Alabama Medicaid DUR Board Meeting Minutes Summary
April 28, 2021

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

Also Present: Lori Thomas, Clemice Hurst, Julie Jordan, Heather Vega, Alex Jenkins, ACHN Pharmacists

Members Absent: none

Call to Order: The DUR meeting was called to order by R. Seaman at approximately 1:02 p.m.

Review and Adoption of Minutes: The minutes of the January 27, 2021 meeting were presented, and D. McConaghy made a motion to approve the minutes. M. Bulloch 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 October 2020. She reported 13,372 total manual requests and 14,859 total electronic requests. From the Prior Authorization and Override Response Time Ratio report for October 2020, L. Thomas reported that approximately 34% of all manual PAs and all overrides were completed in less than two hours. Seventy-seven percent of all manual PAs and 78% of all overrides were completed in less than four hours. Eighty-five percent of all manual PAs and all overrides were completed in less than eight hours. For the month of November 2020, L. Thomas reported 11,527 manual PA requests and 13,167 electronic PA requests were received. She reported that 41% of all manual PAs and 40% of all overrides were completed in less than two hours. Seventy-five percent of all manual PAs and 76% of all overrides were completed in less than four hours. Eighty-four percent of all manual PAs and 86% of all overrides were completed in less than eight hours. For the month of December 2020, L. Thomas reported 11,885 manual PA requests and 13,103 electronic PA requests. L. Thomas reported that approximately 53% of all manual PAs and 51% of all overrides were completed in less than two hours. Eighty-two percent of all manual PA requests and 80% of all overrides were completed in less than four hours. Ninety percent of all manual PA requests and 88% of 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 July 2020 through December 2020. She reported 3,319,373 total prescriptions, 196,406 average recipients per month using pharmacy benefits, and an average paid per prescription of $134.87.

Cost Management Analysis: L. Thomas reported an average cost per claim of $139.04 for December 2020 and emphasized that the table contained the average cost per claim over the past two years. From the 4th Quarter 2020 Drug Analysis, L.Thomas reported 82.7% generic utilization, 8.7% brand single-source, 5% brand multi-source (those requests which required a DAW override), and 3.6% OTC and "other". From the Top 25 Drugs Based on Number of Claims from 10/01/2020 – 12/31/2020, L.Thomas reported the top five drugs: cetirizine, albuterol sulfate HFA, amoxicillin, montelukast sodium, and gabapentin. L. Thomas mentioned that this was identical to 3rd Quarter 2020. K. Newman pointed out that hydrocodone-APAP was previously reported as being sixth, but had moved to ninth for this reported quarter. L. Thomas then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 10/01/2020 – 12/31/2020: Vyvanse®, Focalin XR®, Invega® Sustenna®, Humira® Citrate-free and Suboxone®. 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, Insulins, and Miscellaneous Anticonvulsants.

Therapeutic Drug Class Review: L. Thomas reviewed the Cystic Fibrosis Agents (CFTR Modulators) medication class that requires a Max Cost Override. She reviewed the four medications in this drug class and briefly went over the Max Cost Override criteria. A chart was provided to the DUR Board Members with each medication and the number of override approvals and denials.

RDUR Intervention Report: L. Thomas presented the RDUR Activity Report for October 2020. She reported 500 profiles reviewed and 462 letters sent with 36 responses received as of the date of the report. She reported 19 of 36 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); Drug-Disease Precaution (contraceptive agents and smoking); Appropriate Use (concurrent use of buprenorphine and pure opiate agonists).

Proposed Criteria: L.Thomas presented the proposed set of 43 criteria to the Board and instructed the Board members to mark their ballots. Of the 43 proposed criteria, results from the criteria vote returned 42 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 also informed the Board members that COVID-19 vaccination information could be found on Medicaid's website along with other COVID-related information.

P & T Committee Update: C. Hurst began the P & T Update by informing the Board that the last meeting was held on February 3, 2021, and covered the Skin and Mucous Membrane Agents and Disease-Modifying Antirheumatic Agents. The next P & T Committee meeting will be held on May 5, 2021, and will cover the ADHD Agents, Wakefulness Promoting Agents, and part of the Anti-infectives.

Next Meeting Date: R. Seaman reminded the Board that the next DUR meeting will be held on July 28, 2021. A motion to adjourn the meeting was made by M. Stallworth. D. Powell seconded the motion and the meeting was adjourned at 1:52 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. Ubrogepant / Overuse Alert Message: Ubrelvy (ubrogepant) may be over-utilized. The recommended dose of ubrogepant is 50 mg or 100 mg orally with or without food. If needed, a second dose may be taken at least 2 hours after the initial dose. The maximum dose of ubrogepant in a 24-hour period is 200 mg. The safety of treating more than 8 migraines in a 30-day period has not been established. Conflict Code: ER - Overutilization Drugs/Diseases Util A: Ubrogepant Util B: Util C (Negate): Cirrhosis, CKD 4, CKD 5 Max Dose: 200 mg/day References: Clinical Pharmacology, 2020 Elsevier/Gold Standard. Ubrelvy Prescribing Information, Dec. 2019, Allergan.	___v___	_____	_____
2. Ubrogepant / Overuse Alert Message: Ubrelvy (ubrogepant) may be over-utilized. The recommended initial dose of ubrogepant in patients with severe hepatic impairment (Child-Pugh Class C) or severe renal impairment (CLcr 15-29 mL/min) is 50 mg. If needed, a second dose may be taken at least 2 hours after the initial dose. The maximum dose of ubrogepant in a 24-hour period is 100 mg. The safety of treating more than 8 migraines in a 30-day period has not been established. Conflict Code: ER - Overutilization Drugs/Diseases Util A: Ubrogepant Util B: Util C (Include): Cirrhosis, CKD 4, CKD 5 Max Dose: 100 mg/day References: Clinical Pharmacology, 2020 Elsevier/Gold Standard. Ubrelvy Prescribing Information, Dec. 2019, Allergan.	___v___	_____	_____

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

3. Ubrogepant / ESRD ___√___ _____ _____

Alert Message: The use of Ubrelvy (ubrogepant) should be avoided in patients with end-stage renal disease (CLcr < 15mL/min). Ubrogepant has not been studied in patients with ESRD, and no dosing recommendations can be made for this patient population.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C (Include)
Ubrogepant		ESRD

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

4. Ubrogepant / Therapeutic Appropriateness ___√___ _____ _____

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

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Ubrogepant		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

5. Ubrogepant / Strong CYP3A4 Inhibitors ___√___ _____ _____

Alert Message: The co-administration of Ubrelvy (ubrogepant) with strong CYP3A4 inhibitors is contraindicated. Ubrogepant is a CYP3A4 substrate, and concurrent use with a strong inhibitor may lead to significant increases in ubrogepant exposure. In in vivo studies, the co-administration of ubrogepant with ketoconazole (a strong CYP3A4 inhibitor) resulted in a 9.7-fold and 5.3-fold increase in the AUCinf and Cmax of ubrogepant, respectively.

Conflict Code: DD - Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Ubrogepant	Clarithromycin	Nelfinavir	
	Cobicistat	Posaconazole	
	Conivaptan	Ritonavir	
	Indinavir	Saquinavir	
	Itraconazole	Voriconazole	
	Ketoconazole		

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

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

6. Ubrogepant 100 mg / Moderate CYP3A4 Inhibitors ___√___ _____ _____

Alert Message: When Ubrelvy (ubrogepant) is co-administered with a moderate CYP3A4 inhibitor, the initial dose of ubrogepant should be limited to 50 mg, and the use of a second dose within 24 hours should be avoided. In in vivo drug studies, the co-administration of ubrogepant (a CYP3A4 substrate) with the moderate CYP3A4 inhibitor, verapamil, resulted in an approximate 3.5-fold and 2.8-fold increase in the AUCinf and Cmax of ubrogepant, respectively.

Conflict Code: DD - Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Ubrogepant 100 mg	Aprepitant	Erythromycin	
	Ciprofloxacin	Fluconazole	
	Crizotinib	Fluvoxamine	
	Cyclosporine	Imatinib	
	Diltiazem	Verapamil	
	Dronedarone		

References:
IBM Micromedex DRUGDEX (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA 2020.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

7. Ubrogepant 100 mg / Weak CYP3A4 Inhibitors _____ ___√___ _____

Alert Message: When Ubrelvy (ubrogepant) is co-administered with a weak CYP3A4 inhibitor the initial dose of ubrogepant should be limited to 50 mg and the second dose, if needed, should be limited to 50 mg also. No dedicated drug interaction study has been conducted with ubrogepant (a CYP3A4 substrate) and a weak CYP3A4 inhibitor, but the conservative prediction of the maximal potential increase in ubrogepant exposure with weak CYP3A4 inhibitors is not expected to be more than 2-fold.

Conflict Code: DD - Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Ubrogepant 100 mg	Amiodarone	Lapatinib	
	Chlorzoxazone	Lomitapide	
	Cilostazol	Ranolazine	
	Fosaprepitant	Tacrolimus	
	Istradefylline	Ticagrelor	
	Ivacaftor		

References:
IBM Micromedex DRUGDEX (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA 2020.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

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

8. Ubrogepant / Strong CYP3A4 Inducers ___√___ _____ _____

Alert Message: The concurrent use of Ubrelvy (ubrogepant) with strong CYP3A4 inducers should be avoided. Ubrogepant is a CYP3A4 substrate, and concurrent use with a strong CYP3A4 inducer may result in decreased ubrogepant exposure and loss of efficacy. In in vivo drug studies, the co-administration of ubrogepant with the strong CYP3A4 inhibitor, rifampin, resulted in an approximate 80% reduction in ubrogepant exposure.

Conflict Code: DD - Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Ubrogepant	Carbamazepine	
	Enzalutamide	
	Mitotane	
	Phenobarbital	
	Phenytoin	
	Primidone	
	Rifampin	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

9. Ubrogepant 100 mg / BCRP and/or P-gp Only Inhibitors ___√___ _____ _____

Alert Message: When Ubrelvy (ubrogepant) is co-administered with a BCRP and/or P-gp only inhibitor, the initial dose of ubrogepant should be limited to 50 mg and the second dose, if needed, should be limited to 50 mg also. No dedicated drug interaction study has been conducted with ubrogepant (a BCRP and P-gp substrate) and BCRP and P-gp efflux inhibitors, but an increase in ubrogepant exposure may result from co-administration of these drugs.

Conflict Code: DD - Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Ubrogepant 100 mg	Carvedilol	
	Eltrombopag	
	Quinidine	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

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

10. Ubrogepant / Lactation ___√___ _____ _____

Alert Message: There are no data on the presence of Ubrelvy (ubrogepant) in human milk, the effects of ubrogepant on the breastfed infant, or the effects of ubrogepant on milk production. In lactating rats, oral dosing with ubrogepant resulted in levels of ubrogepant in milk comparable to peak plasma concentrations. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ubrogepant and any potential adverse effects on the breastfed infant from ubrogepant or from the underlying maternal condition.

Conflict Code: MC - Drug/Disease Precaution
Drugs/Diseases

Util A	Util B	Util C
Ubrogepant	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

11. Ubrogepant / Pregnancy / Pregnancy Negating ___√___ _____ _____

Alert Message: There are no adequate data on the developmental risk associated with the use of Ubrelvy (ubrogepant) in pregnant women. In animal studies, adverse effects on embryofetal development were observed following administration of ubrogepant during pregnancy (increased embryofetal mortality in rabbits) or during pregnancy and lactation (decreased body weight in offspring in rats) at doses greater than those used clinically and which were associated with maternal toxicity.

Conflict Code: MC - Drug/Disease Precaution
Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrelvy Prescribing Information, Dec. 2019, Allergan.

12. Levamlodipine / Overuse ___√___ _____ _____

Alert Message: Conjupri (levamlodipine) may be over-utilized. The recommended maximum daily adult dose is 5 mg once daily.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Levamlodipine		

Max Dose: 5 mg/day
Age Range: 18 – 999 yoa

References:
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.
Conjupri Prescribing Information, Dec. 2019, CSPC Ouyi Pharmaceutical Co., Ltd.

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

13. Levamlodipine / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: Conjupri (levamlodipine) may be over-utilized. The effective antihypertensive oral dose in pediatric patients 6 to 17 years of age is 2.5 mg once daily. Doses in excess of 2.5 mg daily have not been studied in pediatric patients.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Levamlodipine		

Age Range: 0 – 17 yoa
Max Dose: 2.5 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Conjupri Prescribing Information, Dec. 2019, CSPC Ouyi Pharmaceutical Co., Ltd.

14. Levamlodipine / Simvastatin ___√____ _____ _____

Alert Message: The dose of simvastatin should be limited to 20 mg daily in patients co-administered Conjupri (levamlodipine). Levamlodipine is the pharmacologically active enantiomer of amlodipine. In a drug study, co-administration of amlodipine with simvastatin resulted in a 77% increase in exposure to simvastatin compared to simvastatin alone.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Levamlodipine	Simvastatin 40 & 80	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Conjupri Prescribing Information, Dec. 2019, CSPC Ouyi Pharmaceutical Co., Ltd.

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

15. Levamlodipine / Moderate & Strong CYP3A4 Inhibitors ___√___ _____ _____

Alert Message: Co-administration of Conjupri (levamlodipine) with moderate or strong CYP3A inhibitors may result in increased systemic exposure to amlodipine and may require levamlodipine dose reduction. Monitor the patient for symptoms of hypotension and edema when amlodipine is co-administered with CYP3A inhibitors to determine the need for dose adjustment.

Conflict Code: DD - Drug/Drug Interaction
Drugs/Diseases

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

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Conjupri Prescribing Information, Dec. 2019, CSPC Ouyi Pharmaceutical Co., Ltd.

16. Levamlodipine / Cyclosporine & Tacrolimus ___√___ _____ _____

Alert Message: The concurrent use of Conjupri (levamlodipine) with cyclosporine or tacrolimus may increase the systemic exposure of the immunosuppressive agent. Frequent monitoring of trough blood levels of cyclosporine and tacrolimus is recommended and adjust the dose when appropriate.

Conflict Code: DD - Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Levamlodipine	Cyclosporine	
	Tacrolimus	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Conjupri Prescribing Information, Dec. 2019, CSPC Ouyi Pharmaceutical Co., Ltd.

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

17. Riluzole Tablets & Film / Overutilization ___√___ _____ _____

Alert Message: Riluzole may be over-utilized. The manufacturer's recommended dosage of riluzole is 50 mg twice daily.

Drugs/Diseases

Util A	Util B	Util C
Riluzole Tablets		
Riluzole Oral Film		

Max Dose: 100 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.

18. Riluzole Suspension / Overutilization ___√___ _____ _____

Alert Message: Tiglutik (riluzole oral suspension) may be over-utilized. The manufacturer's recommended dosage of riluzole oral suspension is 50 mg (10 mL) twice daily, every 12 hours.

Drugs/Diseases

Util A	Util B	Util C
Riluzole Suspension		

Max Dose: 100 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Tiglutik Prescribing Information, September 2018, ITF Pharma.

19. Riluzole – All / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: Cases of drug-induced liver injury, some of which were fatal, have been reported in patients taking riluzole. Patients should be monitored for signs and symptoms of hepatic injury every month for the first three months of treatment and periodically thereafter. The use of riluzole is not recommended if patients develop hepatic transaminases levels greater than 5 times the ULN. Discontinue riluzole if there is evidence of liver dysfunction (e.g., elevated bilirubin).

Drugs/Diseases

Util A	Util B	Util C
Riluzole		

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.

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

20. Riluzole – All / Pulmonary Toxicity ___√___ _____ _____

Alert Message: Interstitial lung disease, including hypersensitivity pneumonitis, has occurred in patients taking riluzole. Discontinue riluzole immediately if interstitial lung disease develops.

Drugs/Diseases

Util A	Util B	Util C
Riluzole	Acute Interstitial Pneumonia	
	Dyspnea	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.

21. Riluzole – All / Fever & Neutropenia ___√___ _____ _____

Alert Message: Cases of severe neutropenia (absolute neutrophil count less than 500 per mm3) within the first 2 months of riluzole treatment have been reported. Advise patients to report febrile illnesses.

Drugs/Diseases

Util A	Util B	Util C
Riluzole	Fever	
	Neutropenia	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.

22. Riluzole – All / CYP1A2 Inhibitors ___√___ _____ _____

Alert Message: The concomitant use of strong or moderate CYP1A2 inhibitors (e.g., ciprofloxacin, fluvoxamine, methoxsalen, mexiletine, oral contraceptive, vemurafenib, zileuton) with riluzole (a CYP1A2 substrate) may increase the risk of riluzole-associated adverse reactions.

Drugs/Diseases

Util A	Util B	Util C
Riluzole	Ciprofloxacin	
	Fluvoxamine	
	Methoxsalen	
	Mexiletine	
	Oral Contraceptives	
	Vemurafenib	
	Zileuton	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.

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

23. Riluzole – All / CYP1A2 Inducers ___√___ _____ _____

Alert Message: Concurrent use of riluzole (a CYP1A substrate) with CYP1A2 inducers may decrease riluzole exposure, which may result in decreased riluzole efficacy.

Drugs/Diseases

Util A	Util B	Util C
Riluzole	Barbiturates	Ritonavir
	Carbamazepine	Ritonavir
	Cannabidiol	Teriflunomide
	Omeprazole	Tipranavir
	Leflunomide	
	Modafinil	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.

24. Riluzole – All / Therapeutic Appropriateness ___√___ _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Riluzole		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.

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

25. Riluzole – All / Hepatotoxic Drugs ___√___ _____ _____

Alert Message: Cases of drug-induced liver injury, some of which were fatal, have been reported in patients taking riluzole. Riluzole-treated patients who take other hepatotoxic drugs may be at an increased risk for hepatotoxicity.

Drugs/Diseases

Util A	Util B	Util C
Riluzole	Alectinib	Ixazomib
	Allopurinol	Ketoconazole
	Amiodarone	Larotrectinib
	Amoxicillin-clavulanate	Maraviroc
	Atorvastatin	Methotrexate
	Azathioprine	Methyldopa
	Busulfan	Minocycline
	Carbamazepine	Nefazodone
	Chlorpromazine	Nitrofurantoin
	Dantrolene	Phenytoin
	Diclofenac	Propylthiouracil
	Didanosine	Pyrazinamide
	Disulfiram	Quinidine
	Efavirenz	Rifampin
	Erythromycin	Simvastatin
	Erlotinib	Sulfasalazine
	Flutamide	Sulindac
	Ibuprofen	Sunitinib
	Idelalisib	Ticlopidine
	Infliximab	TMP-SMZ
	Interferon	Valproate
	Isoniazid	
	Itraconazole	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.
Bjornsson ES. Hepatotoxicity by Drugs: The Most Common Implicated Agents. Int J Mol Sci. 2016;17(2):224. Published 2016 Feb 6. doi:10.3390/ijms17020224

26. Riluzole – All / Nonadherence ___√___ _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing riluzole. Non-adherence 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
Riluzole		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Introna A, D'Errico E, Modugno B, et al., Adherence to Riluzole in Patients with Amyotrophic Lateral Sclerosis: An Observational Study. Neuropsych Dis Treat. 2018;14:193-203.
Viswanathan M, Golin CE, Jones CD, et al. Interventions to Improve Adherence to Self-administered Medications for Chronic Diseases in the United States: A Systematic Review. Ann Intern Med. 2012 Dec 4;157:785–795. doi: 10.7326/0003-4819-157-11-201212040-00538

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

25. Riluzole – All / Pregnancy / Pregnancy Negating ___√___ _____ _____

Alert Message: There are no studies of riluzole in pregnant women, and case reports have been inadequate to inform the drug-associated risk. In studies in which riluzole was administered orally to pregnant animals, developmental toxicity (decreased embryofetal/offspring viability, growth, and functional development) was observed at clinically relevant doses. Based on these results, women should be advised of a possible risk to the fetus associated with the use of riluzole during pregnancy.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.

28. Riluzole – All / Lactation ___√___ _____ _____

Alert Message: It is not known if riluzole is excreted in human milk. Riluzole or its metabolites have been detected in the milk of lactating rats. Women should be advised that many drugs are excreted in human milk and that the potential for serious adverse reactions in nursing infants from riluzole is unknown.

Drugs/Diseases

Util A	Util B	Util C
Riluzole	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.

29. Lemborexant / Overuse ____√____ _____ _____

Alert Message: The recommended dosage of Dayvigo (lemborexant) is 5 mg taken no more than once per night, immediately before going to bed, with at least 7 hours remaining before the planned time of awakening. The dose may be increased to the maximum recommended dose of 10 mg based on clinical response and tolerability.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Lemborexant		Hepatic Impairment
		Weak CYP3A4 Inhibitors

Max Dose: 10 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

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

30. Lemborexant 10 mg / Overuse – Hepatic Impairment ___V___ _____ _____

Alert Message: The maximum recommended dose of Dayvigo (lemborexant) is 5 mg no more than once per night in patients with moderate hepatic impairment. In drug studies, lemborexant exposure (AUC and Cmax) and terminal half-life were increased in patients with moderate hepatic impairment (Child-Pugh Class B). Dosage adjustment is recommended in patients with moderate hepatic impairment (Child-Pugh Class B). No dosage adjustment is recommended in patients with mild hepatic impairment, but they may experience an increased risk of somnolence.

Drugs/Diseases

Util A	Util B	Util C (Include)
Lemborexant 10 mg		Hepatic Impairment

Max Dose: 5 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

31. Lemborexant / Cirrhosis ___V___ _____ _____

Alert Message: Dayvigo (lemborexant) is not recommended in patients with severe hepatic impairment. In drug studies, lemborexant exposure (AUC and Cmax) and terminal half-life were increased in patients with moderate hepatic impairment (Child-Pugh Class B). Lemborexant has not been studied in patients with severe hepatic impairment.

Drugs/Diseases

Util A	Util B	Util C
Lemborexant	Cirrhosis	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

32. Lemborexant / Therapeutic Appropriateness ___V___ _____ _____

Alert Message: Dayvigo (lemborexant) use is contraindicated in patients with narcolepsy. Lemborexant is a central nervous system (CNS) depressant that can impair daytime wakefulness even when used as prescribed.

Drugs/Diseases

Util A	Util B	Util C (Include)
Lemborexant		Narcolepsy

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

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

33. Lemborexant / Sleep Paralysis & Hallucinations ___√___ _____ _____

Alert Message: Sleep paralysis (an inability to move or speak for up to several minutes during sleep-wake transitions) and hypnagogic/hypnopompic hallucinations (including vivid and disturbing perceptions) can occur with the use of Dayvigo (lemborexant). Symptoms similar to mild cataplexy also can occur with lemborexant. Such symptoms can include periods of leg weakness lasting from seconds to a few minutes, can occur either at night or during the day, and may not be associated with an identified triggering event (e.g., laughter or surprise). Prescribers should explain the nature of these events to patients when prescribing lemborexant.

Drugs/Diseases

Util A	Util B	Util C
Lemborexant	Recurrent Sleep Paralysis	
	Hallucinations	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

34. Lemborexant / Complex Sleep Behaviors ___√___ _____ _____

Alert Message: Complex sleep behaviors, including sleep-walking, sleep-driving, and engaging in other activities while not fully awake (e.g., preparing and eating food, making phone calls, having sex), have been reported to occur with the use of hypnotics such as Dayvigo (lemborexant). Discontinue lemborexant immediately if a patient experiences a complex sleep behavior.

Drugs/Diseases

Util A	Util B	Util C
Lemborexant	Sleep Walking	
	Other Parasomnia	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

35. Lemborexant / Suicidal Ideation & Depression ___√___ _____ _____

Alert Message: Worsening of depression or suicidal thinking may occur in patients receiving Dayvigo (lemborexant). Prescribe the lowest number of tablets feasible to avoid intentional overdose. The emergence of any new behavioral sign or symptom of concern requires careful and immediate evaluation.

Drugs/Diseases

Util A	Util B	Util C
Lemborexant	Depression	
	Suicide Attempt	
	Suicidal Ideation	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

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

36. Lemborexant / Compromised Respiratory Function ___√___ _____ _____

Alert Message: The effect of Dayvigo (lemborexant) on respiratory function should be considered if prescribed to patients with compromised respiratory function. Lemborexant has not been studied in patients with moderate to severe obstructive sleep apnea (OSA) or in patients with chronic obstructive pulmonary disease (COPD).

Drugs/Diseases

Util A	Util B	Util C
Lemborexant	COPD	
	OSA	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

37. Lemborexant / Moderate & Strong CYP3A4 Inhibitors ___√___ _____ _____

Alert Message: The concurrent use of Dayvigo (lemborexant) with a moderate or strong CYP3A4 inhibitor should be avoided. Lemborexant is a CYP3A4 substrate, and concomitant use with these drugs has been shown to significantly increase the AUC and Cmax of lemborexant, increase the risk of lemborexant-related adverse reactions.

Drugs/Diseases

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

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at:
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionaLabeling/ucm093664.htm

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

38. Lemborexant 10 mg / Weak CYP3A4 Inhibitors ___√___ _____ _____

Alert Message: The maximum recommended dosage of Dayvigo (lemborexant) is 5 mg no more than once per night when coadministered with weak CYP3A inhibitors. Lemborexant is a CYP3A4 substrate, and physiologically-based pharmacokinetic (PBPK) modeling predicted that concomitant use of weak CYP3A inhibitors increased lemborexant exposure by less than 2-fold.

Conflict Code: DD - Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Lemborexant 10 mg	Chlorzoxazone	
	Cilostazol	
	Fosaprepitant	
	Ivacaftor	
	Lomitapide	
	Ranitidine	
	Ranolazine	
	Tacrolimus	
	Ticagrelor	

Max Dose: 5 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at:
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionaLabeling/ucm093664.htm

39. Lemborexant / Moderate & Strong CYP3A4 Inducers ___√___ _____ _____

Alert Message: The concurrent use of Dayvigo (lemborexant) with moderate or strong CYP3A4 inducers should be avoided. Lemborexant is a CYP3A4 substrate, and concomitant use with these inducers has been shown to decrease lemborexant exposure and may reduce lemborexant-efficacy.

Conflict Code: DD - Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Lemborexant	Apalutamide	Bosentan	
	Carbamazepine	Efavirenz	
	Enzalutamide	Etravirine	
	Lumacaftor	Dexamethasone	
	Mitotane	Modafinil	
	Phenobarbital		
	Phenytoin		
	Primidone		
	Rifabutin		
	Rifampin		
	Rifapentine		

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at:
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionaLabeling/ucm093664.htm

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

40. Lemborexant / CYP2B6 Substrates ___√___ _____ _____

Alert Message: The concurrent use of Dayvigo (lemborexant) with a CYP2B6 substrate may result in the reduced efficacy of the substrate. Lemborexant is CYP2B6 inducer, and concomitant use with a CYP2B6 substrate can lead to decreased substrate exposure. Monitor the patient for adequate CYP2B6 substrate clinical response. Increasing the dose of the substrate may be considered as needed.

Conflict Code: DD - Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Lemborexant	Bupropion	
	Cyclophosphamide	
	Efavirenz	
	Methadone	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer health.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.
Hedrich WD, Hassan HE, Wang H. Insights into CYP2B6-mediated Drug-drug Interactions. Acta Pharm Sin B. 2016;6(5):413–425. doi:10.1016/j.apsb.2016.07.016

41. Lemborexant / Therapeutic Appropriateness ___√___ _____ _____

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

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Lemborexant		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

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

42. Lemborexant / Lactation ___√___ _____ _____

Alert Message: There are no data on the presence of Dayvigo (lemborexant) in human milk, the effects on the breastfed infant, or the effects on milk production. Lemborexant and its metabolites are present in the milk of lactating rats. Infants exposed to lemborexant through breastmilk should be monitored for excessive sedation. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for lemborexant and any potential adverse effects on the breastfed infant from lemborexant or the underlying maternal condition.

Conflict Code: MC – Drug Disease Warning
Drugs/Diseases

Util A	Util B	Util C
Lemborexant	Lactation	

Age Range: 11 – 50 yoa
Gender: Female

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

43. Lemborexant / Pregnancy / Pregnancy Negating ___√___ _____ _____

Alert Message: There are no available data on Dayvigo (lemborexant) use in pregnant women to evaluate for drug-associated risks of major birth defects, miscarriage, or adverse maternal or fetal outcomes. There is a pregnancy exposure registry that monitors pregnancy outcomes in women who are exposed to lemborexant during pregnancy. Healthcare providers are encouraged to register patients in the DAYVIGO pregnancy registry.

Conflict Code: MC – Drug Disease Warning
Drugs/Diseases

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

Age Range: 11 – 50 yoa
Gender: Female

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Dayvigo Prescribing Information, Dec. 2019, Eisai Inc.

Stephanie McGee Azar, Commissioner — (X) Approve ( ) Deny — 5/26/2021 Date

Melinda G. Rowe, MD, MBA, MPH
Assistant Medical Director — (X) Approve ( ) Deny — 5/24/2021 Date

Kathy Hall, Deputy Commissioner — (X) Approve ( ) Deny — 5/24/2021 Date