unique route of administration

Terminology:

- Chairman has been changed to Presiding Officer

Procedure Changes to DUR Board

Elections:

- Elections for Presiding Officer and Vice-Presiding Officer will occur in June. Those elected will assume their positions in September.
    - The presiding officer runs the board meeting and ensures the rules of board are followed.
    - The vice-presiding officer acts as presiding offer when presiding officer is absent or steps down prior to the end of their term.
    - Any member is eligible for either position. The vice-presiding officer will not automatically assume the presiding officer's position at the end of their term. The election for each position will be open in June.

Debate:

- Each member is allowed two 10-minute speeches per day on a question. After the first 10 minutes, the member must wait until everyone has had the opportunity to speak before speaking a second 10 minutes.
- Debate should be germane to the agenda item being discussed
- A call for the orders of the day may occur to keep meeting on track

Minutes:

- Minutes are a record of what is done at the meeting, not what is said.
- Motions are recorded in minutes so please make a clearly worded motion. "I move that…"
- Approval of the minutes:
    - The presiding officer may assume the motion and obtain unanimous consent that the minutes be approved as distributed. If there are corrections to be made, this would require a motion/second/vote.

Old/Unfinished business:

- Reserved for resolving questions or agenda items that were not addressed from the previous meeting

Second Review:

- Purpose is to adopt criteria developed by the Department. Prior authorization becomes effective following this review.
- Needs a motion/second and vote to adopt criteria. Please state motions clearly and completely so they can be recorded in the minutes.
- The original motion can be to adopt the criteria with a change. An amendment motion/second/vote is not needed to change the criteria, only to change the original motion.

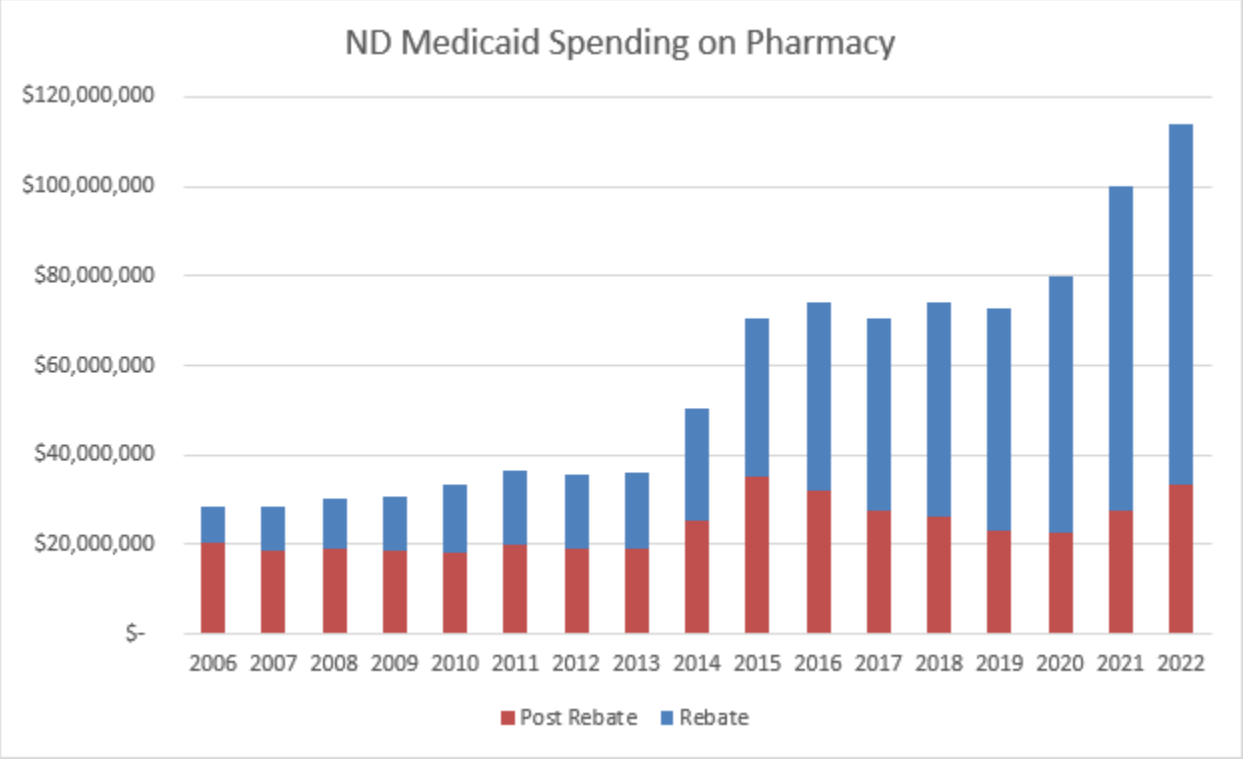
First Review:

- The purpose is to approve the Department to develop prior authorization criteria.
- Needs a motion/second and vote to develop criteria. Please state motions clearly and completely so they can be recorded in the minutes.

Adjournment:

- The presiding officer may adjourn the meeting without a motion/second/vote when it is time based on the agenda or allotted time for the meeting.
    - Adjournment outside of these parameters or an emergency would require a motion/second/vote.

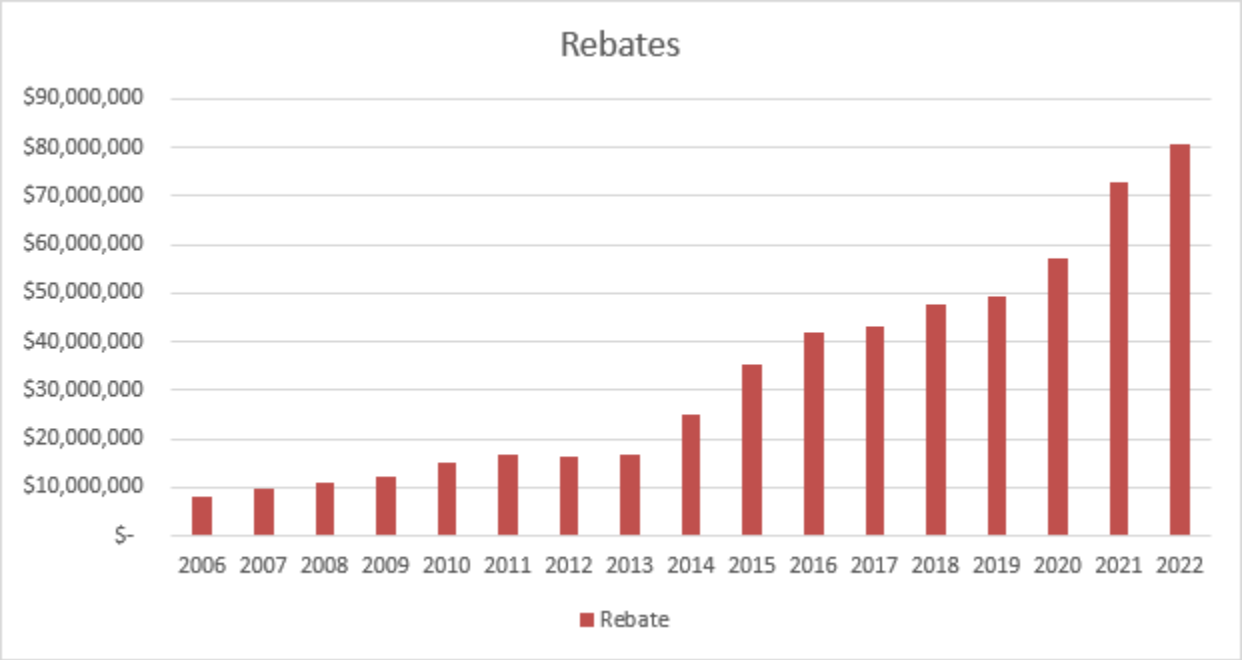
Timeline	
Pre - 2014	Brendan was only staff member
2014	Expansion (managed by Sanford MCO) started
2015	Alexi was hired
2016	Supplement rebates for only FFS
2017	January 1 - MCO supplementals start October 1 – MCO PBM complaint
2019	LeNeika was hired
2020	January 2020 - MCO carve-out March 2020 - COVID



Total payments to pharmacies in 2006 was $28.5 million.
Total payments to pharmacies in 2022 was $113.8 million.

Net pharmacy spend (i.e. post rebate) in 2006 was $20.26 million.
Net pharmacy spend (i.e. post rebate) in 2020 was $22.5 million.

Net pharmacy spend in 2022 was $33.2 million (still lower than $35.1 million in 2015).



MCO Carve Out Decrease in Net Spend

Class	% Decrease
ADHD Stimulants	36.68%
Antidepressants	22.23%
Beta Agonist	68.30%
Hypertension	16.82%
Muscle Relaxant	31.46%
Narcotics	21.79%
Narcotic Treatment	14.53%
NSAIDs/COX2	17.90%
Topical Steroid	29.89%
Total	**25.95%**

Spending Growth

Quarter	Reimb Amt	Net Spend	% Growth qtr/qtr
1Q2019	$ 17,874,850	$ 5,371,480	
2Q2019	$ 18,017,728	$ 5,667,672	5.5%
3Q2019	$ 17,468,060	$ 5,749,207	1.4%
4Q2019	$ 19,373,630	$ 6,458,292	12.3%
1Q2020	$ 18,696,018	$ 5,419,074	-16.1%
2Q2020	$ 18,758,703	$ 5,283,372	-2.5%
3Q2020	$ 20,307,648	$ 5,806,647	9.9%
4Q2020	$ 22,045,832	$ 5,990,144	3.2%
1Q2021	$ 24,272,343	$ 6,340,422	5.8%
2Q2021	$ 24,974,546	$ 6,683,444	5.4%
3Q2021	$ 25,124,024	$ 6,929,321	3.7%
4Q2021	$ 25,801,227	$ 7,431,914	7.3%
1Q2022	$ 27,927,425	$ 7,674,315	3.3%
2Q2022	$ 28,301,349	$ 8,071,019	5.2%
3Q2022	$ 28,153,701	$ 8,352,346	3.5%
4Q2022	$ 29,395,177	$ 9,081,519	8.7%
1Q2023	$ 31,430,413	$ 9,192,116	1.2%

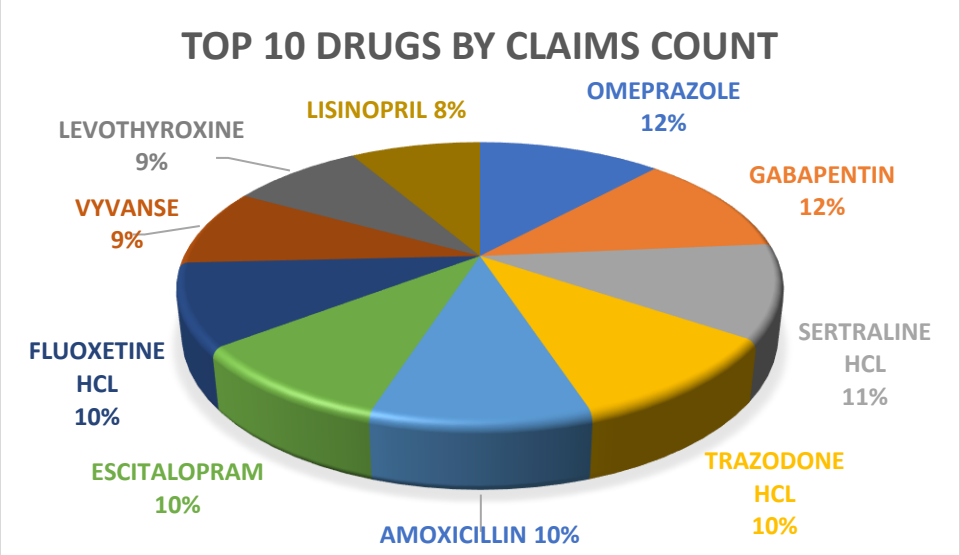
Yearly Average Net Spend Growth between 2018 to 2022

Class	% of total growth
Immunomodulators	35.8%
Oncology	15.5%
Cystic Fibrosis	15.5%
Antipsychotics	11.3%
Eczema	7.4%
HIV	4.8%
Total in these 6 classes	**93.0%**

Top 25 Drugs Based on Number of Claims from 01/01/2023 – 03/31/2023

Drug	Claims	Claims Cost	Patients	Cost / Claim	% Total Claims	Dif.
1. OMEPRAZOLE	5,168	$67,134.97	2,550	$12.99	1.8%	↑1
2. GABAPENTIN	5,144	$75,875.53	2,104	$14.75	1.8%	↓1
3. SERTRALINE HCL	4,829	$65,043.26	2,611	$13.47	1.6%	NC
4. TRAZODONE HCL	4,603	$62,207.79	2,229	$13.51	1.6%	NC
5. AMOXICILLIN	4,331	$61,990.27	4,049	$14.31	1.5%	↑1
6. ESCITALOPRAM OXALATE	4,326	$58,167.97	2,424	$13.45	1.5%	↓1
7. FLUOXETINE HCL	4,289	$57,231.53	2,254	$13.34	1.5%	NC
8. VYVANSE	4,025	$1,076,628.95	1,492	$267.49	1.4%	↑4
9. LEVOTHYROXINE SODIUM	3,940	$63,175.57	1,993	$16.03	1.3%	↓1
10. LISINOPRIL	3,704	$47,540.98	2,178	$12.84	1.3%	↓1
11. ATORVASTATIN CALCIUM	3,594	$52,187.07	2,036	$14.52	1.2%	↓1
12. BUPROPION XL	3,559	$59,034.04	1,844	$16.59	1.2%	↑1
13. PANTOPRAZOLE SODIUM	3,318	$45,639.82	1,597	$13.76	1.1%	↑2
14. HYDROCODONE-APAP	3,071	$44,533.85	1,919	$14.5	1.0%	↑2
15. CYCLOBENZAPRINE HCL	2,954	$34,015.15	1,830	$11.51	1.0%	↑2
16. DULOXETINE HCL	2,896	$46,760.92	1,485	$16.15	1.0%	↑2
17. AMOXICILLIN-CLAV	2,872	$51,727.21	2,690	$18.01	1.0%	↓6
18. CLONIDINE HCL	2,868	$35,256.33	1,403	$12.29	1.0%	↑2
19. ONDANSETRON ODT	2,852	$39,375.67	2,235	$13.81	1.0%	↑10
20. PREDNISONE	2,851	$32,716.26	2,296	$11.48	1.0%	↓6
21. HYDROXYZINE HCL	2,744	$37,909.69	1,676	$13.82	0.9%	↑2
22. BUPRENORPHINE-NALOX	2,741	$115,663.22	676	$42.2	0.9%	↓3
23. VENTOLIN HFA	2,740	$175,388.73	2,692	$64.01	0.9%	↑8
24. LAMOTRIGINE	2,740	$39,392.44	1,087	$14.38	0.9%	↓3
25. BUSPIRONE HCL	2,606	$39,980.16	1,351	$15.34	0.9%	↑1

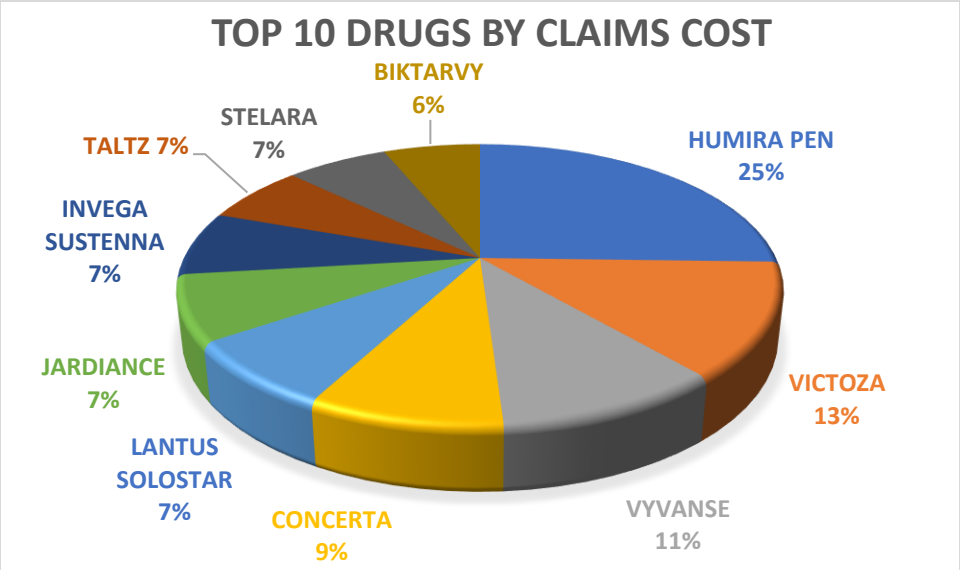
Total Claims	**292,740**



Top 25 Drugs Based on Total Claims Cost from 01/01/2023 – 03/31/2023

Drug	Claims	Claims Cost	Patients	Cost / Patient	% Total Cost	Dif.
1. HUMIRA PEN	295	$2,350,137.28	126	$36,582.22	6.2%	NC
2. VICTOZA	1448	$1,282,349.00	689	$3,624.68	3.4%	NC
3. VYVANSE	4,025	$1,076,628.95	1,492	$721.6	2.8%	NC
4. CONCERTA	2,301	$830,334.49	920	$902.54	2.2%	NC
5. LANTUS SOLOSTAR	1,360	$710,813.88	824	$862.64	1.9%	NC
6. JARDIANCE	1,067	$703,553.04	539	$1,305.29	1.9%	↑1
7. INVEGA SUSTENNA	271	$700,417.71	110	$6,367.43	1.9%	↓1
8. TALTZ AUTOINJECTOR	95	$667,695.10	34	$19,638.09	1.8%	↑2
9. STELARA	28	$655,455.02	18	$36,414.17	1.7%	NC
10. BIKTARVY	294	$610,112.83	129	$4,729.56	1.6%	↑1
11. MAVYRET	43	$522,443.63	28	$18,658.70	1.4%	↑9
12. VRAYLAR	520	$508,917.03	216	$2,356.10	1.3%	↑1
13. LATUDA	600	$482,987.32	244	$1,979.46	1.3%	↓5
14. ADDERALL XR	2,446	$436,081.56	990	$440.49	1.2%	NC
15. ELIQUIS	777	$419,051.56	354	$1,183.76	1.1%	↑2
16. SYMBICORT	1,159	$403,187.69	649	$621.24	1.1%	↓1
17. ADVAIR DISKUS	988	$361,302.25	538	$671.57	1.0%	↓1
18. NOVOLOG FLEXPEN	500	$358,449.53	299	$1,198.83	0.9%	NC
19. TRIKAFTA	16	$327,967.39	8	$40,995.92	0.9%	↓7
20. ABILIFY MAINTENA	137	$318,799.65	55	$5,796.36	0.8%	↑2
21. NORDITROPIN	83	$292,477.87	39	$7,499.43	0.8%	↓2
22. DUPIXENT	83	$285,163.36	34	$8,387.16	0.8%	↑7
23. XIFAXAN	96	$273,891.47	50	$5,477.83	0.7%	↑1
24. ORKAMBI	17	$237,449.07	6	$39,574.85	0.6%	↑1
25. INGREZZA	31	$236,023.46	11	$21,456.68	0.6%	↑13

Total Claims Cost	**$37,820,109.62**



Top 15 Therapeutic Classes Based on Number of Claims from 01/01/2023 – 03/31/2023

Therapeutic Class Description	Claims	Claims Cost	Patients	Cost/Claim	% Total Claims	Dif.
1. ANTIDEPRESSANTS	33,334	$705,163.73	13,454	$21.15	11.4%	NC
2. ANTICONVULSANTS	15,057	$631,660.79	5,140	$41.95	5.1%	NC
3. ANTIPSYCHOTIC AGENTS	10,460	$2,930,543.30	3,971	$280.17	3.6%	NC
4. PROTON-PUMP INHIBITORS	8,874	$158,311.36	4,276	$17.84	3.0%	NC
5. ANXIOLYTICS, SEDATIVES, HYPNOTICS	8,235	$120,581.28	4,112	$14.64	2.8%	↑1
6. AMPHETAMINES	8,181	$1,570,707.77	3,118	$191.99	2.8%	↑1
7. PENICILLIN ANTIBIOTICS	7,625	$122,940.30	6,743	$16.12	2.6%	↓2
8. OPIATE AGONISTS	7,590	$120,179.61	3,890	$15.83	2.6%	NC
9. NSAIDS	6,860	$99,441.64	4,472	$14.5	2.3%	NC
10. RESPIRATORY/CNS STIMULANTS	6,516	$1,112,383.00	2,335	$170.72	2.2%	↑1
11. STATINS	6,265	$92,382.41	3,522	$14.75	2.1%	↓1
12. BETA BLOCKING AGENTS	5,836	$105,231.85	3,155	$18.03	2.0%	NC
13. ADRENALS	4,735	$63,404.81	3,728	$13.39	1.6%	NC
14. BETA-ADRENERGIC AGONISTS	4,637	$274,032.69	4,218	$59.1	1.6%	NC
15. ACE INHIBITORS	4,618	$74,798.49	2,693	$16.2	1.6%	NC

Top 15 Therapeutic Classes Based on Claims Cost from 01/01/2023 – 03/31/2023

Therapeutic Class Description	Claims	Claims Cost	Patients	Cost/Patient	% Total Cost	Dif.
1. DMARDS	647	$3,812,849.15	261	$14,608.62	10.1%	NC
2. ANTIPSYCHOTIC AGENTS	10,460	$2,930,543.30	3,971	$737.99	7.7%	NC
3. SKIN/MUCOUS MEMBRANE AGENTS	799	$2,428,124.70	471	$5,155.25	6.4%	↑1
4. INSULINS	3,777	$1,986,331.84	1,456	$1,364.24	5.3%	↓1
5. ANTINEOPLASTIC AGENTS	703	$1,594,212.85	293	$5,441.00	4.2%	↑1
6. AMPHETAMINES	8,181	$1,570,707.77	3,118	$503.75	4.2%	↓1
7. INCRETIN MIMETICS	1,647	$1,454,711.44	718	$2,026.06	3.8%	NC
8. ANTIRETROVIRALS	934	$1,318,023.91	323	$4,080.57	3.5%	↑2
9. CORTICOSTEROIDS (RESPIRATORY)	3,949	$1,148,808.86	2,278	$504.31	3.0%	↑11
10. RESPIRATORY AND CNS STIMULANTS	6,516	$1,112,383.00	2,335	$476.4	2.9%	↓1
11. SGLT-2 INHIBITORS	1,528	$980,293.29	764	$1,283.11	2.6%	NC
12. ANTIDEPRESSANTS	33,334	$705,163.73	13,454	$52.41	1.9%	↑1
13. HCV ANTIVIRALS	66	$699,062.52	43	$16,257.27	1.8%	↑1
14. ANTICONVULSANTS	15,057	$631,660.79	5,140	$122.89	1.7%	↓2
15. ANTICOAGULANTS	1,668	$594,279.60	685	$867.56	1.6%	↑2

PDL Update

Drug Name	PA Status	Class
Altuviiio	PA	Extended half-life factor VIII products
Atorvaliq	PA	Non-Solid Dosage Forms
Austedo XR	PA	Tardive Dyskinesia
Cuvrior	PA	Wilson's Disease
Daybue	PA	Medications that cost greater than 3000
Joenja	PA	Medications that cost greater than 3000
Lumryz	PA	Narcolepsy
mesalamine HD	PA	Ulcerative Colitis
Nityr	PA	Preferred Dosage Forms
Pradaxa pellets	PA	Anticoagulants - oral
Rezvoglar	PA	Insulin
Skyclarys	PA	Medications that cost greater than 3000
Tezspire	PA	Eosinophilic Asthma
Vowst	PA	Clostridioides difficile-associated diarrhea (CDAD)

Update to Hepatitis C

Initial Criteria - Approval Duration: Based on label recommendations

- The member must have life expectancy greater than 12 months.
- The member and prescriber attestation forms must be attached to request
- The member must have established compliant behavior including attending scheduled provider visits (defined as 1 or less no-shows) and filling all maintenance medications on time for the past 90 days, as evidenced by pharmacy claims history.
- Chronic Hepatitis C must be documented by one of the following (within the last 12 months):
  - Liver fibrosis F1 and below or unknown: 2 positive HCV RNA levels at least 6 months apart
  - Liver fibrosis F2 and above: 1 positive HCV RNA test

Non-Solid Dosage Form Agents Criteria:

- Epclusa pellet packs: Members that weigh 30 kg or greater must meet Non-Solid Dosage Preparations criteria in addition to Hepatitis C criteria
- Mavyret pellet packs: Members that weigh 45 kg or greater must meet Non-Solid Dosage Preparations criteria in addition to Hepatitis C criteria

Non-Preferred Agents Criteria:

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

For FIRST TIME treatments with Direct Acting Antivirals:

One of the following criteria must be met (1,2 or 3):

1. The member has completed 2 visits in the Harm Reduction MTM Program
2. The member does not have history of alcohol abuse or IV drug use within the past 5 years
3. The member has a history of alcohol use disorder or IV drug use within the past 5 years with one of the following criteria met:

Currently enrolled or has completed a substance use treatment program within the past 12 months	• 1 negative IV drug test (if history of IV drug use) or 1 negative alcohol test (if history of alcohol use disorder) within 30 days of the request date
Has not completed a substance use treatment program within the past 12 months	• 2 negative IV drug tests (if history of IV drug use) or 2 negative alcohol tests (if history of alcohol use disorder), dated at least 3 months apart, with the most current test completed within 30 days of the request date **OR** • Provider must submit chart notes documenting that the member has maintained sobriety for the past year or since last substance use treatment program completion

For <u>RE-TREATMENT</u> after Direct Acting Antivirals:

- Prescriber must be, or in consult with, a hepatology, gastroenterology, or infectious disease specialist (including via Project ECHO)
- The following criteria is met (as applicable due to reason for retreatment):

<table>
<tr><th colspan="3">Reason for retreatment:</th></tr>
<tr><td rowspan="4">Due to drugs of abuse by injection</td><td colspan="2">• The member is receiving treatment or must have received treatment for substance use disorder since initial Hepatitis C treatment with Direct Acting Antivirals, and the provider/facility name must be provided with the request.</td></tr>
<tr><td>Liver fibrosis F2 and below (or unknown)</td><td>Liver fibrosis F3 and above</td></tr>
<tr><td>• The provider must submit chart notes documenting that the member has abstained from drugs of abuse for the past year</td><td rowspan="2">• Two drug tests: 1 test completed 3 months prior to request and 1 test within 30 days of the request date</td></tr>
<tr><td>• Two drug tests: 1 test completed 6 months (+/- 1 months) prior to request and 1 test within 30 days of the request date</td></tr>
<tr><td rowspan="3">Due to non-compliance (defined as a medication possession ratio (MPR) of less than 80%)</td><td>Liver fibrosis F2 and below (or unknown)</td><td>Liver fibrosis F3 and above</td></tr>
<tr><td>• The member must have established compliant behavior including attending scheduled provider visits (defined as 1 or less no-shows) and filling all maintenance medications on time for the past 180 days, as evidenced by pharmacy claims history.</td><td>• The member must have established compliant behavior including attending scheduled provider visits (defined as 1 or less no-shows) and filling all maintenance medications on time for the past 90 days, as evidenced by pharmacy claims history.</td></tr>
<tr><td colspan="2">• The member has participated in 2 MTM sessions addressing adherence barriers within the past 180 days</td></tr>
<tr><td>Resistance</td><td colspan="2">• FIRST TIME treatment with Direct Acting Antivirals criteria must be met</td></tr>
</table>

Hepatitis C Treatments
Prior Authorization Form

Fax Completed Form to:
855-207-0250
For questions regarding this Prior authorization, call
866-773-0695

Prior Authorization Vendor for ND

ND Medicaid requires that members receiving a prescription for hepatitis C treatments must meet the criteria listed in the preferred drug list (PDL). Please see the PDL at www.hidesigns.com/assets/files/ndmedicaid/NDPDL.pdf

Part I: TO BE COMPLETED BY PRESCRIBER

Member Name		Member Date of Birth	Weight (kg)	Member Medicaid ID Number
Prescriber Name		Specialist involved in therapy		
Prescriber NPI		Telephone Number		Fax Number
Requested Drug and Dose:	**Duration requested:**	**Member's liver fibrosis score (RNA levels must be within the last 12 months):** □ Unknown – Attach 2 positive HCV RNA levels at least 6 months apart □ F0-F1 - Attach 2 positive HCV RNA levels at least 6 months apart □ F2 or above – Attach 1 positive RNA HCV level		
Diagnosis: □ HCV □ OTHER	**Genotype:**	**Member's Child–Pugh Class:** □ A □ B □ C □ N/A		

This request is for
- □ Initial treatment for Hepatitis C
- □ Re-treatment after Interferon and/or Ribavirin
- □ Re-treatment after Direct Acting Antiviral; Drug Name _____

Reason for re-treatment
- □ Re-infection due to IV Drug Use
- □ Non-compliance with previous regimen (MPR < 80%)
- □ Resistance
- □ Other _____

Does member have history of:
- □ HIV/HCV co-infection
- □ Liver or kidney transplant
- □ HCV-uninfected transplant recipient who received an organ from HCV-viremic donor
- □ Decompensated cirrhosis
  - Is member going to take Ribavirin alongside treatment? □ YES □ NO

Is the member's life expectancy greater than one year?	□ YES □ NO
Does the member attend scheduled visits with no more than 1 no-show and fill maintenance medications on time?	□ YES □ NO

Does member have history within the past 5 years of Alcohol Use Disorder or IV Drug Use?
- □ **Alcohol Use Disorder:**
  - □ Member is currently enrolled or has completed treatment program within past 12 months
    - □ 1 negative alcohol test completed within 30 days of the request date is attached
  - □ Member has not completed substance use treatment program within past 12 months
    - □ 2 negative alcohol tests dated at least 3 months apart, with most recent completed within 30 days of the request date
  - □ Chart notes attached documenting 2 completed visits in Harm Reduction MTM Program
- □ **IV Drug Use:**
  - □ Member is currently enrolled or has completed treatment program within past 12 months
    - □ 1 negative IV drug test completed within 30 days of the request date is attached
  - □ Member has not completed substance use treatment program within past 12 months
    - □ 2 negative IV drug tests dated at least 3 months apart, with most recent completed within 30 days of the request date
  - □ Chart notes attached documenting 2 completed visits in Harm Reduction MTM Program

Treatment Program Name: _____

Prescriber (or Staff) / Pharmacy Signature**	Date

**: *By completing this form, I hereby certify that the above request is true, accurate and complete. That the request is medically necessary, does not exceed the medical needs of the member, and is clinically supported in the member's medical records. I also understand that any misrepresentations or concealment of any information requested in the prior authorization request may subject me to audit and recoupment.*

Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

Hepatitis C Member Consent Form

I am planning to live in North Dakota during the entire treatment period. I will complete the entire course of treatment, attend office visits, and have laboratory tests as ordered by my healthcare provider during the treatment period.

I will notify my chosen pharmacy of a need to refill one week prior to running out of medication. I understand I must take my medication each day as directed for the entire course of treatment. If the medication does not work due to missed doses, I may not be approved for re-treatment.

I understand to keep my liver healthy, I must not drink alcohol or use illicit injectable drugs prior to, during, or after my treatment. If indicated, I will participate in a treatment program to remain abstinent.

I understand that after treatment, I can be re-infected with Hepatitis C. My provider has educated me on routes of Hepatitis C transmission, and I will avoid or modify high risk activities to avoid re-infection.

I understand that medications that treat Hepatitis C may be harmful to unborn babies. I will use methods to avoid getting pregnant or another person pregnant during treatment and when advised by my provider or pharmacist, for at least 6 months after treatment is complete. If I become pregnant and stop treatment before it is completed, I may not be approved for re-treatment.

Member Signature _____Date __/__/____

Pharmacy or Prescriber Representative:

Signature _____Date __/__/____

By signature, the pharmacy or prescriber representative confirms the consent form has been reviewed with the member.

Hepatitis C Prescriber Agreement Form

I agree that I will counsel my patient on how, where, and when to obtain refills of their hepatitis C medications.

I agree that I will have intermittent telephone check-ins with my patient, at minimum at 2 weeks and 6 weeks of treatment. I will assess continued adherence with medication, labs, and office visits, treatment tolerability, as well as medication changes that may affect treatment.

I have reviewed my patient's medications for drug interactions that would make Hepatitis C medications less effective or cause other adverse effects.

I have reviewed the treatment plan with my patient including medications, lab, vaccinations, and follow-up visits.

I have assessed my patient's readiness for treatment and believe they are ready and willing to comply with the treatment plan. I have assessed social and psychological stability, substance use, compliance to follow up visits and medications, pregnancy status, and concurrent health risks.

I understand that ND Medicaid tracks refill history and may contact me to provide additional information in the event of a dropped or late refill.

I have a dedicated individual or team which may include pharmacy and nursing support to fulfill the elements of this form and have listed key members contact information below.

Name: _____ Location: _____

Phone #: _____

Name: _____ Location: _____

Phone #: _____

Pharmacy or Prescriber Representative:

Signature_____ **Date** __/__/____

Update to Chronic Kidney Disease (Filspari)

Chronic Kidney Disease

Dual endothelin angiotensin receptor antagonist

CLINICAL PA REQUIRED
FILSPARI (sparsentan)

Prior Authorization Criteria

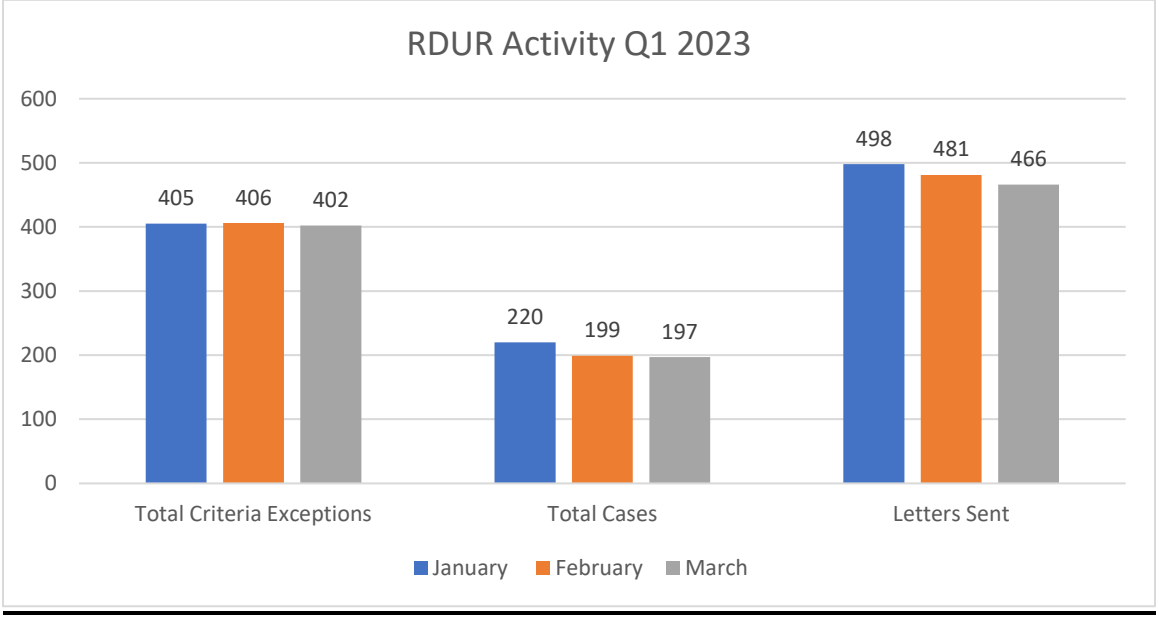
Initial Criteria - Approval Duration: 12 months

- If member is on renal dialysis, Medicare eligibility must be ruled out.
- The member must be on the following at the target or maximally tolerated dose, as evidenced by paid claims or pharmacy printouts:
  - An ACE-inhibitor or an ARB
  - A SGLT-2 inhibitor

Filspari Only

- The medication is prescribed by, or in consultation with, a nephrologist
- The diagnosis has been confirmed with kidney biopsy
- The member must have eGFR ≥ 30.
- The member must be experiencing proteinuria > 1 gram/day or UPCR ≥ 1.5 g/g (documentation must be attached) despite 3-month trials with good compliance of the following in combination at the target or maximally tolerated dose, as evidenced by paid claims or pharmacy printouts:
  - ACE inhibitor or an ARB
  - A SGLT-2 inhibitor

RDUR Activity Overview: Q1 2023



January Cases by Type of Criteria		
Criteria Description	**# of Cases**	**% of Cases**
Adverse Effects	3	1.4%
Clinical Appropriateness	23	10.5%
Drug-Disease Interactions	104	47.3%
Drug-Drug Conflicts	90	40.8%

February Cases by Type of Criteria		
Criteria Description	**# of Cases**	**% of Cases**
Clinical Appropriateness	133	66.8%
Drug-Disease Interactions	21	10.6%
Drug-Drug Conflicts	45	22.6%

March Cases by Type of Criteria		
Criteria Description	**# of Cases**	**% of Cases**
Adverse Effects	31	15.7%
Clinical Appropriateness	106	53.8%
Drug-Disease Interactions	1	0.6%
Drug-Drug Conflicts	59	29.9%

Second Reviews

Hyperparathyroidism

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
calcitrol capsule	doxercalciferol capsule
paricalcitrol capsule	HECTOROL (doxercalciferol) CAPSULE
	RAYALDEE ER (calcifediol)
	ROCALTROL (calcitriol)
	ZEMPLAR (paricalcitrol) CAPSULE

Prior Authorization Criteria

- See Preferred Dosage Form criteria

Influenza

PREFERRED AGENTS (NO PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
oseltamivir	TAMIFLU (oseltamivir)
	XOFLUZA (baloxavir marboxil)

Electronic Age Verification

- Xofluza: The member must be 5 years of age or older

Prior Authorization Criteria

Initial Criteria - Approval Duration: 5 days

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

Neuromyelitis Optica Spectrum Disorder

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
ENSPRING (satralizumab-mwge)	SOLIRIS (eculizumab) – *Medical Billing Only*
UPLIZNA (inebilizumab) – *Medical Billing Only*	

Prior Authorization Criteria

Initial Criteria - Approval Duration: 6 months

- The member must meet FDA-approved label for use (e.g., use outside of studied population will be considered investigational).
- The requested medication must be prescribed by, or in consult with, a neurologist
- The member has positive serologic test for anti-AQP4 antibodies.
- The member has a history of ≥ 1 relapses that required rescue therapy within the past 12 months
- The member has an Expanded Disability Status Score (EDSS) of ≤ 6.5

Non-Preferred Agents Criteria

- The member must have had a 3-month trial with each of the preferred agents

Renewal Criteria - Approval Duration: 12 months

- The member must have experienced stabilization, slowing of disease progression, or improvement of the condition since starting treatment with the requested medication, as evidenced by medical documentation (e.g., chart notes) attached to the request (subject to clinical review) including:
  - Reduction in relapse rate
  - Reduction in symptoms (e.g., pain, fatigue, motor function)

Urea Cycle Agents

Hyperammonemia

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
BUPHENYL (sodium phenylbutyrate)	RAVICTI (glycerol phenylbutyrate)
PHEBURANE (sodium phenylbutyrate)	
sodium phenylbutyrate	

NAS Deficiency

PREFERRED AGENTS (CLINICAL PA REQUIRED)	NON-PREFERRED AGENTS (PA REQUIRED)
carglumic acid	CARBAGLU (carglumic acid)

Prior Authorization Criteria

See Medications that cost over $3000/month criteria

Non-Preferred Agents Criteria

- Carbaglu: See Preferred Dosage Form criteria
- Ravicti: The member is unable to tolerate sodium phenylbutyrate due to sodium content or GI distress

NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
2ND QUARTER 2023

Criteria Recommendations ***Approved Rejected***

1. Odevixibat / Overuse _____ _____

Alert Message: Bylvay (odevixibat) may be over-utilized. The recommended dosage of odevixibat is 40 mcg/kg once daily in the morning with a meal. If there is no improvement in pruritus after 3 months, the dosage may be increased in 40 mcg/kg increments up to 120 mcg/kg once daily not to exceed a total daily dose of 6 mg.

Drugs/Diseases

Util A	Util B	Util C
Odevixibat		

Max Dose: 6 mg/day

References:
Bylvay Prescribing Information, Oct. 2022, Albireo Pharm, Inc.
Clinical Pharmacology, 2023 Elsevier/Gold Standard.

2. Odevixibat / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Bylvay (odevixibat) for the treatment of pruritus in progressive familial intrahepatic cholestasis (PFIC) in adult patients, including those 65 years of age and older, have not been established.

Drugs/Diseases

Util A	Util B	Util C
Odevixibat		

Age Range: 18 - 999 yoa

References:
Bylvay Prescribing Information, Oct. 2022, Albireo Pharm, Inc.
Clinical Pharmacology, 2023 Elsevier/Gold Standard.

3. Odevixibat / Vitamin Deficiency _____ _____

Alert Message: Bylvay (odevixibat) may affect the absorption of fat-soluble vitamins (FSV). Obtain serum FSV levels at baseline and monitor during treatment, along with any clinical manifestations. If FSV deficiency is diagnosed, supplement with FSV. Discontinue odevixibat if FSV deficiency persists or worsens despite adequate FSV supplementation.

Drugs/Diseases

Util A	Util B	Util C
Odevixibat	Vitamin Deficiency A, D, E, & K	

References:
Bylvay Prescribing Information, Oct. 2022, Albireo Pharm, Inc.
Clinical Pharmacology, 2023 Elsevier/Gold Standard.

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

4. Odevixibat / Liver Test Abnormalities & Portal HTN _____ _____

Alert Message: Bylvay (odevixibat) can cause elevations of liver tests or worsening of liver tests relative to baseline values. Obtain baseline liver tests and monitor during treatment. Dose reduction or treatment interruption of odevixibat may be required if abnormalities occur. For persistent or recurrent liver test abnormalities, consider treatment discontinuation. Permanently discontinue treatment if a patient progresses to portal hypertension or experiences a hepatic decompensation event (e.g., variceal hemorrhage, ascites, hepatic encephalopathy).

Drugs/Diseases

Util A	Util B	Util C
Odevixibat	Abnormal Liver Function Studies	
	Ascites	
	Hepatic Encephalopathy	
	Portal Hypertension	
	Liver Failure	

References:

Bylvay Prescribing Information, Oct. 2022, Albireo Pharm, Inc.
Clinical Pharmacology, 2023 Elsevier/Gold Standard.

5. Odevixibat / Diarrhea _____ _____

Alert Message: Bylvay (odevixibat) treatment may cause diarrhea. If diarrhea occurs, monitor for dehydration and treat promptly. Interrupt odevixibat dosing if a patient experiences persistent diarrhea. Restart odevixibat at 40 mcg/kg/day when diarrhea resolves, and increase the dose as tolerated if appropriate. If diarrhea persists and no alternate etiology is identified, stop odevixibat treatment.

Drugs/Diseases

Util A	Util B	Util C
Odevixibat	Diarrhea	

References:

Bylvay Prescribing Information, Oct. 2022, Albireo Pharm, Inc.

6. Odevixibat / Bile Acid Resins _____ _____

Alert Message: Bile acid binding resins may bind Bylvay (odevixibat) in the gut, which may reduce odevixibat efficacy. Administer bile acid binding resins (e.g., cholestyramine, colesevelam, or colestipol) at least 4 hours before or 4 hours after administration of odevixibat.

Drugs/Diseases

Util A	Util B	Util C
Odevixibat	Cholestyramine	
	Colesevelam	
	Colestipol	

References:

Bylvay Prescribing Information, Oct. 2022, Albireo Pharm, Inc.
Clinical Pharmacology, 2023 Elsevier/Gold Standard.

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

7. Odevixibat / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no human data on Bylvay (odevixibat) use in pregnant persons to establish a drug-associated risk of major birth defects, miscarriage, or adverse developmental outcomes. Based on findings from animal reproduction studies, odevixibat may cause cardiac malformations when a fetus is exposed during pregnancy.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Bylvay Prescribing Information, Oct. 2022, Albireo Pharm, Inc.
Clinical Pharmacology, 2023 Elsevier/Gold Standard.

8. Odevixibat / Lactation _____ _____

Alert Message: There are no data on the presence of Bylvay (odevixibat) in human milk, the effects on the breastfed infant, or the effects on milk production. Odevixibat has low absorption following oral administration, and breastfeeding is not expected to result in exposure of the infant to odevixibat at the recommended doses; however, odevixibat may reduce the absorption of fat-soluble vitamins (FSV). Monitor FSV levels and increase FSV intake, if FSV deficiency is observed during lactation. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for odevixibat and any potential adverse effects on the breastfed child from odevixibat or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Odevixibat	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Bylvay Prescribing Information, Oct. 2022, Albireo Pharm, Inc.
Clinical Pharmacology, 2023 Elsevier/Gold Standard.

9. Sotorasib / Overuse _____ _____

Alert Message: Lumakras (sotorasib) may be over-utilized. The recommended dosage of sotorasib is 960 mg (eight 120 mg tablets) orally once daily until disease progression or unacceptable toxicity.

Drugs/Diseases

Util A	Util B	Util C
Sotorasib		

Max Dose:

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lumakras Prescribing Information, November 2022, Amgen Inc.

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

10. Sotorasib / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of Lumakras (sotorasib) have not been established in pediatric patients.

Drugs/Diseases

Util A	Util B	Util C
Sotorasib		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lumakras Prescribing Information, November 2022, Amgen Inc.

11. Sotorasib / Hepatotoxicity _____ _____
Alert Message: Lumakras (sotorasib) can cause hepatotoxicity, which may lead to drug-induced liver injury and hepatitis. Monitor liver function tests (ALT, AST, and total bilirubin) prior to the start of sotorasib, every 3 weeks for the first 3 months of treatment, then once a month or as clinically indicated, with more frequent testing in patients who develop transaminase and/or bilirubin elevations. Withhold, dose reduce or permanently discontinue sotorasib based on severity of adverse reaction.

Drugs/Diseases

Util A	Util B	Util C
Sotorasib		

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lumakras Prescribing Information, November 2022, Amgen Inc.

12. Sotorasib / Interstitial Lung Disease & Pneumonitis _____ _____
Alert Message: Lumakras (sotorasib) can cause ILD/pneumonitis, which can be fatal. Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, fever). Immediately withhold sotorasib in patients with suspected ILD/pneumonitis and permanently discontinue sotorasib if no other potential causes of ILD/pneumonitis are identified.

Drugs/Diseases

Util A	Util B	Util C
Sotorasib	Cough	
	Dyspnea	
	Fever	
	Acute Interstitial Pneumonia	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lumakras Prescribing Information, November 2022, Amgen Inc.

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

13. Sotorasib / Proton Pump Inhibitors _____ _____

Alert Message: The solubility of Lumakras (sotorasib) is pH-dependent. Coadministration of sotorasib with gastric acid-reducing agents decreased sotorasib concentrations, which may reduce the efficacy of sotorasib. Avoid coadministration of sotorasib with proton pump inhibitors (PPIs), H2 receptor antagonists, and locally acting antacids. If coadministration with an acid-reducing agent cannot be avoided, administer sotorasib 4 hours before or 10 hours after administration of a locally acting antacid.

Drugs/Diseases

Util A	Util B	Util C
Sotorasib	Antacids	
	H-2 Blockers	
	PPIs	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lumakras Prescribing Information, November 2022, Amgen Inc.

14. Sotorasib / Strong CYP3A4 Inducers _____ _____

Alert Message: Avoid the coadministration of Lumakras (sotorasib) with strong CYP3A4 inducers. Sotorasib is a CYP3A4 substrate. Coadministration of sotorasib with a strong CYP3A4 inducer decreased sotorasib concentrations, which may reduce the efficacy of sotorasib.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lumakras Prescribing Information, November 2022, Amgen Inc.

15. Sotorasib / CYP3A4 Substrates w/ NTI _____ _____

Alert Message: Lumakras (sotorasib) is a CYP3A4 inducer. Coadministration of sotorasib with a CYP3A4 substrate has been shown in drug interaction studies to decrease the substrate plasma concentrations, which may reduce the efficacy of the substrate. Avoid coadministration of sotorasib with CYP3A4 sensitive substrates, for which minimal concentration changes may lead to therapeutic failures of the substrate. If concurrent use cannot be avoided, increase the sensitive CYP3A4 substrate dosage in accordance with the substrate's prescribing information.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lumakras Prescribing Information, November 2022, Amgen Inc.

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

16. Sotorasib / P-gp Substrates w/ NTI _____ _____

Alert Message: Lumakras (sotorasib) is a P-gp inhibitor. Coadministration of sotorasib with a P-gp substrate has been shown in drug interaction studies to increase the P-gp substrate plasma concentrations, which may increase the adverse reactions of the substrate. Avoid coadministration of sotorasib with P-gp substrates, for which minimal concentration changes may lead to serious toxicities. If coadministration cannot be avoided, decrease the P-gp substrate dosage in accordance with the substrate's official prescribing information.

Drugs/Diseases

Util A	Util B		Util C
Sotorasib	Cyclosporine	Sirolimus	
	Digoxin	Tacrolimus	
	Everolimus		

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lumakras Prescribing Information, November 2022, Amgen Inc.

17. Sotorasib / BCRP Substrates _____ _____

Alert Message: Lumakras (sotorasib) is a BCRP inhibitor. Coadministration of sotorasib with a BCRP substrate has been shown in drug interaction studies to increase the substrate plasma concentrations, which may increase the risk of adverse reactions of the substrate. When coadministered with sotorasib, monitor for adverse reactions of the BCRP substrate and decrease the BCRP substrate dosage in accordance with the substrate's prescribing information.

Drugs/Diseases

Util A	Util B		Util C
Sotorasib	Alpelisib	Prazosin	
	Atorvastatin	Rosuvastatin	
	Dantrolene	Sulfasalazine	
	Dolutegravir	Talazoparib	
	Methotrexate	Tenofovir	
	Pazopanib	Topotecan	
	Pibrentasvir		

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lumakras Prescribing Information, November 2022, Amgen Inc.

18. Sotorasib / Lactation _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Sotorasib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Lumakras Prescribing Information, November 2022, Amgen Inc.

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

19. Sotorasib / Non-adherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Lumakras (sotorasib). 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

Sotorasib

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Ruddy K, Mayer E, Partridge A. Patient Adherence and Persistence With Oral Anticancer Treatment. CA Cancer J Clin 2009;59:56-66.
Greer JA, Amoyal N, Nisotel L, et al. Systemic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist. 2016;21:354-376.
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.1273

20. Tasimelteon LQ / Overutilization _____ _____

Alert Message: The recommended dosage of Hetlioz LQ (tasimelteon oral suspension) in pediatric patients 3 to 15 years of age weighing more than 28 kg is 20 mg one hour before bedtime, at the same time every night. The recommended dosage in pediatric patients 3 to 15 years of age weighing 28 kg of less is 0.7 mg/kg one hour before bedtime, at the same time every night.

Drugs/Diseases

Util A Util B Util C

Tasimelteon LQ

Max Dose: 20 mg/day

Age Range 3 - 15 yoa

References:

Hetlioz & Hetlioz LQ Prescribing Information, Dec. 2020, Vanda Pharmaceuticals Inc.
Clinical Pharmacology, 2023, Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.

21. Tasimelteon LQ / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Hetlioz LQ (tasimelteon oral suspension) for the treatment of nighttime sleep disturbances in SMS have not been established in patients younger than 3 years old.

Drugs/Diseases

Util A Util B Util C

Tasimelteon LQ

Age Range 0 – 2 yoa

References:

Hetlioz & Hetlioz LQ Prescribing Information, Dec. 2020, Vanda Pharmaceuticals Inc.
Clinical Pharmacology, 2023, Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.

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

22. Methylphenidate ER Tabs / Overutilization _____ _____

Alert Message: Relexxii (methylphenidate extended-release tablets) may be over-utilized. The manufacturer's recommended maximum daily dose of methylphenidate extended-release tablets for pediatric patients 6 to 12 years of age is 54 mg once daily.

Drugs/Diseases

Util A	Util B	Util C
Methylphenidate ER Tabs		

Max Dose: 54 mg/day

Age Range 6 - 12 yoa

References:

Relexxii Prescribing Information, June 2022, Vertical Pharmaceuticals, LLC.

Clinical Pharmacology, 2023, Elsevier/Gold Standard.

Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.

23. Opioids / CNS Depressants _____ _____

Alert Message: The concomitant use of opioids with CNS depressants, including alcohol, can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death. Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate. Limit dosages and durations to the minimum required. Follow patients closely for signs of respiratory depression and sedation.

Drugs/Diseases

Util A	Util B	Util C
Benzhydrocodone	CNS Depressants	
Codeine		
Fentanyl		
Dihydrocodeine		
Hydrocodone		
Hydromorphone		
Levorphanol		
Meperidine		
Methadone		
Morphine		
Oxycodone		
Oxymorphone		
Tapentadol		
Tramadol		
Buprenorphine (pain)		

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

Criteria Recommendations ***Approved Rejected***

24. Dextromethorphan/Bupropion / Overuse _____ _____
Alert Message: Auvelity (dextromethorphan/bupropion) may be over-utilized. The maximum recommended dosage of dextromethorphan/bupropion is one tablet twice daily, given at least 8 hours apart. Do not exceed two doses within the same day.

Drugs/Diseases

Util A	Util B	Util C
Dextromethorphan/Bupropion		

Max Dose: 2 tablets/day

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Auvelity Prescribing Information, August 2022, Axsome Therapeutics.

25. Dextromethorphan/Bupropion / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of Auvelity (dextromethorphan/bupropion) have not been established in pediatric patients.

Drugs/Diseases

Util A	Util B	Util C
Dextromethorphan/Bupropion		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Auvelity Prescribing Information, August 2022, Axsome Therapeutics.

26. Dextromethorphan/Bupropion / Contraindicated Disease States _____ _____
Alert Message: The use of Auvelity (dextromethorphan/bupropion) is contraindicated in patients with seizure disorders, a current or prior diagnosis of bulimia or anorexia nervosa, and those who are undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiepileptic medications. The bupropion component of the combination product can cause seizures.

Drugs/Diseases

Util A	Util B	Util C (Include)
Dextromethorphan/Bupropion		Seizures Bulimia Anorexia

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Auvelity Prescribing Information, August 2022, Axsome Therapeutics.

Criteria Recommendations ***Approved Rejected***

27. Dextromethorphan/Bupropion / MAO Inhibitors _____ _____

Alert Message: The use of Auvelity (dextromethorphan/bupropion) is contraindicated in patients taking, or within 14 days of stopping, MAOIs due to the risk of serious and possibly fatal drug interactions, including hypertensive crisis and serotonin syndrome. Starting dextromethorphan/bupropion in a patient treated with reversible MAOIs such as linezolid or intravenous methylene blue is contraindicated.

Drugs/Diseases

Util A	Util B	Util C
Dextromethorphan/Bupropion	Isocarboxazid	
	Phenelzine	
	Tranylcypromine	
	Linezolid	
	Methylene Blue	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Auvelity Prescribing Information, August 2022, Axsome Therapeutics.

28. Dextromethorphan/Bupropion / Severe Renal Impairment _____ _____

Alert Message: The pharmacokinetics of Auvelity (dextromethorphan/bupropion) have not been evaluated in patients with severe renal impairment. Dextromethorphan/bupropion is not recommended in patients with severe renal impairment (eGFR 15 to 29 mL/minute/1.73m2).

Drugs/Diseases

Util A	Util B	Util C (Include)
Dextromethorphan/Bupropion		CKD Stage 4

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Auvelity Prescribing Information, August 2022, Axsome Therapeutics.

29. Dextromethorphan/Bupropion / Severe Hepatic Impairment _____ _____

Alert Message: The pharmacokinetics of Auvelity (dextromethorphan/bupropion) have not been evaluated in patients with severe hepatic impairment. Dextromethorphan/bupropion is not recommended in patients with severe hepatic renal impairment (Child-Pugh C).

Drugs/Diseases

Util A	Util B	Util C (Include)
Dextromethorphan/Bupropion		Cirrhosis
		Liver Failure

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Auvelity Prescribing Information, August 2022, Axsome Therapeutics.

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

30. Dextromethorphan/Bupropion / Overuse – Mod Renal Imp. _____ _____
Alert Message: Auvelity (dextromethorphan/bupropion) may be over-utilized. The maximum recommended dosage of dextromethorphan/bupropion in patients with moderate renal impairment (eGFR 30 to 59 mL/min/1.73m2) is one tablet once daily in the morning.

Drugs/Diseases

Util A	Util B	Util C (Include)
Dextromethorphan/Bupropion		CKD Stage 3

Max Dose: 1 tablet/day

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Auvelity Prescribing Information, August 2022, Axsome Therapeutics.

31 Dextromethorphan/Bupropion / Strong CYP2D6 Inhibitors _____ _____
Alert Message: Concomitant use of Auvelity (dextromethorphan/bupropion) with strong CYP2D6 inhibitors increases plasma concentrations of the dextromethorphan component of the combination product. Dosage adjustment is necessary when dextromethorphan/bupropion is co-administered with strong inhibitors of CYP2D6. The recommended dosage of dextromethorphan/bupropion, when co-administered with strong CYP2D6 inhibitors, is one tablet once daily in the morning. Monitor patients for adverse reactions potentially attributable to dextromethorphan, such as somnolence and dizziness.

Drugs/Diseases

Util A	Util B	Util C (Include)
Dextromethorphan/Bupropion		Fluoxetine
		Dacomitinib
		Paroxetine
		Quinidine

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Auvelity Prescribing Information, August 2022, Axsome Therapeutics.

32. Dextromethorphan/Bupropion / Strong CYP2B6 Inducers _____ _____
Alert Message: Concomitant use of Auvelity (dextromethorphan/bupropion) with strong CYP2B6 inducers decreases plasma concentrations of both bupropion and dextromethorphan and may decrease efficacy. Avoid co-administration of dextromethorphan/bupropion with strong CYP2B6 inducers.

Drugs/Diseases

Util A	Util B	Util C
Dextromethorphan/Bupropion	Phenobarbital	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Auvelity Prescribing Information, August 2022, Axsome Therapeutics.

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

33. Dextromethorphan/Bupropion / Drug That Decrease Seizure Threshold _____ _____

Alert Message: Coadministration of Auvelity (dextromethorphan/bupropion) and drugs that lower the seizure threshold should be approached with caution. Drugs such as antidepressants, antipsychotics, theophylline, and systemic steroids may have an additive effect with the bupropion component of the combination product, thereby increasing the risk of seizures.

Drugs/Diseases

Util A	Util B 1209	Util C
Dextromethorphan/Bupropion	Antidepressants	
	Antipsychotics	
	Baclofen	
	Metoclopramide	
	Theophylline	
	Tramadol	
	Steroids	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Auvelity Prescribing Information, August 2022, Axsome Therapeutics.

34. Dextromethorphan/Bupropion / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on animal studies, Auvelity (dextromethorphan/bupropion) may cause fetal harm when administered during pregnancy. Dextromethorphan/bupropion is not recommended during pregnancy. If a female becomes pregnant while being treated with dextromethorphan/bupropion, discontinue treatment and counsel the patient about the potential risk to a fetus.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Dextromethorphan/Bupropion	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Auvelity Prescribing Information, August 2022, Axsome Therapeutics.

35. Dextromethorphan/Bupropion / Lactation _____ _____

Alert Message: Because of the potential for neurotoxicity, advise patients that breastfeeding is not recommended during treatment with Auvelity (dextromethorphan/bupropion) and for 5 days following the final dose.

Drugs/Diseases

Util A	Util B	Util C
Dextromethorphan/Bupropion	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Auvelity Prescribing Information, August 2022, Axsome Therapeutics.

Criteria Recommendations ***Approved Rejected***

36. Dextromethorphan/Bupropion / Non-adherence _____ _____
Alert Message: Based on refill history, your patient may be under-utilizing Auvelity (dextromethorphan/bupropion). 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
Dextromethorphan/Bupropion		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Iuga AO, McGuire MJ. Adherence and Health Care Costs. Risk Manag Healthc Policy. 2014 Feb 20;7:35-44.
Chong WW, Aslani P, Chen TF. Effectiveness of Interventions to Improve Antidepressant Medication Adherence: A Systematic Review. Int J Clin Pract. 2011 Sep;65(9)954-975.

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

37. Tivozanib / Overuse _____ _____
Alert Message: Fotivda (tivozanib) may be over-utilized. The recommended dosage of tivozanib is 1.34 mg taken orally once daily for 21 days on treatment, followed by 7 days off treatment for a 28-day cycle.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Tivozanib		Moderate Hepatic Impairment Severe Hepatic Impairment

Max Dose: 1.34 mg/day

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Fotivda Prescribing Information, March 2021, Aveo Pharmaceuticals, Inc.

38. Tivozanib 1.34 mg / Overuse Hepatic Impairment _____ _____
Alert Message: Fotivda (tivozanib) may be over-utilized. The recommended dosage of tivozanib in patients with moderate hepatic impairment (total bilirubin > 1.5 to 3 times UKN with any AST) is 0.89 mg taken orally once daily for 21 days on treatment, followed by 7 days off treatment for a 28-day cycle. The recommended dosage of tivozanib in patients with severe hepatic impairment has not been established.

Drugs/Diseases

Util A	Util B	Util C
Tivozanib 1.34	Moderate Liver Impairment Severe Liver Impairment	

Max Dose: 0.89 mg/day

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Fotivda Prescribing Information, March 2021, Aveo Pharmaceuticals, Inc.

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

39. Tivozanib / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of Fotivda (tivozanib) in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C
Tivozanib		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Fotivda Prescribing Information, March 2021, Aveo Pharmaceuticals, Inc.

40. Tivozanib / Cardiac Failure _____ _____
Alert Message: Fotivda (tivozanib) can cause serious, sometimes fatal, cardiac failure. Tivozanib has not been studied in patients with symptomatic cardiac failure within the preceding 6 months before tivozanib treatment initiation. Periodically monitor patients for symptoms of cardiac failure throughout treatment with tivozanib. Management of cardiac failure events may require interruption, dose reduction, or permanent discontinuation of tivozanib therapy.

Drugs/Diseases

Util A	Util B	Util C
Tivozanib	Cardiac Failure	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Fotivda Prescribing Information, March 2021, Aveo Pharmaceuticals, Inc.

41. Tivozanib / Hypertension _____ _____
Alert Message: Fotivda (tivozanib) can cause severe hypertension and hypertensive crisis. Control blood pressure prior to treatment with tivozanib. Monitor blood pressure after 2 weeks and at least monthly thereafter during treatment with tivozanib. Treat patients with antihypertensive therapy when hypertension occurs during treatment with tivozanib. Withhold tivozanib for severe hypertension despite optimal anti-hypertensive therapy. For persistent hypertension, despite the use of anti-hypertensive medications, reduce the tivozanib dose. Discontinue tivozanib if hypertension is severe and persistent despite anti-hypertensive therapy and dose reduction of tivozanib, or in patients who experience hypertensive crisis.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Tivozanib	Hypertension	Antihypertensive Agents

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Fotivda Prescribing Information, March 2021, Aveo Pharmaceuticals, Inc.

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

42. Tivozanib / Cardiac Ischemia & Arterial Thromboembolic Events _____ _____

Alert Message: Fotivda (tivozanib) can cause serious, sometimes fatal, cardiac ischemia and arterial thromboembolic events. Tivozanib has not been studied in patients who had an arterial thrombotic event, myocardial infarction, or unstable angina within the preceding 6 months before tivozanib treatment initiation. Closely monitor patients who are at risk for or have a history of these events (such as myocardial infarction and stroke) during treatment with ‘ tivozanib. Discontinue tivozanib in patients who develop any severe or life-threatening arterial thromboembolic event.

Drugs/Diseases

Util A	Util B	Util C
Tivozanib	Arterial Embolism and Thrombosis	
	Myocardial Infarction	
	Unstable Angina	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Fotivda Prescribing Information, March 2021, Aveo Pharmaceuticals, Inc.

43. Tivozanib / Venous Thromboembolic Events _____ _____

Alert Message: Fotivda (tivozanib) can cause serious, sometimes fatal, venous thromboembolic events. Closely monitor patients who are at risk for or have a history of these events during treatment with tivozanib. Discontinue tivozanib in patients who develop any severe or life-threatening venous thromboembolic event.

Drugs/Diseases

Util A	Util B	Util C
Tivozanib	Venous Embolism and Thrombosis	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Fotivda Prescribing Information, March 2021, Aveo Pharmaceuticals, Inc.

44. Tivozanib / Hemorrhagic Events _____ _____

Alert Message: Fotivda (tivozanib) can cause serious, sometimes fatal, hemorrhagic events. Tivozanib has not been studied in patients with significant bleeding within the preceding 6 months before tivozanib treatment initiation. Closely monitor patients who are at risk for or who have a history of bleeding during treatment with tivozanib. Discontinue tivozanib in patients who develop severe or life-threatening hemorrhagic events.

Drugs/Diseases

Util A	Util B	Util C
Tivozanib	Hemorrhage	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Fotivda Prescribing Information, March 2021, Aveo Pharmaceuticals, Inc.

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

45. Tivozanib / Proteinuria _____ _____

Alert Message: Fotivda (tivozanib) can cause proteinuria. In clinical trial experience, proteinuria occurred in 8% of tivozanib-treated patients, with 2% of events Grade 3. Of the patients who developed proteinuria, 3/81 (3.7%) had acute kidney injury either concurrently or later during treatment. Monitor patients for proteinuria before initiation of, and periodically throughout, treatment with tivozanib. For patients who develop moderate to severe proteinuria reduce the dose or interrupt tivozanib treatment. Discontinue tivozanib in patients who develop nephrotic syndrome.

Drugs/Diseases

Util A	Util B	Util C
Tivozanib	Proteinuria	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Fotivda Prescribing Information, March 2021, Aveo Pharmaceuticals, Inc.

46. Tivozanib / Thyroid Dysfunction _____ _____

Alert Message: Fotivda (tivozanib) can cause thyroid dysfunction. In clinical trial experience, thyroid dysfunction events in tivozanib patients occurred in 11%, with 0.3% Grade 3 or 4 events. Hypothyroidism was reported in 8% of patients and hyperthyroidism was reported in 1% of patients. Monitor thyroid function before initiation of, and periodically throughout, treatment with tivozanib. Treat hypothyroidism and hyperthyroidism to maintain euthyroid state before and during treatment with tivozanib.

Drugs/Diseases

Util A	Util B	Util C
Tivozanib	Hyperthyroidism	
	Hypothyroidism	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Fotivda Prescribing Information, March 2021, Aveo Pharmaceuticals, Inc.

47. Tivozanib / Reversible Posterior Leukoencephalopathy Syndrome _____ _____

Alert Message: Reversible posterior leukoencephalopathy syndrome (RPLS), a syndrome of subcortical vasogenic edema diagnosed by MRI, can occur with Fotivda (tivozanib). Evaluation for RPLS in any patient presenting with seizures, headaches, visual disturbances, confusion, or altered mental function. Discontinue tivozanib in patients who develop RPLS.

Drugs/Diseases

Util A	Util B	Util C
Tivozanib	Altered Mental Function	
	Headaches	
	Seizures	
	Visual Disturbances	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Fotivda Prescribing Information, March 2021, Aveo Pharmaceuticals, Inc.

Criteria Recommendations	*Approved*	*Rejected*

48. Tivozanib / Strong CYP3A4 Inducers _____ _____

Alert Message: Avoid concomitant use of strong CYP3A inducers with Fotivda (tivozanib). Concomitant use of tivozanib with a strong CYP3A inducer decreases tivozanib exposure, which may reduce tivozanib anti-tumor activity.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Fotivda Prescribing Information, March 2021, Aveo Pharmaceuticals, Inc.

49. Tivozanib / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on findings from animal studies and its mechanism of action, Fotivda (tivozanib) can cause fetal harm when administered to a pregnant woman. In embryo-fetal developmental studies, oral administration of tivozanib to pregnant animals during the period of organogenesis caused maternal toxicity, fetal malformations, and embryo-fetal death at doses below the maximum recommended clinical dose on a mg/m2 basis. Advise the pregnant patient of the potential risk to the fetus.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Fotivda Prescribing Information, March 2021, Aveo Pharmaceuticals, Inc.

50. Tivozanib / Lactation _____ _____

Alert Message: There are no data on the presence of Fotivda (tivozanib) in human milk or the effects of tivozanib on the breastfed child or milk production. Because of the potential for serious adverse reactions in a breastfed child, advise a lactating woman not to breastfeed during treatment with tivozanib and for one month after the last dose.

Drugs/Diseases

Util A	Util B	Util C
Tivozanib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Fotivda Prescribing Information, March 2021, Aveo Pharmaceuticals, Inc.

51. Tivozanib / Therapeutic Appropriateness _____ _____
Alert Message: Advise females of reproductive potential to use effective contraception during treatment with Fotivda (tivozanib) and for one month after the last dose. Based on findings from animal studies and its mechanism of action, tivozanib can cause fetal harm when administered to a pregnant woman.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Tivozanib		Contraceptives

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Fotivda Prescribing Information, March 2021, Aveo Pharmaceuticals, Inc.

52. Tivozanib / Therapeutic Appropriateness _____ _____
Alert Message: Advise males with female partners of reproductive potential to use effective contraception during treatment with Fotivda (tivozanib) and for one month after the last dose.

Drugs/Diseases

Util A	Util B	Util C
Tivozanib		

Gender: Male

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Fotivda Prescribing Information, March 2021, Aveo Pharmaceuticals, Inc.

53. Tivozanib / Non-adherence _____ _____
Alert Message: Based on refill history, your patient may be under-utilizing Fotivda (tivozanib). 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
Tivozanib		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Ruddy K, Mayer E, Partridge A. Patient Adherence and Persistence With Oral Anticancer Treatment. CA Cancer J Clin 2009;59:56-66.

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

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.1273

Criteria Recommendations ***Approved Rejected***

54. Aripiprazole ER Injection 675mg / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of Aristada Initio (aripiprazole lauroxil extended-release injection) in patients less than 18 years of age have not been evaluated.

Drugs/Diseases

Util A	Util B	Util C
Aripiprazole 675mg Injection		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Aristada Initio Prescribing Information, March 2021, Alkermes, Inc.

55. Aripiprazole ER Injection / Therapeutic Appropriateness _____ _____
Alert Message: The safety and effectiveness of Aristada (aripiprazole lauroxil extended-release injection) in patients less than 18 years of age have not been evaluated.

Drugs/Diseases

Util A	Util B	Util C
Aripiprazole ER Injection		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Aristada Prescribing Information, March 2021, Alkermes, Inc.

56. Aripiprazole ER Injection 441mg / Strong CYP3A4 Inducers _____ _____
Alert Message: Aripiprazole is a CYP3A4 substrate, and concomitant use with a strong CYP3A4 inducer can result in decreased aripiprazole exposure. If Aristada 441 mg (aripiprazole extended-release injection) is used with a strong CYP3A4 inducer for more than 2 weeks, consider increasing the dose of aripiprazole to the next higher strength, 662 mg. No dosage adjustment is needed for the 662 mg, 882 mg, or 1064 mg dose.

Drugs/Diseases

Util A	Util B		Util C
Aripiprazole ER Inj 441mg	Apalutamide	Phenobarbital	
	Carbamazepine	Phenytoin	
	Enzalutamide	Primidone	
	Mitotane	Rifampin	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Aristada Prescribing Information, March 2021, Alkermes, Inc.

57. Aripiprazole ER Injection / Strong 3A4 & 2D6 Inhibitors _____ _____

Alert Message: Aripiprazole is a CYP3A4 and CYP2D6 substrate, and concomitant use with a strong CYP3A4 or CYP2D6 inhibitor can result in increased aripiprazole exposure. If Aristada (aripiprazole lauroxil extended-release injection) is used with a strong CYP3A4 inhibitor or CYP2D6 inhibitor for more than 2 weeks, reduce the dose of aripiprazole to the next lower strength. No dosage adjustment is necessary for patients taking the 441 mg aripiprazole injection, if tolerated. Avoid the use of aripiprazole 662 mg, 882 mg, or 1064 mg with drugs that strongly inhibit both CYP3A4 and CPY2D6.

Drugs/Diseases

Util A	Util B	Util C
Aripiprazole ER Inj 662mg	Clarithromycin	Bupropion
Aripiprazole ER Inj 882mg	Cobicistat	Fluoxetine
Aripiprazole ER Inj 1064mg	Itraconazole	Paroxetine
	Ketoconazole	Quinidine
	Nefazodone	Terbinafine
	Nelfinavir	
	Posaconazole	
	Ritonavir	
	Voriconazole	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Aristada Prescribing Information, March 2021, Alkermes, Inc

58. Aripiprazole ER 675 mg Injection / Aripiprazole ER Maintenance Injec _____ _____

Alert Message: Aristada Initio (aripiprazole lauroxil 675 mg extended-release injection) is only to be used as a single dose to initiate Aristada (aripiprazole lauroxil extended-release injection) treatment or as a single dose to re-initiate Aristada treatment following a missed dose of Aristada. Aristada Initio is not for repeated dosing.

Drugs/Diseases

Util A	Util B	Util C
Aristada Initio	Aristada	

Day Supply
Util A: Aristada Initio - 90 days
Util B: Aristada - 90 days

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Aristada Prescribing Information, March 2021, Alkermes, Inc

59. Paliperidone ER q 6 mo Injection / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Invega Hafyera (6-month paliperidone extended-release injection) in patients less than 18 years of age have not been established. The use of extended-release injectable paliperidone is not recommended in pediatric patients because of the potential longer duration of an adverse event. In clinical trials of oral paliperidone, there were notably higher incidences of dystonia, hyperkinesia, tremor, and parkinsonism in the adolescent population as compared to the adult studies.

Drugs/Diseases

Util A	Util B	Util C
Paliperidone 6 mo Inject		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Invega Hafyera Prescribing Information, August 2021, Janssen Pharmaceuticals, Inc.

60. Paliperidone ER q 6 mo Injection / Renal Impairment _____ _____

Alert Message: The use of Invega Hafyera (6-month paliperidone extended-release injection) is not recommended for use in patients with mild, moderate, or severe renal impairment (creatinine clearance < 90 mL/min) because necessary dosage adjustment is not possible with available strengths of the paliperidone injection. Paliperidone is substantially excreted by the kidney, and clearance is decreased in patients with renal impairment.

Drugs/Diseases

Util A	Util B	Util C
Paliperidone 6-Mo Inject	Renal Impairment	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Invega Hafyera Prescribing Information, August 2021, Janssen Pharmaceuticals, Inc.

61. Paliperidone ER 3 mo Injection / Moderate to Severe Renal Impairment _____ _____

Alert Message: The use of Invega Trinza (3-month paliperidone extended-release injection) is not recommended in patients with moderate or severe renal impairment (creatinine clearance < 50 mL/min). Paliperidone is substantially excreted by the kidney, and clearance is decreased in patients with renal impairment.

Drugs/Diseases

Util A	Util B	Util C
Paliperidone 3 mo Inject	CKD Stage 3, 4 & 5 ESRD	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Invega Trinza Prescribing Information, August 2021, Janssen Pharmaceuticals, Inc.

62. Paliperidone ER 3 mo Injection / Mild Renal Impairment _____ _____

Alert Message: Dose reduction of Invega Trinza (3-month paliperidone extended-release injection) is recommended for patients with mild renal impairment. Paliperidone is substantially excreted by the kidney, and clearance is decreased in patients with renal impairment. For patients with mild renal impairment (creatinine clearance >/= 50 mL/min to < 80 mL/min (Cockcroft-Gault Formula), adjust the dosage and stabilize the patient using the 1-month paliperidone palmitate extended-release injectable suspension, then transition to 3-month paliperidone extended-release injection.

Drugs/Diseases

Util A	Util B	Util C
Paliperidone 3 mo Inject	CKD Stage 2	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Invega Trinza Prescribing Information, August 2021, Janssen Pharmaceuticals, Inc.

63. Paliperidone ER Monthly Injection / Mod to Severe Renal Impairment _____ _____

Alert Message: Use of Invega Sustenna (monthly paliperidone extended-release injection) is not recommended in patients with moderate or severe renal impairment (creatinine clearance < 50 mL/min). Paliperidone is substantially excreted by the kidney and clearance is decreased in patients with renal impairment.

Drugs/Diseases

Util A	Util B	Util C
Paliperidone Monthly Inject	CKD Stage 3, 4 & 5 ESRD	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Invega Sustenna Prescribing Information, July 2022, Janssen Pharmaceuticals, Inc.

64. Paliperidone ER 234 mg Monthly Injection / Mild Renal Impairment _____ _____

Alert Message: Dose reduction of Invega Sustenna (monthly paliperidone extended-release injection) is recommended for patients with mild renal impairment (creatinine clearance ≥ 50 mL/min to < 80 mL/min). Paliperidone is substantially excreted by the kidney and clearance is decreased in patients with renal impairment. The maximum monthly dose of the paliperidone injection is 156 mg for patients with mild renal impairment. Use of monthly paliperidone extended-release injection is not recommended in patients with moderate or severe renal impairment (creatinine clearance < 50 mL/min).

Drugs/Diseases

Util A	Util B	Util C
Paliperidone Monthly Inject 234mg	CKD Stage 2	

Max Dose: 156 mg/month

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Invega Sustenna Prescribing Information, July 2022, Janssen Pharmaceuticals, Inc.

Criteria Recommendations ***Approved Rejected***

65. Paliperidone ER Injections - All / Strong CYP3A4 & P-gp Inducers _____ _____

Alert Message: The concurrent use of paliperidone extended-release injection (e.g., Invega Sustenna, Invega Trinza, or Invega Hafyera) with a strong CYP3A4 or P-gp inducer may decrease the exposure to paliperidone. Paliperidone is a CYP3A4 and P-gp substrate. Avoid using strong CYP3A4 or P-gp inducers with a paliperidone injection during the dosing interval for the injection, if possible. If administering a strong inducer is necessary, consider managing the patient using paliperidone extended-release tablets.

Drugs/Diseases

Util A	Util B	Util C
Paliperidone Injections	Apalutamide	
	Carbamazepine	
	Phenobarbital	
	Phenytoin	
	Primidone	
	Rifampin	

References:

Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Invega Hafyera Prescribing Information, August 2021, Janssen Pharmaceuticals, Inc.
Invega Sustenna Prescribing Information, July 2022, Janssen Pharmaceuticals, Inc.
Invega Trinza Prescribing Information, August 2021, Janssen Pharmaceuticals, Inc.

66. Fingolimod / Overuse _____ _____

Alert Message: Tascenso ODT (fingolimod) may be over-utilized. The manufacturer's maximum recommended dose of fingolimod for adults and pediatric patients 10 years of age and older weighing more than 40 kg is 0.5 mg daily. In pediatric patients 10 years of age and older weighing less than or equal to 40 kg, the recommended dosage of fingolimod is 0.25 mg orally once daily.

Drugs/Diseases

Util A	Util B	Util C
Fingolimod		

Max Dose: 0.5 mg/day

Age Range: 10 – 999 yoa

References:

Tascenso ODT Prescribing Information, Dec. 2022, Cycle Pharmaceuticals Ltd.
Clinical Pharmacology, 2023 Elsevier/Gold Standard.

67. Fingolimod / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Tascenso ODT (fingolimod) have not been established in patients less than 10 years of age.

Drugs/Diseases

Util A	Util B	Util C
Fingolimod		

Age Range: 0 – 9 yoa

References:

Tascenso ODT Prescribing Information, Dec. 2022, Cycle Pharmaceuticals Ltd.

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

68. Fingolimod / Class Ia or Class III Antiarrhythmic Drugs _____ _____

Alert Message: Concurrent use of Tascenso ODT (fingolimod) with Class Ia or Class III antiarrhythmic drugs is contraindicated. Initiation of fingolimod results in decreased heart rate, and Class Ia/III antiarrhythmics have been associated with cases of torsades de pointes in patients with bradycardia.

Drugs/Diseases

Util A	Util B		Util C
Fingolimod	Quinidine (Ia)	Amiodarone (III)	
	Procainamide (Ia)	Sotalol (III)	
	Disopyramide (Ia)		

References:

Tascenso ODT Prescribing Information, Dec. 2022, Cycle Pharmaceuticals Ltd.

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

Criteria Recommendations ***Approved Rejected***

69. Fingolimod / Cardiovascular Risk _____ _____

Alert Message: Tascenso ODT (fingolimod) is contraindicated in patients who have experienced myocardial infarction, unstable angina, stroke, TIA, decompensated heart failure requiring hospitalization, or Class III/IV heart failure in the last 6 months. Patients with these preexisting conditions may poorly tolerate fingolimod-induced bradycardia or experience serious rhythm disturbances after the first dose of fingolimod.

Drugs/Diseases

Util A	Util B	Util C (Include)
Fingolimod		Myocardial Infarction
		Unstable Angina
		Stroke/TIA
		Heart Failure

References:

Tascenso ODT Prescribing Information, Dec. 2022, Cycle Pharmaceuticals Ltd.

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

70. Fingolimod / 2nd or 3rd Degree Heart Block & Sick Sinus Syndrome _____ _____

Alert Message: The use of Tascenso ODT (fingolimod) is contraindicated in patients with a history or presence of Mobitz Type II second- or third-degree atrioventricular (AV) block or sick sinus syndrome unless the patient has a functioning pacemaker.

Drugs/Diseases

Util A	Util B	Util C (Include)
Fingolimod		Mobitz Type II AV Block
		Sick Sinus Syndrome

References:

Tascenso ODT Prescribing Information, Dec. 2022, Cycle Pharmaceuticals Ltd.

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

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

71. Fingolimod / QT Prolongation _____ _____

Alert Message: All patients should have an electrocardiogram (ECG) prior to initiation of Tascenso ODT (fingolimod) therapy. The use of fingolimod is contraindicated in patients with QT prolongation (defined as a baseline QTc interval >/= 500 msec).

Drugs/Diseases

Util A	Util B	Util C (Include)
Fingolimod		QT Prolongation

References:
Tascenso ODT Prescribing Information, Dec. 2022, Cycle Pharmaceuticals Ltd.
Clinical Pharmacology, 2023 Elsevier/Gold Standard.

72. Fingolimod / Macular Edema _____ _____

Alert Message: Patients with a history of uveitis and patients with diabetes mellitus are at increased risk of macular edema during Tascenso ODT (fingolimod) therapy. It is recommended that these patients undergo an adequate ophthalmologic evaluation and have regular follow-up evaluations while receiving fingolimod therapy.

Drugs/Diseases

Util A	Util B	Util C (Include)
Fingolimod		Diabetes Mellitus
		Uveitis

References:

Tascenso ODT Prescribing Information, Dec. 2022, Cycle Pharmaceuticals Ltd.

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

73. Fingolimod / Increased Risk of Infection Meds _____ _____

Alert Message: Tascenso ODT (fingolimod) therapy leads to a dose-dependent reduction in peripheral lymphocyte count, and concomitant use with antineoplastic, immunosuppressive, or immune modulating therapies would be expected to increase the risk of immunosuppression.

Drugs/Diseases

Util A	Util B	Util C
Fingolimod	Antineoplastic Agents	
	Immunosuppressants	
	Immune Modulating therapies	

References:
Tascenso ODT Prescribing Information, Dec. 2022, Cycle Pharmaceuticals Ltd.
Clinical Pharmacology, 2023 Elsevier/Gold Standard.

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

74. Fingolimod / Ketoconazole _____ _____

Alert Message: Ketoconazole is a potent inhibitor of CYP3A and CYP4F. The blood levels of Tascenso ODT (fingolimod) and its active metabolite fingolimod-phosphate are increased by 1.7-fold when used concomitantly with ketoconazole. If ketoconazole and fingolimod must be co-administered, patients should be closely monitored, as the risk of adverse reactions is greater.

Drugs/Diseases

Util A	Util B	Util C
Fingolimod	Ketoconazole	

References:

Tascenso ODT Prescribing Information, Dec. 2022, Cycle Pharmaceuticals Ltd.
Clinical Pharmacology, 2023 Elsevier/Gold Standard.

75. Fingolimod / Cardiovascular Drugs _____ _____

Alert Message: Patients receiving concurrent therapy with Tascenso ODT (fingolimod) and drugs that slow heart rate or atrioventricular (AV) conduction (e.g., beta-blockers or digoxin) should be carefully evaluated prior to starting therapy. Concomitant treatment may be associated with severe bradycardia or heart block.

Drugs/Diseases

Util A	Util B	Util C
Fingolimod	Digoxin	
	Beta-blockers	
	Verapamil	
	Diltiazem	

References:

Tascenso ODT Prescribing Information, Dec. 2022, Cycle Pharmaceuticals Ltd.
Clinical Pharmacology, 2023 Elsevier/Gold Standard.

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

76. Fingolimod / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Based on findings from animal studies, Tascenso ODT (fingolimod) may cause fetal harm when administered to a pregnant woman. In animal reproduction studies conducted in rats and rabbits, developmental toxicity was observed with administration of fingolimod at doses less than the recommended human dose. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Because it takes approximately 2 months to eliminate fingolimod from the body, advise females of reproductive potential to use effective contraception to avoid pregnancy during and for 2 months after stopping fingolimod treatment.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Fingolimod	Pregnancy ICD-9s	Delivery
		Miscarriage
		Abortion

References:

Tascenso ODT Prescribing Information, Dec. 2022, Cycle Pharmaceuticals Ltd.

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

77. Fingolimod / Lactation _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Fingolimod	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Tascenso ODT Prescribing Information, Dec. 2022, Cycle Pharmaceuticals Ltd.

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

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

78. Fingolimod / Drugs that Prolong QT Interval _____ _____

Alert Message: Tascenso ODT (fingolimod) should be used with extreme caution with drugs that prolong the QT interval. Drugs that prolong the QT interval have been associated with cases of torsades de pointes in patients with bradycardia.

Drugs/Diseases

Util A	Util B				Util C
Fingolimod	Albuterol	Alfuzosin	Amantadine	Amitriptyline	
	Asenapine	Atazanavir	Atomoxetine	Azithromycin	
	Chloral Hydrate	Chloroquine	Chlorpromazine	Ciprofloxacin	
	Citalopram	Clarithromycin	Clomipramine	Clozapine	
	Crizotinib	Dasatinib	Desipramine	Diphenhydramine	
	Dofetilide	Dolasetron	Doxepin	Dronedarone	
	Droperidol	Erythromycin	Escitalopram	Famotidine	
	Felbamate	Fesoterodine	Flecainide	Fluconazole	
	Fluoxetine	Fluphenazine	Formoterol	Foscarnet	
	Fosphenytoin	Galantamine	Gemifloxacin	Granisetron	
	Haloperidol	Ibutilide	Iloperidone	Imipramine	
	Indapamide	Isradipine	Itraconazole	Lapatinib	
	Levalbuterol	Levofloxacin	Lithium	Maprotiline	
	Mefloquine	Methadone	Mexiletine	Moexipril	
	Moxifloxacin	Naratriptan	Nelfinavir	Nicardipine	
	Nilotinib	Norfloxacin	Nortriptyline	Octreotide	
	Ofloxacin	Ondansetron	Paliperidone	Paroxetine	
	Pazopanib	Pentamidine	Perphenazine	Pimozide	
	Posaconazole	Propafenone	Protriptyline	Quetiapine	
	Quinine	Ranolazine	Risperidone	Ritonavir	
	Salmeterol	Sertraline	Solifenacin	Tamoxifen	
	Sumatriptan	Sunitinib	Tacrolimus	Tocainide	
	Telithromycin	Thioridazine	Tizanidine	Tolterodine	
	Trazodone	Trifluoperazine	Trimipramine	Voriconazole	
	Vandetanib	Vardenafil	Venlafaxine	Ziprasidone	

*Amiodarone, disopyramide, ketoconazole, procainamide, quinidine and sotalol are not included. They are addressed in separate criteria.

References:
Tascenso ODT Prescribing Information, Dec. 2022, Cycle Pharmaceuticals Ltd.
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
AriCERT: Drugs that Prolong the QT Interval and/or Induce Torsades de Pointes.
Available at: www.azcer.org.

Criteria Recommendations	*Approved*	*Rejected*

79. Fingolimod / Severe Hepatic Impairment _____ _____

Alert Message: Because Tascenso ODT (fingolimod) exposure is doubled in patients with severe hepatic impairment, these patients should be closely monitored during treatment with fingolimod, as the risk of adverse reactions is greater.

Drugs/Diseases

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

References:

Tascenso ODT Prescribing Information, Dec. 2022, Cycle Pharmaceuticals Ltd.

Clinical Pharmacology, 2023 Elsevier/Gold Standard.

80. Fingolimod ODT / Nonadherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Tascenso ODT (fingolimod). 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 (Include)
Fingolimod ODT		

References:

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

McKay KA, Tremlett H, Patten SB, et al. Determinants of Non-Adherence to Disease-Modifying Therapies in Multiple Sclerosis: A Cross-Canada Prospective Study. Mult Scler. 2016;23(4):588-596.

Joplin S, van der Zwan R, Joshua F, Wong PK. Medication Adherence in Patients with Rheumatoid Arthritis: The Effect of Patient Education, Health Literacy, and Musculoskeletal Ultrasound. Biomed Res Int. 2015;2015:150658.

Criteria Recommendations ***Approved Rejected***

81. Ca/Mg/K/Na Oxybates / Overuse (Adults) _____ _____
Alert Message: Xywav (calcium/magnesium/potassium/sodium oxybates) may be over-utilized. The recommended dosage range for adults with narcolepsy and idiopathic hypersomnia is 6 to 9 mg per night. Doses higher than 9 g per night have not been studied and ordinarily should not be administered.

Drugs/Diseases

Util A	Util B	Util C
Ca/Mg/K/Na Oxybates		

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

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Xywav Prescribing Information, March 2022, Jazz Pharmaceuticals, Inc.

82. Ca/Mg/K/Na Oxybates / Overuse – Narcolepsy (Pediatric) _____ _____ Alert Message: For pediatric patients 7 years of age and older, Xywav (calcium/magnesium/potassium/sodium oxybates) is administered orally twice per night. The recommended starting pediatric dosage, titration regimen, and maximum total nightly dosage are based on patient weight. The dosage may be gradually titrated based on efficacy and tolerability. Refer to the official prescribing information for pediatric dosing. Doses higher than 9 g per night have not been studied and ordinarily should not be administered.

Drugs/Diseases

Util A	Util B	Util C (Include)
Ca/Mg/K/Na Oxybates		Narcolepsy w/ cataplexy

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

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Xywav Prescribing Information, March 2022, Jazz Pharmaceuticals, Inc.

83. Ca/Mg/K/Na Oxybates / Therapeutic Appropriateness (Pediatric) _____ _____
Alert Message: The safety and effectiveness of Xywav (calcium/magnesium/potassium/sodium oxybates) for the treatment of cataplexy or excessive daytime sleepiness in pediatric patients below the age of 7 years have not been established.

Drugs/Diseases

Util A	Util B	Util C (Include)
Ca/Mg/K/Na Oxybates		Narcolepsy w/ Cataplexy

Age Range: 0 – 6 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Xywav Prescribing Information, March 2022, Jazz Pharmaceuticals, Inc.

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

84. Ca/Mg/K/Na Oxybates / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Xywav (calcium/magnesium/potassium/sodium oxybates) for the treatment of idiopathic hypersomnia in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C (Include)
Ca/Mg/K/Na Oxybates		Idiopathic hypersomnia

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Xywav Prescribing Information, March 2022, Jazz Pharmaceuticals, Inc.

85. Ca/Mg/K/Na Oxybates / Black Box Warning _____ _____

Alert Message: The active moiety of Xywav (calcium/magnesium/potassium/sodium oxybates) is oxybate or gamma-hydroxybutyrate (GHB). Abuse or misuse of illicit GHB, either alone or in combination with other CNS depressants, is associated with CNS adverse reactions, including seizure, respiratory depression, decreases in the level of consciousness, coma, and death. Because illicit use and abuse of GHB have been reported, healthcare providers should carefully evaluate patients for a history of drug abuse and follow them closely, particularly for signs of misuse or abuse of GHB. If abuse is suspected, treatment with Ca/Mg/K/Na oxybates should be discontinued.

Drugs/Diseases

Util A	Util B	Util C
Ca/Mg/K/Na Oxybates	History of Drug Abuse	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Xywav Prescribing Information, March 2022, Jazz Pharmaceuticals, Inc.

86. Ca/Mg/K/Na Oxybates / Contraindication _____ _____

Alert Message: Xywav (calcium/magnesium/potassium/sodium oxybates) is contraindicated for use in patients with succinic semialdehyde dehydrogenase deficiency.

Drugs/Diseases

Util A	Util B	Util C (Include)
Ca/Mg/K/Na Oxybate		Succinic Semialdehyde Dehydrogenase Deficiency

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Xywav Prescribing Information, March 2022, Jazz Pharmaceuticals, Inc.

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

87. Ca/Mg/K/Na Oxybates / Sedative Hypnotics (Contraindication) _____ _____

7lert Message: Xywav (calcium/magnesium/potassium/sodium oxybates) is contraindicated in combination with alcohol and sedative-hypnotics. The calcium/magnesium/potassium/sodium oxybates product is a central nervous system (CNS) depressant. Clinically significant respiratory depression and obtundation have occurred in adult patients taking sodium oxybate (the same active moiety as Ca/Mg/K/Na oxybates) at recommended doses in clinical trials and may occur in patients treated with Ca/Mg/K/Na oxybates at recommended doses.

Drugs/Diseases

Util A	Util B		Util C
Ca/Mg/K/Na Oxybates	Estazolam	Temazepam	
	Eszopiclone	Triazolam	
	Flurazepam	Zaleplon	
	Lemborexant	Zolpidem	
	Quazepam		
	Phenobarbital		
	Ramelteon		
	Suvorexant		
	Tasimelteon		

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Xywav Prescribing Information, March 2022, Jazz Pharmaceuticals, Inc.

88. Ca/Mg/K/Na Oxybates / Divalproex Sodium _____ _____

Alert Message: The concurrent use of Xywav (calcium/magnesium/potassium/sodium oxybates) with divalproex sodium may result in an increased risk of CNS depression. In drug studies, coadministration of sodium oxybate and divalproex sodium resulted in 25% increase in the sodium oxybate AUC. When initiating divalproex sodium in patients taking a stable dosage of Ca/Mg/K/Na oxybates, a reduction of the Ca/Mg/K/Na oxybates dosage by at least 20% is recommended with initial concomitant use. When initiating Ca/Mg/K/Na oxybate in patients already taking divalproex sodium, a lower starting dosage of Ca/Mg/K/Na oxybate is recommended. Subsequently, the dosage of Ca/Mg/K/Na oxybates can be adjusted based on individual clinical response and tolerability.

Drugs/Diseases

Util A	Util B	Util C
Ca/Mg/K/Na Oxybates	Divalproex Sodium	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Xywav Prescribing Information, March 2022, Jazz Pharmaceuticals, Inc.

89. Ca/Mg/K/Na Oxybates / CNS Depressants _____ _____

Alert Message: The concurrent use of Xywav (calcium/magnesium/potassium/sodium oxybates) with other CNS depressants may increase the risk of respiratory depression, hypotension, profound sedation, syncope, and death. The Ca/Mg/K/Na oxybates product is a central nervous system depressant. If the use of CNS depressants in combination with Ca/Mg/K/Na oxybates is required, dose reduction or discontinuation of one or more CNS depressants (including Ca/Mg/K/Na oxybates) should be considered.

Drugs/Diseases

Util A	Util B	Util C
Ca/Mg/K/Na Oxybates	CNS Depressants	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Xywav Prescribing Information, March 2022, Jazz Pharmaceuticals, Inc.

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

90. Ca/Mg/K/Na Oxybates / Depression & Suicide _____ _____

Alert Message: Depression, and suicidal ideation and behavior can occur in patients treated with Xywav (calcium/magnesium/potassium/sodium oxybates). The emergence of depression in patients treated with Ca/Mg/K/Na oxybates requires careful and immediate evaluation. Patients with a previous history of a depressive illness and/or suicide attempt should be monitored carefully for the emergence of depressive symptoms while taking Ca/Mg/K/Na oxybates.

Drugs/Diseases

Util A	Util B	Util C
Ca/Mg/K/Na Oxybates	Depression	
	Suicidal Ideation	

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Xywav Prescribing Information, March 2022, Jazz Pharmaceuticals, Inc.

91. Ca/Mg/K/Na Oxybates / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no adequate data on the developmental risks associated with the use of Xywav (calcium/magnesium/potassium/sodium oxybates) during human pregnancy. Animal studies produced no clear evidence of developmental toxicity; however, increased stillbirths and decreased postnatal viability and growth were seen at clinically relevant doses.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Ca/Mg/K/Na Oxybates	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2023 Elsevier/Gold Standard.
Facts & Comparisons, 2023 Updates, Wolters Kluwer Health.
Xywav Prescribing Information, March 2022, Jazz Pharmaceuticals, Inc.

92. Ca/Mg/K/Na Oxybates / Lactation _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Ca/Mg/K/Na Oxybates	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.
Xywav Prescribing Information, March 2022, Jazz Pharmaceuticals, Inc.