Alabama Medicaid DUR Board Meeting Minutes Summary
October 26, 2022

Members Present: Kelli Littlejohn Newman, Crystal Deas, Dan McConaghy, Marilyn Bulloch, Rachel Seaman, Mary Stallworth, Bernie Olin, Kelly Tate, Melinda Rowe

Also Present: Lori Thomas, Clemice Hurst, Julie Jordan, Heather Vega, LaQwanda Eddings-Haygood, ACHN Pharmacists

Members Absent: Nina Ford Johnson, Amber Clark, Danielle Powell

Call to Order: The DUR meeting was called to order by C. Deas at approximately 1:04 p.m.

Review and Adoption of Minutes: The minutes of the July 20, 2022 meeting were presented, and M. Bulloch made a motion to approve the minutes. K. Tate seconded the motion, and the motion was approved unanimously.

Prior Authorization and Overrides Update: L. Thomas began the Prior Authorization and Overrides Update with the Monthly Manual Prior Authorizations and Overrides Report for the month of April 2022. She reported 13,389. There were 16,241 total electronic requests for the month of April 2022. From the Prior Authorization and Override Response Time Ratio report for April 2022, L. Thomas reported that approximately 22% of all manual PAs and 20% of all overrides were completed in less than two hours. Fifty-seven percent of all manual PAs and 53% of all overrides were completed in less than four hours. Eighty-nine percent of all manual PAs and 88% of all overrides were completed in less than eight hours. For the month of May 2022, L. Thomas reported 13,563 manual PA requests and 15,254 electronic PA requests were received. She reported that 16% of all manual PAs and all overrides were completed in less than two hours. Fifty-one percent of all manual PAs and 56% of all overrides were completed in less than four hours. Seventy percent of all manual PAs and 75% of all overrides were completed in less than eight hours. For the month of June 2022, L. Thomas reported 14,013 manual PA requests and 15,386 electronic PA requests. L. Thomas reported that approximately 24% of all manual PAs and 23% of all overrides were completed in less than two hours. Sixty-three percent of all manual PA requests and 61% of all overrides were completed in less than four hours. Eighty-nine percent of all manual PA and all overrides were completed in less than eight hours.

Program Summary Review: L. Thomas briefly reviewed the Alabama Medicaid Program Summary for the months of October 2021 through March 31, 2022. She reported 3,795,091 total prescriptions, 230,082 average recipients per month using pharmacy benefits, and an average paid per prescription of $145.11.

Cost Management Analysis: L. Thomas reported an average cost per claim of $146.35 for June 2022 and compared previous months contained in the table. From the 2nd Quarter Drug Analysis, L. Thomas reported 82.8% generic utilization, 7.7% brand single-source, 5.5% brand multi-source (those requests which required a DAW override), and 3.9% OTC and "other". From the Top 25 Drugs Based on Number of Claims from 04/01/2022-06/30/2022, L. Thomas reported the top five drugs: cetirizine, amoxicillin, albuterol sulfate HFA, fluticasone propionate, and montelukast sodium. She reported that this report was similar to the 1st Quarter 2022 utilization report. L. Thomas then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 04/01/2022-06/30/2022: Humira® Citrate-free, Vyvanse®, Trikafta®, Invega® Sustenna®, and Trulicity®. From the Top 15 Therapeutic Classes by Total Cost of Claims for the same time frame, L. Thomas reported the top five classes: Antipsychotic Agents, Disease-modifying Antirheumatic Agents, Respiratory and CNS Stimulants, Skin and Mucous Membrane Agents, and Miscellaneous Anticonvulsants.

Review of Palivizumab Utilization for the 2021 - 2022 Season: Due to the atypical nature of the 2021 – 2022 RSV season with statistically significant virus positivity rates into the summer of 2022, the COVID-19 pandemic, and after discussion with pediatric and pulmonary experts throughout the state, Alabama Medicaid allowed Synagis® dosing beyond the typical October through March timeframe. For this utilization report, the 2021-2022 Synagis® season was defined as October 2021 through August 2022. L. Thomas explained that during a typical RSV season, RSV activity in Alabama becomes significant in September or October. The season usually peaks in December and becomes statistically non-significant in January or February. According to the National Respiratory and Enteric Virus Surveillance System (NREVSS) website, RSV activity in Alabama became significant in the week ending 10/02/2021. After a level of significance was reached, the number of positive antigen detection tests dropped significantly until week ending 06/11/2022. A drastic increase was then seen week ending 08/20/2022 and a level of statistical significance remained at the time of the report. L. Thomas reminded the Board that each recipient could receive a maximum of 5 doses per season and that all policies relating to Synagis® were based on clinical literature and recommendations. For the 2021-22 season, there were 2,970 claims for 592 recipients. The average cost per claim was $2,759 while the average cost per recipient was $13,843. L. Thomas pointed out that there were 1,763 prior authorizations requested over the course of the season, with an approval rate of 68%. L. Thomas briefly reviewed the top dispensing pharmacies and the top PA denial reasons. L. Thomas also reviewed the graphs comparing the total spend of all drugs compared to the total spend of Synagis® per RSV season.

RDUR Intervention Report: L. Thomas presented the RDUR Activity Report for July 2021. She reported 500 profiles reviewed and 692 letters sent with 56 responses received as of the date of the report. She reported 26 of 53 physicians indicated that they found the RDUR letters "useful" or "extremely useful". The criteria for the cycle of intervention letters included Drug-Drug Interaction (Support Act criteria – pure opioid agonists and benzodiazepines); Drug-Drug Interaction (Support Act criteria – pure opioid agonists and antipsychotics); Therapeutic Appropriateness (pregabalin and history of substance abuse/dependence); Appropriate Use (concurrent use of buprenorphine and pure opiate agonists). L. Thomas also presented the RDUR Activity Report for October 2021. She reported 500 profiles reviewed and 635 letters sent with 43 responses received as of the date of the report. She reported 20 of 35 physicians indicated that they found the RDUR letters "useful" or "extremely useful". The criteria for the cycle of intervention letters included Drug-Drug Interaction (Support Act criteria – pure opioid agonists and benzodiazepines); Drug-Drug Interaction (Support Act criteria – pure opioid agonists and antipsychotics); Therapeutic Appropriateness (diabetes and hypertension); Appropriate Use (concurrent use of buprenorphine and pure opiate agonists).

Proposed Criteria: L. Thomas presented the proposed set of 48 criteria to the Board and instructed the Board members to mark their ballots. Of the 48 proposed criteria, results from the criteria vote returned 47 approved and 1 approved as amended.

Medicaid Update: K. Newman reminded the Board members that all updated Medicaid drug lists and ALERTs were provided to them electronically and are also available online. K. Newman reminded the Board members that the Agency is still preparing for the unwinding of the national COVID-19 PHE. K. Newman reviewed changes to the Hepatitis C medication criteria and the ALERT regarding Paxlovid prescribing by pharmacists.

P & T Committee Update: C. Hurst began the P & T Update by informing the Board that the last P & T meeting was held on August 10, 2022, and covered the respiratory agents; eye, ear, nose, and throat preparations; complement inhibitors for hereditary angioedema; and growth hormone agents. The next meeting is scheduled for November 9, 2022 and will cover the calcitonin gene-related peptide antagonists; proton-pump inhibitors; skeletal muscle relaxants; opiate agonists and partial agonists; selective serotonin agonists; antiemetics; and anxiolytics, sedatives, and hypnotics.

Next Meeting Date: C. Deas reminded the Board that the next DUR meeting will be held on January 25, 2023. A motion to adjourn the meeting was made by D. McConaghy and M. Bulloch seconded the motion. The meeting was adjourned at 1:55 p.m.

Respectfully submitted,

Lori Thomas, PharmD

Lori Thomas, PharmD.

ALABAMA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*
1. Finerenone / Overuse Alert Message: Kerendia (finerenone) may be over-utilized. The recommended maintenance finerenone dose is 20 mg once daily. Drugs/Diseases Util A: Finerenone Max Dose: 20 mg/day References: Clinical Pharmacology, 2021 Elsevier/Gold Standard. Kerendia Prescribing Information, July 2021, Bayer HealthCare Pharmaceuticals.	√		
2. Finerenone / Therapeutic Appropriateness Alert Message: The safety and efficacy of Kerendia (finerenone) have not been established in patients below 18 years of age. Drugs/Diseases Util A: Finerenone Age Range: 0 – 17 yoa References: Clinical Pharmacology, 2021 Elsevier/Gold Standard. Kerendia Prescribing Information, July 2021, Bayer HealthCare Pharmaceuticals.	√		
3. Finerenone / Strong CYP3A4 Inhibitors Alert Message: The concurrent use of Kerendia (finerenone) with strong CYP3A inhibitors is contraindicated. Finerenone is a CYP3A4 substrate, and concomitant use with a strong CYP3A4 inhibitor may increase the risk of finerenone-related adverse reactions. Drugs/Diseases Util A: Finerenone Util B: Clarithromycin, Cobicistat, Darunavir, Indinavir, Itraconazole, Ketoconazole, Nefazodone Util C: Nelfinavir, Posaconazole, Ritonavir, Saquinavir, Voriconazole References: Clinical Pharmacology, 2021 Elsevier/Gold Standard. Kerendia Prescribing Information, July 2021, Bayer HealthCare Pharmaceuticals.	√		

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

4. Finerenone / Adrenal Insufficiency ___√___ _____ _____

Alert Message: Kerendia (finerenone) is contraindicated in patients with adrenal insufficiency. Finerenone is a nonsteroidal, selective antagonist of the mineralocorticoid receptor (MR), which is activated by aldosterone and cortisol and regulates gene transcription.

Drugs/Diseases

Util A	Util B	Util C
Finerenone	Adrenal Insufficiency	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Kerendia Prescribing Information, July 2021, Bayer HealthCare Pharmaceuticals.

5. Finerenone / Hyperkalemia ___√___ _____ _____

Alert Message: Kerendia (finerenone) can cause hyperkalemia. The risk for developing hyperkalemia increases with decreasing kidney function and is greater in patients with higher baseline potassium levels or other risk factors for hyperkalemia. Measure serum potassium and eGFR in all patients before initiation of treatment with finerenone and dose accordingly. Do not initiate finerenone if serum potassium is > 5.0 mEq/L. Measure serum potassium periodically during treatment with finerenone and adjust dose accordingly. More frequent monitoring may be necessary for patients at risk for hyperkalemia, including those on concomitant medications that impair potassium excretion or increase serum potassium.

Drugs/Diseases

Util A	Util B	Util C (Include)
Finerenone		Hyperkalemia

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Kerendia Prescribing Information, July 2021, Bayer HealthCare Pharmaceuticals.

6. Finerenone / Moderate or Weak CYP3A4 Inhibitors ___√___ _____ _____

Alert Message: Kerendia (finerenone) is a CYP3A4 substrate. Concomitant use of finerenone with a moderate or weak CYP3A4 inhibitor increases finerenone exposure, which may increase the risk of finerenone adverse reactions. Monitor serum potassium during drug initiation or dosage adjustment of either finerenone or the moderate or weak CYP3A4 inhibitor and adjust finerenone dosage as appropriate.

Drugs/Diseases

Util A	Util B				Util C
Finerenone	Atazanavir	Diltiazem	Verapamil	Istradefylline	
	Aprepitant	Dronedarone	Chlorzoxazone	Ivacaftor	
	Cimetidine	Erythromycin	Cilostazol	Lomitapide	
	Ciprofloxacin	Fluconazole	Cimetidine	Ranitidine	
	Crizotinib	Fluvoxamine	Clotrimazole	Ranolazine	
	Cyclosporine	Imatinib	Fosaprepitant	Ticagrelor	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Kerendia Prescribing Information, July 2021, Bayer HealthCare Pharmaceuticals.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

7. Finerenone / Strong and Moderate CYP3A4 Inducers ___√_____ _____ _____

Alert Message: Avoid concomitant use of Kerendia (finerenone) with strong or moderate CYP3A4 inducers. Finerenone is a CYP3A4 substrate. Concomitant use of finerenone with a strong or moderate CYP3A4 inducer decreases finerenone exposure, which may reduce the efficacy of finerenone.

Drugs/Diseases

Util A	Util B	Util C
Finerenone	Apalutamide	Mitotane
	Bosentan	Phenobarbital
	Butalbital	Phenytoin
	Carbamazepine	Primidone
	Efavirenz	Rifabutin
	Enzalutamide	Rifampin
	Etravirine	Rifapentine

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Kerendia Prescribing Information, July 2021, Bayer HealthCare Pharmaceuticals.

8. Finerenone / Pregnancy / Pregnancy Negating ___√_____ _____ _____

Alert Message: There are no available data on Kerendia (finerenone) use in pregnancy to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Animal studies have shown developmental toxicity at exposures about 4 times those expected in humans. The clinical significance of these findings is unclear.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Kerendia Prescribing Information, July 2021, Bayer HealthCare Pharmaceuticals.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

9. Finerenone / Lactation ___V___ _____ _____

Alert Message: There are no data on the presence of Kerendia (finerenone) or its metabolite in human milk, the effects on the breastfed infant, or the effects of the drug on milk production. In a pre- and postnatal developmental toxicity study in rats, increased pup mortality and lower pup weight were observed at about 4 times the AUCunbound expected in humans. These findings suggest that finerenone is present in rat milk. When a drug is present in animal milk, it is likely that the drug will be present in human milk. Because of the potential risk to breastfed infants from exposure to finerenone, avoid breastfeeding during treatment and for 1 day after treatment.

Drugs/Diseases

Util A	Util B	Util C
Finerenone	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Kerendia Prescribing Information, July 2021, Bayer HealthCare Pharmaceuticals.

10. Finerenone / Severe Hepatic Impairment ___V___ _____ _____

Alert Message: Kerendia (finerenone) use should be avoided in patients with severe hepatic impairment. In clinical studies, finerenone mean AUC was increased by 38%, and the Cmax was unchanged in cirrhotic patients with moderate hepatic impairment (Child-Pugh B) compared to healthy control subjects. The effect of severe hepatic impairment (Child-Pugh C) on finerenone exposure was not studied.

Drugs/Diseases

Util A	Util B	Util C
Finerenone	Cirrhosis	
	Hepatic Failure	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Kerendia Prescribing Information, July 2021, Bayer HealthCare Pharmaceuticals.

11. Finerenone / Medications Causing Increased Potassium ___V___ _____ _____

Alert Message: Kerendia (finerenone) can cause hyperkalemia. More frequent monitoring may be necessary for patients at risk for hyperkalemia, including those on concomitant medications that impair potassium excretion or increase serum potassium.

Drugs/Diseases

Util A	Util B	Util C
Finerenone	ACE Inhibitors	
	Aliskiren	
	ARBs	
	Eplerenone	
	Potassium Sparing Diuretics	
	Potassium Supplements	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Kerendia Prescribing Information, July 2021, Bayer HealthCare Pharmaceuticals.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

12. Finerenone / Non-adherence ___√___ _____ _____

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

Drugs/Diseases
Util A Util B Util C
Finerenone

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Mechta Nielsen T, Frojk Juhl M, Feldt-Rasmussen B, Thomsen T. Adherence to Medication in Patients with Chronic Kidney Disease: A Systematic Review of Qualitative Research. Clin Kidney J. 2018. Aug;11(4):513-527.
Burnier M, Pruijm M, Wuerzner G. et al. Drug Adherence in Chronic Kidney Disease and Dialysis. Nephrol Dial Transplant 2015; 30: 39–44.
Kleinsinger, Fred. The Unmet Challenge of Medication Nonadherence. The Permanente Journal. Vol. 22 (2018): 18-033. doi:10.7812/TPP/18-033.

13. Olanzapine/Samidorphan / Overuse ___√___ _____ _____

Alert Message: Lybalvi (olanzapine/samidorphan) may be over-utilized. The maximum recommended dose of olanzapine/samidorphan is 20 mg/10 mg per day.

Drugs/Diseases
Util A Util B Util C
Olanzapine/Samidorphan

Max Dose: 20mg/10mg per day

References:
Lybalvi Prescribing Information, June 2021, Alkermes.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

14. Olanzapine/Samidorphan / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: The safety and effectiveness of Lybalvi (olanzapine/samidorphan) have not been established in pediatric patients.

Drugs/Diseases
Util A Util B Util C
Olanzapine/Samidorphan

Age Range: 0 – 17 yoa

References:
Lybalvi Prescribing Information, June 2021, Alkermes.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

15. Olanzapine/Samidorphan / Opioid Withdrawal ___√___ _____ _____

Alert Message: The use of Lybalvi (olanzapine/samidorphan) is contraindicated in patients undergoing acute opioid withdrawal. The samidorphan component of the combination product is an opioid antagonist and can precipitate opioid withdrawal in patients who are dependent on opioids. If olanzapine/samidorphan use is being considered in a patient receiving opioids, the initiation of olanzapine/samidorphan must be delayed for a minimum of at least a 7-day opioid-free interval after the last use of short-acting opioids and a 14-day opioid-free interval after the last use of a long-acting opioid.

Drugs/Diseases

Util A	Util B	Util C
Olanzapine/Samidorphan	Opioid Dependence w/ Withdrawal	
	Opioid Use w/ Withdrawal	
	Opioid Related Disorders w/ Withdrawal	

References:
Lybalvi Prescribing Information, June 2021, Alkermes.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

16. Olanzapine/Samidorphan / Opioids ___√___ _____ _____

Alert Message: The use of Lybalvi (olanzapine/samidorphan) is contraindicated in patients using opioids. Olanzapine/samidorphan can precipitate opioid withdrawal. If olanzapine/samidorphan use is being considered in a patient receiving opioids, the initiation of olanzapine/samidorphan must be delayed for a minimum of at least a 7-day opioid-free interval after the last use of a short-acting opioid and a 14-day opioid-free interval after the last use of a long-acting opioid.

Drugs/Diseases

Util A	Util B	Util C
Olanzapine/Samidorphan	Benzhydrocodone	
	Codeine	
	Fentanyl	
	Dihydrocodeine	
	Hydrocodone	
	Hydromorphone	
	Levorphanol	
	Meperidine	
	Morphine	
	Oxycodone	
	Oxymorphone	
	Tapentadol	
	Tramadol	
	Buprenorphine (pain)	

References:
Lybalvi Prescribing Information, June 2021, Alkermes.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

17. Olanzapine/Samidorphan / Tardive Dyskinesia ___√___ _____ _____

Alert Message: Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may develop in patients treated with antipsychotic drugs. Therefore, Lybalvi (olanzapine/samidorphan) should be prescribed in a manner that is most likely to reduce the risk of tardive dyskinesia. The risk of developing tardive dyskinesia and the likelihood that it will become irreversible increases with the duration of treatment and the cumulative dose. If signs and symptoms of tardive dyskinesia appear in a patient on olanzapine/samidorphan, drug discontinuation should be considered.

Drugs/Diseases

Util A	Util B	Util C
Olanzapine/Samidorphan	Tardive Dyskinesia	

References:
Lybalvi Prescribing Information, June 2021, Alkermes.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

18. Olanzapine/Samidorphan / Anticholinergic (Antimuscarinic) Effects ___√___ _____ _____

Alert Message: Olanzapine, a component of Lybalvi (olanzapine/samidorphan), exhibits in vitro muscarinic receptor affinity. In premarketing clinical trials with oral olanzapine, olanzapine was associated with constipation, dry mouth, and tachycardia, all adverse reactions possibly related to cholinergic antagonism. Such adverse reactions were not often the basis for discontinuations, but olanzapine/samidorphan should be used with caution in patients with a current diagnosis or prior history of urinary retention, clinically significant prostatic hypertrophy, constipation, or a history of paralytic ileus or related conditions. In post-marketing experience, the risk for severe adverse reactions (including fatalities) was increased with concomitant use of anticholinergic medications.

Drugs/Diseases

Util A	Util B	Util C
Olanzapine/Samidorphan	Urinary Retention	
	Prostatic Hypertrophy	
	Constipation	
	Paralytic Ileus	

References:
Lybalvi Prescribing Information, June 2021, Alkermes.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

19. Olanzapine/Samidorphan / Strong CYP1A2 Inhibitors ___√___ _____ _____

Alert Message: Concomitant use of Lybalvi (olanzapine/samidorphan) with a strong CYP1A2 inhibitor can increase olanzapine AUC and Cmax, which may increase the risk of olanzapine/samidorphan adverse reactions. Consider reducing the dosage of the olanzapine component olanzapine/samidorphan when used concomitantly with strong CYP1A2 inhibitors.

Drugs/Diseases

Util A	Util B	Util C
Olanzapine/Samidorphan	Ciprofloxacin	
	Fluvoxamine	

References:
Lybalvi Prescribing Information, June 2021, Alkermes.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

20. Olanzapine/Samidorphan / Strong CYP3A4 Inducers ___√___ _____ _____

Alert Message: Concomitant use of Lybalvi (olanzapine/samidorphan) with strong CYP3A4 inducers is not recommended. Concurrent use of strong 3A4 inducers with olanzapine/samidorphan may reduce olanzapine/samidorphan efficacy. The samidorphan component of the combination product is a CYP3A4 substrate and olanzapine is a CYP1A2 substrate. In drug interaction studies, coadministration of (olanzapine/samidorphan) with a strong CYP3A4 inducer significantly decreased AUCinf of the samidorphan component.

Drugs/Diseases

Util A	Util B	Util C
Olanzapine/Samidorphan	Apalutamide	
	Carbamazepine	
	Enzalutamide	
	Mitotane	
	Phenobarbital	
	Phenytoin	
	Primidone	
	Rifampin	

References:
Lybalvi Prescribing Information, June 2021, Alkermes.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

21. Olanzapine/Samidorphan / CYP1A2 Inducers ___√___ _____ _____

Alert Message: Concomitant use of Lybalvi (olanzapine/samidorphan) with a CYP1A2 inducer decreases olanzapine exposure, which may reduce olanzapine/samidorphan efficacy. Consider increasing the dosage of the olanzapine component in olanzapine/samidorphan when used concomitantly with CYP1A2 inducers.

Drugs/Diseases

Util A	Util B	Util C
Olanzapine/Samidorphan	Ritonavir	

References:
Lybalvi Prescribing Information, June 2021, Alkermes.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

22. Olanzapine/Samidorphan / CNS Depressants ___√___ _____ _____

Alert Message: Concomitant use of Lybalvi (olanzapine/samidorphan) with CNS depressants may potentiate the orthostatic hypotension observed with olanzapine. Olanzapine/samidorphan should be used with caution in patients receiving CNS depressants.

Drugs/Diseases

Util A	Util B	Util C
Olanzapine/Samidorphan	CNS Depressants	

References:
Lybalvi Prescribing Information, June 2021, Alkermes.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

23. Olanzapine/Samidorphan / Anticholinergic Agents ___√___ _____ _____

Alert Message: Lybalvi (olanzapine/samidorphan) should be used with caution in patients receiving medications having anticholinergic (antimuscarinic) effects. Concomitant treatment with an olanzapine-containing medication and other drugs with anticholinergic activity can increase the risk for severe gastrointestinal adverse reactions related to hypomotility.

Drugs/Diseases

Util A	Util B	Util C
Olanzapine/Samidorphan	Anticholinergic Agents	

References:
Lybalvi Prescribing Information, June 2021, Alkermes.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

24. Olanzapine/Samidorphan / Levodopa and Dopamine Agonists ___√___ _____ _____

Alert Message: Concomitant use of Lybalvi (olanzapine/samidorphan) is not recommended with levodopa and dopamine agonists. The olanzapine component in the combination agent is a dopamine antagonist, and concurrent use can antagonize the effects of levodopa and dopamine agonists.

Drugs/Diseases

Util A	Util B	Util C
Olanzapine/Samidorphan	Apomorphine	
	Bromocriptine	
	Cabergoline	
	Levodopa	
	Pramipexole	
	Ropinirole	
	Rotigotine	

References:
Lybalvi Prescribing Information, June 2021, Alkermes.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

25. Olanzapine/Samidorphan / Pregnancy / Pregnancy Negating ___√___ _____ _____

Alert Message: Neonates exposed to antipsychotic drugs, including the olanzapine component of Lybalvi (olanzapine/samidorphan), during the third trimester, are at risk for extrapyramidal and/or withdrawal symptoms following delivery. There are no available data on the use of samidorphan or the combination of olanzapine and samidorphan in pregnant women to determine a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. There are risks to the mother associated with untreated schizophrenia or bipolar I disorder and with exposure to antipsychotics, including olanzapine/samidorphan, during pregnancy.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Olanzapine/Samidorphan	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Lybalvi Prescribing Information, June 2021, Alkermes.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

26. Olanzapine/Samidorphan / Lactation ___√___ _____ _____

Alert Message: Olanzapine, a component of Lybalvi (olanzapine/samidorphan) is present in human milk. There are reports of excess sedation, irritability, poor feeding, and extrapyramidal symptoms (tremors and abnormal muscle movements) in infants exposed to olanzapine through breast milk. There are no data on the presence of samidorphan or the combination of olanzapine and samidorphan in human milk, the effects on the breastfed infant, or the effects on milk production. The development and health benefits of breastfeeding should be considered along with the mother's clinical need for olanzapine/samidorphan and any potential adverse effects on the breastfed infant from olanzapine/samidorphan or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Olanzapine/Samidorphan	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Lybalvi Prescribing Information, June 2021, Alkermes.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

27. Olanzapine/Samidorphan / Non-adherence ___√___ _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Olanzapine/Samidorphan		

References:
Theida P, et.al., An Economic Review of Compliance with Medication Therapy in the Treatment of Schizophrenia, Psychiatric Services, 2003;54:508-516.
Acsher-Svanum H, Zhu B, Faries DE, et al., The Cost of Relapse and the Predictors of Relapse in the Treatment of Schizophrenia. BMC Psychiatry 2010, 10:2.
Berger A, Edelsbery J, Sanders KN, et al., Medication Adherence and Utilization in Patients with Schizophrenia or Bipolar Disorder Receiving Aripiprazole, Quetiapine, or Ziprasidone at Hospital Discharge: A Retrospective Cohort Study. BMC Psychiatry 2012,12:99.
Stephenson JJ, Tuncelli O, Gu T, et al., Adherence to Oral Second-Generation Antipsychotic Medications in Patients with Schizophrenia and Bipolar Disorder: Physicians' Perceptions of Adherence vs. Pharmacy Claims. Int J Clin Pract, June 2012, 66, 6, 565-573.
Morken G, Widen JH, Grawe RW. Non-adherence to Antipsychotic Medication, Relapse and Rehospitalization in Recent-Onset Schizophrenia. BMC Psychiatry. 2008, 8:32.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

28. Amphetamine XR Tablets / Overuse _____ __√____ _____

Alert Message: Dyanavel XR tablets (amphetamine extended-release) may be over-utilized. The maximum recommended dosage of extended-release amphetamine is 20 mg once daily.

Drugs/Diseases

Util A	Util B	Util C
Amphetamine XR Tabs		

Age Range: 6 – 12 yoa
Max Dose: 20 mg/day

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Dyanavel XR Prescribing Information, Nov. 2021, Tris Pharma Inc.

29. Amphetamine XR Tablets / Overuse __√____ _____ _____

Alert Message: The safety and efficacy of Dyanavel XR tablets (amphetamine extended-release tablets) in pediatric patients younger than 6 years old with ADHD have not been established.

Drugs/Diseases

Util A	Util B	Util C
Amphetamine XR Tabs		

Age Range: 0 - 5 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Dyanavel XR Prescribing Information, Nov. 2021, Tris Pharma Inc.

30. Relugolix / Overuse ___√____ _____ _____

Alert Message: Orgovyx (relugolix) may be over-utilized. Initiate treatment of relugolix with a loading dose of 360 mg on the first day and continue treatment with a 120 mg dose taken orally once daily at approximately the same time each day.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Relugolix		Carbamazepine Phenytoin Rifampin

Max Dose: 120 mg/day

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Orgovyx Prescribing information, Dec. 2020, Myovant Sciences, Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

31. Relugolix / Therapeutic Appropriateness ___√___ _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Relugolix		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Orgovyx Prescribing information, Dec. 2020, Myovant Sciences, Inc.

32. Relugolix / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: Orgovyx (relugolix) may prolong the QT/QTc interval. Consider whether the benefits of androgen deprivation therapy outweigh the potential risks in patients with congenital long QT syndrome, congestive heart failure, or frequent electrolyte abnormalities and in patients taking drugs known to prolong the QT interval.

Drugs/Diseases

Util A	Util B	Util C
Relugolix	Long QT Syndrome	
	Congestive Heart Failure	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Orgovyx Prescribing information, Dec. 2020, Myovant Sciences, Inc.

33. Relugolix / P-gp Inhibitors ___√___ _____ _____

Alert Message: The concurrent use of Orgovyx (relugolix) with oral P-gp inhibitors should be avoided. If co-administration is unavoidable, take relugolix first and separate dosing of the oral P-gp inhibitor by at least 6 hours and monitor for relugolix adverse reactions. Relugolix is a P-gp substrate, and concomitant use with a P-gp inhibitor may increase the AUC and Cmax of relugolix increases in the risk of relugolix-related adverse events. Treatment with relugolix may be interrupted for up to two weeks if a course of treatment with a P-gp inhibitor is required.

Drugs/Diseases

Util A	Util B				Util C
Relugolix	Amiodarone	Flibanserin	Lomitapide	Ritonavir	
	Brigatinib	Fostamatinib	Mefloquine	Rolapitant	
	Cabozantinib	Glecaprevir	Mifepristone	Sapropterin	
	Carvedilol	Ibrutinib	Nelfinavir	Saquinavir	
	Clarithromycin	Isavuconazonium	Neratinib	Sarecycline	
	Cobicistat	Istradefylline	Osimertinib	Sorafenib	
	Cyclosporine	Itraconazole	Pibrentasvir	Ticagrelor	
	Daclatasvir	Ivacaftor	Ponatinib	Tolvaptan	
	Dronedarone	Ketoconazole	Posaconazole	Velpatasvir	
	Elagolix	Lapatinib	Propafenone	Vemurafenib	
	Erythromycin	Lasmiditan	Quinidine	Verapamil	
	Etravirine	Ledipasvir	Ranolazine	Voxilaprevir	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Orgovyx Prescribing information, Dec. 2020, Myovant Sciences, Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

34. Relugolix / Drugs Causing Qt Prolongation ___√___ _____ _____

Alert Message: Orgovyx (relugolix) may prolong the QT/QTc interval. Consider whether the benefits of androgen deprivation therapy outweigh the potential risks in patients with congenital long QT syndrome, congestive heart failure or frequent electrolyte abnormalities and in patients taking drugs known to prolong the QT interval.

Drugs/Diseases

Util A	Util B	Util C		
Relugolix	Abiraterone	Efavirenz	Levofloxacin	Rilpivirine
	Alfuzosin	Eliglustat	Lithium	Risperidone
	Amiodarone	Encorafenib	Lofexidine	Ritonavir
	Amitriptyline	Entrectinib	Loperamide	Romidepsin
	Anagrelide	Eribulin	Maprotiline	Saquinavir
	Aripiprazole	Erythromycin	Methadone	Sertraline
	Arsenic Trioxide	Escitalopram	Metoclopramide	Siponimod
	Asenapine	Ezogabine	Midostaurin	Solifenacin
	Atazanavir	Famotidine	Mifepristone	Sotalol
	Atomoxetine	Felbamate	Mirabegron	Sunitinib
	Azithromycin	Fingolimod	Mirtazapine	Tacrolimus
	Bedaquiline	Flecainide	Moexipril	Tamoxifen
	Bortezomib	Fluconazole	Moxifloxacin	Telavancin
	Bendamustine	Fluoxetine	Nelfinavir	Tetrabenazine
	Bosutinib	Fluvoxamine	Nilotinib	Thioridazine
	Buprenorphine	Foscarnet	Nortriptyline	Tizanidine
	Ceritinib	Galantamine	Ofloxacin	Tolterodine
	Chloroquine	Ganciclovir	Ondansetron	Toremifene
	Chlorpromazine	Gemifloxacin	Osimertinib	Tramadol
	Cilostazol	Gilteritinib	Oxaliplatin	Trazodone
	Ciprofloxacin	Glasdegib	Paliperidone	Trimipramine
	Citalopram	Granisetron	Panobinostat	Valbenazine
	Clarithromycin	Haloperidol	Paroxetine	Vandetanib
	Clomipramine	Hydroxychloroquine	Pasireotide	Vemurafenib
	Clozapine	Hydroxyzine	Pazopanib	Venlafaxine
	Crizotinib	Ibutilide	Pentamidine	Voriconazole
	Dabrafenib	Iloperidone	Pimavanserin	
	Dasatinib	Imipramine	Pimozide	
	Desipramine	Indapamide	Pitolisant	
	Deutetrabenazine	Indinavir	Posaconazole	
	Diphenhydramine	Ivabradine	Procainamide	
	Disopyramide	Itraconazole	Promethazine	
	Dofetilide	Ivosidenib	Propafenone	
	Dolasetron	Ketoconazole	Quetiapine	
	Donepezil	Lapatinib	Quinidine	
	Doxepin	Lefamulin	Quinine	
	Dronedarone	Lenvatinib	Ranolazine	
	Droperidol	Leuprolide	Ribociclib	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Orgovyx Prescribing information, Dec. 2020, Myovant Sciences, Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

35. Relugolix / Combined P-gp & Strong CYP3A4 Inducers ___√___ _____ _____

Alert Message: The concurrent use of Orgovyx (relugolix) with a combined P-gp and strong CYP3A4 inducers should be avoided. Relugolix is a P-gp and CYP3A4 substrate, and co-administration with a combined inducer of P-gp and CYP3A4 inducer can decrease the AUC and Cmax of relugolix. If concomitant use is unavoidable, increase the relugolix dose to 240 mg once daily. After discontinuation of the combined P-gp and CYP3A4 inducer, resume the recommended relugolix dose of 120 mg once daily.

Drugs/Diseases

Util A	Util B	Util C
Relugolix	Carbamazepine	
	Phenytoin	
	Rifampin	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Orgovyx Prescribing information, Dec. 2020, Myovant Sciences, Inc.

36. Relugolix / Pregnancy / Pregnancy Negating ___√___ _____ _____

Alert Message: Based on animal findings and mechanism of action, Orgovyx (relugolix) can cause fetal harm and loss of pregnancy when administered to a pregnant patient. There are no human data on the use of relugolix in pregnant patients to inform of drug-associated risk. In animal reproductive studies, administration of relugolix to pregnant rabbits during organogenesis caused embryo-lethality at maternal exposures that were 0.3 times the human exposure at the recommended relugolix dose.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Orgovyx Prescribing information, Dec. 2020, Myovant Sciences, Inc.

37. Relugolix / Lactation ___√___ _____ _____

Alert Message: The safety and efficacy of Orgovyx (relugolix) at the recommended dose of 120 mg per day have not been established in females. There are no data on the presence of relugolix in human milk, the effects on the breastfed child, or the effects on milk production. Relugolix and its metabolites were present in the milk of lactating rats.

Drugs/Diseases

Util A	Util B	Util C
Relugolix	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

38. Relugolix / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: Based on findings in animal studies and mechanism of action, advise male patients with partners of reproductive potential to use effective contraception during treatment and for 2 weeks after the last dose of Orgovyx (relugolix).

Drugs/Diseases
Util A Util B Util C
Relugolix

Gender: Male

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Orgovyx Prescribing information, Dec. 2020, Myovant Sciences, Inc.

39. Relugolix / Non-adherence ___√___ _____ _____

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

Drugs/Diseases
Util A Util B Util C
Relugolix

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

40. Decitabine/Cedazuridine / Overuse ___√___ _____ _____

Alert Message: Inqovi (decitabine/cedazuridine) may be over-utilized. The recommended dosage of decitabine/cedazuridine is 1 tablet (containing 35 mg decitabine and 100 mg cedazuridine) orally once daily on Days 1 through 5 of each 28-day cycle for a minimum of 4 cycles until disease progression or unacceptable toxicity.

Conflict Code: ER - Overutilization
Drugs/Disease
Util A Util B Util C
Decitabine/Cedazuridine

Max Dose: 1 tablet/day

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Inqovi Prescribing Information, July 2020, Taiho Oncology, Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

41. Decitabine/Cedazuridine / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: The safety and effectiveness of Inqovi (decitabine/cedazuridine) have not been established in pediatric patients.

Drugs/Disease

Util A	Util B	Util C
Decitabine/Cedazuridine		

Age Range: 0 – 17 yoa

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Inqovi Prescribing Information, July 2020, Taiho Oncology, Inc.

42. Decitabine/Cedazuridine / CDA Substrates ___√___ _____ _____

Alert Message: The coadministration of Inqovi (decitabine/cedazuridine) with drugs that are metabolized by CDA should be avoided. The cedazuridine component of the combination product is an inhibitor of the cytidine deaminase (CDA) enzyme. Concurrent use of decitabine/cedazuridine with drugs that are metabolized by CDA may result in increased systemic exposure of the CDA substrate with the potential for increased substrate toxicity.

Drugs/Disease

Util A	Util B	Util C
Decitabine/Cedazuridine	Azacitidine Cytarabine Gemcitabine	

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Inqovi Prescribing Information, July 2020, Taiho Oncology, Inc.

43. Decitabine/Cedazuridine / Capecitabine ___√___ _____ _____

Alert Message: The coadministration of Inqovi (decitabine/cedazuridine) with capecitabine should be avoided. The cedazuridine component of the combination product is an inhibitor of the cytidine deaminase (CDA) enzyme. Capecitabine is a prodrug that depends on CDA for conversion to the active metabolite 5-fluorouracil. Concurrent use of these agents may result in decreased effectiveness of capecitabine.

Drugs/Disease

Util A	Util B	Util C
Decitabine/Cedazuridine	Capecitabine	

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Inqovi Prescribing Information, July 2020, Taiho Oncology, Inc.

44. Decitabine/Cedazuridine / Pregnancy / Pregnancy Negating ___√___

Alert Message: Based on findings from human data, animal studies, and its mechanism of action, Inqovi (decitabine/cedazuridine) can cause fetal harm when administered to a pregnant woman. In nonclinical studies with decitabine in mice and rats, decitabine was teratogenic, fetotoxic, and embryotoxic at doses less than the recommended human dose. Advise pregnant women of the potential risk to a fetus.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Decitabine/Cedazuridine	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Inqovi Prescribing Information, July 2020, Taiho Oncology, Inc.

45. Decitabine/Cedazuridine / Lactation ___√___

Alert Message: There are no data on the presence of cedazuridine, decitabine, or their metabolites in human milk or on their effects on the breastfed child or milk production. Because of the potential for serious adverse reactions in the breastfed child, advise women not to breastfeed during treatment with Inqovi (decitabine/cedazuridine) and for at least 2 weeks after the last dose.

Drugs/Diseases

Util A	Util B	Util C
Decitabine/Cedazuridine	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Inqovi Prescribing Information, July 2020, Taiho Oncology, Inc.

46. Decitabine/Cedazuridine / Therapeutic Appropriateness ___√___

Alert Message: Advise females of reproductive potential to use effective contraception during treatment with Inqovi (decitabine/cedazuridine) and for 6 months after the last dose. Based on findings from human data, animal studies, and its mechanism of action, Inqovi (decitabine/cedazuridine) can cause fetal harm when administered to a pregnant woman.

Drugs/Disease

Util A	Util B	Util C
Decitabine/Cedazuridine		

Gender: Female
Age Range: 11 – 50 yoa

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Inqovi Prescribing Information, July 2020, Taiho Oncology, Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

47. Decitabine/Cedazuridine / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: Advise males with female partners of reproductive potential to use effective contraception during treatment with Inqovi (decitabine/cedazuridine) and for 3 months after the last dose.

Drugs/Disease
Util A Util B Util C
Decitabine/Cedazuridine

Gender: Male

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Inqovi Prescribing Information, July 2020, Taiho Oncology, Inc.

48. Decitabine/Cedazuridine / Non-adherence ___√___ _____ _____

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

Drugs/Diseases
Util A Util B Util C
Decitabine/Cedazuridine

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

Stephanie McGee Azar, Commissioner — (✓) Approve ( ) Deny — 11/18/2022 Date

Melinda Rowe, MD, Assistant Medical Director — (X) Approve ( ) Deny — 11/18/2022 Date

Ginger Wettingfeld, Deputy Commissioner — (✓) Approve ( ) Deny — 11/18/22 Date