

Alabama Medicaid DUR Board Meeting Minutes
January 22, 2020

Members Present: Kelli Littlejohn Newman, Rachel Seaman, Robert Moon, Jessica Jackson, Crystal Deas, Kelly Tate

Also Present: Tiffany Minnifield, Lori Thomas, Clemice Hurst, Julie Jordan, Alex Jenkins, Scott Donald, Taleshia Core

Present via Conference Call: Lacy Miller, Kristian Testerman, Kristin Kennamer, Lisa Lewis, Emily Arnold, Lydia Rather, Debbie Mullinax

Members Absent: Mary Stallworth, Dan McConaghy, Clinton Martin, Danielle Powell

Call to Order: The DUR meeting was called to order by R. Seaman at approximately 1:07p.m.

Review and Adoption of Minutes: The minutes of the October 23, 2019 meeting were presented and R. Moon made a motion to approve the minutes. C. Deas 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 July 2019. She reported 12,038 total manual requests and 22,051 total electronic requests. From the Prior Authorization and Override Response Time Ratio report for July 2019, L. Thomas reported that approximately 86% of all manual PAs and 85% of all overrides were completed in less than two hours. Ninety-five percent of all manual PAs and all overrides were completed in less than four hours. Ninety-seven percent of all manual PAs and all overrides were completed in less than eight hours. For the month of August 2019, L. Thomas reported 12,813 manual PA requests and 23,780 electronic PA requests were received. She reported that 82% of all manual PAs and 77% of all overrides were completed in less than two hours. Ninety-five percent of all manual PAs and 94% of all overrides were completed in less than four hours. Ninety-six percent of all manual PAs and 95% of all overrides were completed in less than eight hours. For the month of September 2019, L. Thomas reported 11,274 manual PA requests and 21,560 electronic PA requests. L. Thomas reported that approximately 83% of all manual PAs and 82% of all overrides were completed in less than two hours. Ninety-four percent of all manual PA requests and overrides were completed in less than four hours. Ninety-six percent of all manual PA requests and overrides were completed in less than eight hours.

Program Summary Review: L.Thomas briefly reviewed the Alabama Medicaid Program Summary for the months of April 2019 through September 2019. She reported 3,463,563 total prescriptions, 209,604 average recipients per month using pharmacy benefits, and an average paid per prescription of \$120.52.

Cost Management Analysis: L.Thomas reported an average cost per claim of \$115.22 for September 2019 and emphasized that the table contained the average cost per claim over the past two years. From the 3rd Quarter 2019 Drug Analysis, L.Thomas reported 81% generic utilization, 9% brand single-source, 7% brand multi-source (those requests which required a DAW override), and 4% OTC and "other". From the Top 25 Drugs Based on Number of Claims from 07/01/2019 – 09/30/2019, L.Thomas reported the top five drugs: cetirizine, amoxicillin, ProAir[®] HFA, montelukast sodium, and gabapentin. L. Thomas then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 07/01/2019 – 09/30/2019: Vyvanse[®], Focalin XR[®], Invega[®] Sustenna[®], Concerta[®], and Suboxone[®]. L. Thomas emphasized this information was identical to 2nd Quarter 2019. 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, Respiratory and CNS Stimulants, Insulins, Miscellaneous Anticonvulsants, and Amphetamines.

RDUR Intervention Report: L. Thomas presented the RDUR Activity Report for October 2019. She reported 509 profiles reviewed and 723 letters sent with 56 responses received as of the date of the report. She reported 31 of 49 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); Appropriate Use (concurrent use of buprenorphine and pure opiate agonists).

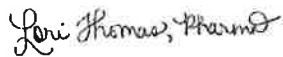
Proposed Criteria: L. Thomas presented the proposed set of 37 criteria to the Board. T. Minnifield instructed the Board members to mark their ballots. Of the 37 proposed criteria, results from the criteria vote returned 37 approved.

Medicaid Update: T. Minnifield reminded the Board members that all updated Medicaid drug lists and ALERTs were provided to them electronically and are also available online. T. Minnifield also reminded the Board members that the next DUR Meeting would be April 22, 2020. K. Newman reviewed the Morphine Milligram Equivalent (MME) Edit implemented in May 2019 and informed the Board members that currently the hard edit is set at 200 MME/day. J. Jackson asked if resources were available for providers to have a better understanding of tapering opioids. K. Newman mentioned the resources available from the Centers of Disease Control and Prevention (CDC).

P & T Committee Update: C. Hurst began the P & T Update by informing the Board that the last meeting was held on November 6, 2019, and covered the Platelet Aggregation Inhibitors; Cardiac Agents; and the Antihyperlipidemics. The next P & T Committee meeting will be held on February 5, 2020 and will cover the Antihypertensive Agents.

Next Meeting Date: R. Seaman reminded the Board that the next DUR meeting will be held on April 22, 2020. A motion to adjourn the meeting was made by R. Moon. K. Tate seconded the motion and the meeting was adjourned at 1:33 p.m.

Respectfully submitted,



Lori Thomas, PharmD.

**ALABAMA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS**

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

1. Revefenacin / Overutilization

_v_____

Alert Message: The recommended dose of Yupelri (revefenacin) inhalation solution is one 175 mcg unit-dose vial administered once daily by nebulizer using a mouthpiece.

Drugs/Diseases

Util A Util B Util C

Revefenacin

Max Dose: 1 inhalation/day

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

2. Revefenacin / Glaucoma

_v_____

Alert Message: Yupelri (revefenacin) should be used with caution in patients with narrow-angle glaucoma. Revefenacin is a long-acting muscarinic antagonist, and its use in this patient population can worsen the condition.

Drugs/Diseases

Util A Util B Util C (Include)

Revefenacin Glaucoma

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

3. Revefenacin / Urinary Retention, Prost Hyperplasia & Bladder Neck Obs

_v_____

Alert Message: Yupelri (revefenacin) should be used with caution in patients with urinary retention. Prescribers and patients should be alert for signs and symptoms of urinary retention (e.g., difficulty passing urine, painful urination), especially in patients with prostatic hyperplasia or bladder-neck obstruction. Instruct patients to consult a healthcare provider immediately if any of these signs or symptoms develop.

Drugs/Diseases

Util A Util B Util C

Revefenacin Urinary Retention
 Prostatic Hyperplasia
 Bladder-Neck Obstruction

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

4. Revefenacin / Anticholinergics

v _____

Alert Message: The concurrent use of Yupelri (revefenacin) with anticholinergic agents should be avoided. Revefenacin is a long-acting muscarinic antagonist, and co-administration with anticholinergics may lead to an increase in anticholinergic adverse effects.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>				<u>Util C</u>
Revefenacin	Trihexyphenidyl	Trospium	Cyclizine	Oxybutynin	
	Benztropine	Hyoscyamine	Dicyclomine	Trimethobenzamide	
	Orphenadrine	Scopolamine	Diphenhydramine	Flavoxate	
	Darifenacin	Propantheline	Meclizine	Metscopolamine	
	Fesoterodine	Mepenzolate	Solifenacin	Tolterodine	

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

5. Revefenacin / OATP1B1 & OATP1B3 Inhibitors

v _____

Alert Message: The concurrent use of Yupelri (revefenacin) with OATP1B1 and OATP1B3 inhibitors is not recommended. The active metabolite of revefenacin is a substrate of OATP1B1 and OATP1B3. Co-administration of revefenacin with an inhibitor of these uptake transporters can result in increased systemic exposure to the active metabolite.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Revefenacin	Rifampicin	Letemovir
	Cyclosporine	Lopinavir
	Clarithromycin	Obeticholic Acid
	Atazanavir	Paritaprevir/Ombitasvir/Ritonavir
	Cobicistat	Rifampin
	Daclatasvir	Velpatasvir/Sofosbuvir/Voxilaprevir
	Eltrombopag	Velpatasvir/Sofosbuvir
	Erythromycin	Teriflunomide
	Gemfibrozil	
	Glecaprevir/Pibrentasvir	

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

6. Revefenacin / Therapeutic Appropriateness

v _____

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

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Revefenacin		

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

7. Revefenacin / Hepatic Impairment

Alert Message: Yupelri (revefenacin) is not recommended for use in patients with any degree of hepatic impairment. In a pharmacokinetic study, the systemic exposure of revefenacin was unchanged while that of its active metabolite was increased in subjects with moderate hepatic impairment. The safety of revefenacin has not been evaluated in COPD patients with mild-to-severe hepatic impairment.

___v___

Drugs/Diseases

Util A

Util B

Util C (Include)

Revefenacin

Hepatic Impairment

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

8. Revefenacin / Pregnancy / Pregnancy Negating

Alert Message: There are no adequate and well-documented studies with Yupelri (revefenacin) in pregnant women. Women should be advised to contact their physician if they become pregnant while taking revefenacin.

___v___

Drugs/Diseases

Util A

Util B

Util C (Negating)

Revefenacin

Pregnancy

Miscarriage

Delivery

Abortion

Gender: Female

Age Range: 11 – 50 yoa

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

9. Revefenacin / Lactation

Alert Message: There is no information regarding the presence of Yupelri (revefenacin) in human milk, the effects on the breastfed infant, or the effects on milk production. However, revefenacin was present in the milk of lactating rats following dosing during pregnancy and lactation. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for revefenacin, and any potential adverse effects on the breastfed infant from revefenacin or from the underlying maternal condition.

___v___

Drugs/Diseases

Util A

Util B

Util C

Revefenacin

Lactation

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

10. Revefenacin / Nonadherence

v _____

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

Revefenacin

References:

van Boven JF, Chavannes NH, van der Molen T, et al. Clinical and Economic Impact of Non-adherence in COPD: A Systematic Review. *Respir Med.* 2015 Jan;108(1):103-113.

Restrepo RD, Alvarez MT, Wittnebel LD, et al., Medication Adherence Issues in Patients Treated for COPD. *International Journal of COPD.* 2008;3(3):371-384.

Simoni-Wastila L, Wei Y, Qian J, et al., Association of Chronic Obstructive Pulmonary Disease Maintenance Medication Adherence With All-Cause Hospitalization and Spending in a Medicare Population. *Am J Geriatr Pharmacother.* 2012 Jun;10(3):201-210.

Lareau SC, Yawn BP. Improving Adherence with Inhaler Therapy in COPD. *International Journal COPD.* 2010 Nov 24;5:401-406.

11. Erenumab-aooe / Overutilization

v _____

Alert Message: Aimovig (erenumab-aooe) may be over-utilized. The recommended dosage of erenumab-aooe is 70 mg injected subcutaneously once monthly. Some patients may benefit from a dosage of 140 mg injected subcutaneously once monthly.

Drugs/Diseases

Util A

Util B

Util C

Erenumab-aooe

Max Dose: 2 pens per month

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.

Aimovig Prescribing Information, May 2018, Amgen Inc.

12. Erenumab-aooe / Therapeutic Appropriateness (0 – 17 yoa)

v _____

Alert Message: The safety and effectiveness of Aimovig (erenumab-aooe) in pediatric patients have not been established.

Drugs/Diseases

Util A

Util B

Util C

Erenumab-aooe

Age Range: 0 - 17 yoa

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.

Aimovig Prescribing Information, May 2018, Amgen Inc.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

13. Erenumab-aooe / Lactation

 v _____ _____

Alert Message: There are no data on the presence of Aimovig (erenumab-aooe) 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 erenumab-aooe and any potential adverse effects on the breastfed infant from erenumab-aooe or from the underlying maternal condition.

Drugs/Diseases

Util A Util B Util C
Erenumab-aooe Lactation

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Aimovig Prescribing Information, May 2018, Amgen Inc.

14. Erenumab-aooe / Nonadherence

 v _____ _____

Alert Message: Based on refill history, your patient may be underutilizing Aimovig (erenumab-aooe). Nonadherence 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
Erenumab-aooe

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med. 2005; 353(5):487–497.
Aimovig Prescribing Information, May 2018, Amgen Inc.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

15. Fremanezumab-vfrm / Therapeutic Appropriateness (0 – 17 yoa)

 v _____ _____

Alert Message: The safety and effectiveness of Ajovy (fremanezumab-vfrm) in pediatric patients have not been established.

Drugs/Diseases

Util A Util B Util C
Fremanezumab-vfrm

Age Range: 0 - 17 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Ajovy Prescribing Information, Sept. 2018, Teva Pharmaceuticals.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

16. Fremanezumab-vfrm / Lactation

 v _____ _____

Alert Message: There are no data on the presence of Ajovy (fremanezumab-vfrm) in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for fremanezumab-vfrm and any potential adverse effects on the breastfed infant from fremanezumab-vfrm or from the underlying maternal condition.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Fremanezumab-vfrm	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Ajovy Prescribing Information, Sept. 2018, Teva Pharmaceuticals.

17. Fremanezumab-vfrm / Pregnancy / Pregnancy Negating

 v _____ _____

Alert Message: There are no adequate data on the developmental risk associated with the use of Ajovy (fremanezumab-vfrm) in pregnant women. Fremanezumab-vfrm has a long half-life. This should be taken into consideration for women who are pregnant or plan to become pregnant while using this drug.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>
Fremanezumab-vfrm	Pregnancy	Miscarriage Delivery Abortion

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Ajovy Prescribing Information, Sept. 2018, Teva Pharmaceuticals.

18. Prucalopride / Overutilization

 v _____ _____

Alert Message: Motegrity (prucalopride) may be over-utilized. The manufacturer's recommended dosage prucalopride for the treatment of chronic idiopathic constipation in adults is 2 mg once daily.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>
Prucalopride		CKD Stage 4 CKD Stage 5

Max Dose: 2 mg/day

References:
Motegrity Prescribing Information, Dec. 2018, Shire US, Inc.
Facts & Comparisons, 2019 Updated, Wolters Kluwer Healthcare.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

19. Prucalopride / Overutilization

Alert Message: Motegrity (prucalopride) may be over-utilized. The manufacturer's recommended dosage of prucalopride for the treatment of chronic idiopathic constipation in adults with severe renal impairment (CrCL < 30 mL/min) is 1 mg once daily. Prucalopride is known to be substantially excreted by the kidney, and the risk of adverse reactions may be greater in patients with impaired renal function.

v _____

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Prucalopride		CKD Stage 4 CKD Stage 5

Max Dose: 1 mg/day

References:

Motegrity Prescribing Information, Dec. 2018, Shire US, Inc.
Facts & Comparisons, 2019 Updated, Wolters Kluwer Healthcare.

20. Prucalopride / End-Stage Renal Disease

Alert Message: The use of Motegrity (prucalopride) should be avoided in patients with end-stage renal disease requiring dialysis. The pharmacokinetics of prucalopride in patients with end-stage renal disease or undergoing dialysis is not fully known.

v _____

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Prucalopride		End-Stage Renal Disease

References:

Motegrity Prescribing Information, Dec. 2018, Shire US, Inc.
Facts & Comparisons, 2019 Updated, Wolters Kluwer Healthcare.

21. Prucalopride / Contraindications

Alert Message: Motegrity (prucalopride) is contraindicated in patients with intestinal perforation or obstruction due to a structural or functional disorder of the gut wall; obstructive ileus; severe inflammatory conditions of the intestinal tract such as Crohn's disease, ulcerative colitis, and toxic megacolon/megarectum.

v _____

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Prucalopride	Gastrointestinal Obstruction Crohn's Disease Perforation of Intestine Obstructive Ileus Ulcerative Colitis Toxic Megacolon	

References:

Motegrity Prescribing Information, Dec. 2018, Shire US, Inc.
Facts & Comparisons, 2019 Updated, Wolters Kluwer Healthcare.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

22. Prucalopride / Suicidal Ideation & Behavior

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Alert Message: Monitor all patients treated with Motegrity (prucalopride) for persistent worsening of depression or the emergence of suicidal thoughts and behaviors. Counsel patients, their caregivers, and family members of patients to be aware of any unusual changes in mood or behavior and alert the healthcare provider. Instruct patients to discontinue prucalopride immediately and contact their healthcare provider if they experience any of these symptoms.

Drugs/Diseases

Util A

Util B

Util C (Include)

Prucalopride

Suicidal Ideation
Suicide Attempt
Depression

References:

Motegrity Prescribing Information, Dec. 2018, Shire US, Inc.
Facts & Comparisons, 2019 Updated, Wolters Kluwer Healthcare.

23. Prucalopride / Therapeutic Appropriateness

 v

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

Drugs/Diseases

Util A

Util B

Util C

Prucalopride

Age Range: 0 – 17 yoa

References:

Motegrity Prescribing Information, Dec. 2018, Shire US, Inc.
Facts & Comparisons, 2019 Updated, Wolters Kluwer Healthcare.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

24. Prucalopride / Lactation

v _____

Alert Message: Motegrity (prucalopride) is present in breast milk. There are no data on the effects of prucalopride on the breastfed child or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for prucalopride and any potential adverse effects on the breastfed child from prucalopride or from the underlying maternal condition.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Prucalopride	Lactation Disorders of Lactation	

Gender: Female

Age Range: 11 – 50 yoa

References:

Motegrity Prescribing Information, Dec. 2018, Shire US, Inc.
Facts & Comparisons, 2019 Updated, Wolters Kluwer Healthcare.

25. Prucalopride / Pregnancy / Pregnancy Negating

v _____

Alert Message: Available data from case reports with Motegrity (prucalopride) use in pregnant women are insufficient to identify any drug-associated risks of miscarriage, major birth defects, or adverse maternal or fetal outcomes. Cases of spontaneous abortion have been observed during clinical studies, although, in the presence of other risk factors, the relationship to prucalopride is unknown.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>
Prucalopride	Pregnancy	Miscarriage Abortion Delivery

Gender: Female

Age Range: 11 – 50 yoa

References:

Motegrity Prescribing Information, Dec. 2018, Shire US, Inc.
Facts & Comparisons, 2019 Updated, Wolters Kluwer Healthcare.
Active Risk Identification and Assessment (ARIA) Sufficiency Memo for Pregnancy Safety Concerns, Epidemiology: ARIA Sufficiency Memo Version. Department of Health and Human Services, FDA, Center for Drug Evaluations and Research, Office of Surveillance and Epidemiology (OSE). [December 14, 2018].
Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/210166Orig1s000OtherR.pdf

26. Clobazam / TA - Therapeutic Appropriateness (<2 yoa)

v _____

Alert Message: The safety and effectiveness of Sympazan (clobazam) in patients less than 2 years of age have not been established.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Clobazam		

Age Range: 0-1 yoa

References:

Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

27. Clobazam / Overutilization (2-9 yoa)

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Alert Message: Sympazan (clobazam) may be over-utilized. Patients weighing 30 kg or less should have clobazam therapy initiated at 5 mg daily and titrated as tolerated to 20 mg daily. Patients weighing greater than 30 kg should have therapy initiated at 10 mg daily and titrated as tolerated to a maximum of 40 mg daily.

Drugs/Diseases

Util A Util B Util C
Clobazam

Max Dose: 20 mg/day
Age Range: 2-9 yoa

References:
Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

28. Clobazam / Nonadherence

 v

Alert Message: Based on the refill history, your patient may be underutilizing Sympazan (clobazam). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs. If the patient is discontinuing clobazam, it should be withdrawn gradually by decreasing the total daily dose by 5 - 10 mg/day on a weekly basis until discontinued in order to avoid seizure occurrence or withdrawal symptoms.

Drugs/Diseases

Util A Util B Util C
Clobazam

References:
Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Faught E, Duh MS, Weiner JR, et al. Nonadherence to Antiepileptic Drugs and Increased Mortality, Findings from the RANSOM Study. Neurology 2008;71(20): 1572-1578.
Hodges JC, Treadwell J, Malphrus AD, et al., Identification and Prevention of Antiepileptic Drug Noncompliance: The Collaborative Use of State-Supplied Pharmaceutical Data. ISRN Pediatr. 2014 Feb 19:1-8.
Viswanathan M, Golin CE, Jones DC, et al., Interventions to Improve Adherence to Self-administered Medications for Chronic Disease in the United States: A Systemic Review. Ann Intern Med. 2012;157:785-792.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

29. Clobazam / Moderate & Strong CYP2C19 Inhibitors

Alert Message: Sympazan (clobazam) is a CYP2C19 substrate, and concurrent use with a strong or moderate CYP2C19 inhibitor may result in increased exposure to the active metabolite of clobazam (N-desmethyloclobazam). Dosage adjustment of clobazam may be necessary.

 v _____ _____

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Clobazam	Fluconazole Fluvoxamine Ticlopidine Omeprazole Esomeprazole Fluoxetine Voriconazole	

References:

Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

30. Clobazam / CNS Depressants

Alert Message: Sympazan (clobazam) has a CNS depressant effect, and concurrent use with other CNS depressants may result in potentiated depressants effects.

 v _____ _____

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Clobazam	Narcotics Barbiturates Benzodiazepines Sedative/Hypnotics Muscle Relaxants Antihistamines Antipsychotics	

References:

Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

31. Clobazam / CYP3A4 Metabolized Hormonal Contraceptives

Alert Message: Sympazan (clobazam) is a weak CYP3A4 inducer and concurrent use with CYP3A4-mediated hormonal contraceptives may diminish the effectiveness of the contraceptive agent. The manufacturer recommends the use of additional non-hormonal form of contraception when using clobazam.

 v _____ _____

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Clobazam	CYP3A4 Metabolized Hormonal Contraceptives	

References:

Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

32. Clobazam / Substance Abuse

v _____

Alert Message: Sympazan (clobazam) should be used with caution in patients with a history of substance abuse because of the predisposition of such patients to habituation and dependence. Clobazam is a benzodiazepine. In clinical trials, cases of dependency were reported following abrupt discontinuation of clobazam.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Clobazam	Drug Abuse	

References:

Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

33. Clobazam / CYP2D6 Metabolized Drugs

v _____

Alert Message: Sympazan (clobazam) is a CYP2D6 inhibitor, and concurrent use with drugs metabolized by CYP2D6 may cause increased plasma concentrations of the substrate. Dosage adjustment of the CYP2D6 substrate may be required.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>			<u>Util C</u>
Clobazam	Dextromethorphan	Aripiprazole	Paroxetine	Ondansetron
	Atomoxetine	Carvedilol	Donepezil	Promethazine
	Metoprolol	Duloxetine	Propafenone	Chlorpheniramine
	Nebivolol	Flecainide	Propranolol	
	Perphenazine	Fluoxetine	Risperidone	
	Tolterodine	Fluvoxamine	Tamoxifen	
	Venlafaxine	Haloperidol	Timolol	
	Thioridazine	Mexiletine	Tramadol	
	Tricyclic Antidepressants	Oxycodone	Amphetamine	

References:

Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

34. Clobazam / Alcohol Abuse / Dependence

v _____

Alert Message: A review of the patient’s diagnostic profile reveals that they may consume alcohol. The concurrent use of Sympazan (clobazam) with alcohol has been reported to increase the maximum plasma exposure of clobazam by approximately 50%. Caution patients against the use of alcohol while taking clobazam.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Clobazam	Alcohol Dependence	
	Acute Alcohol Intoxication	
	Other/Unspecified Alcohol Dependence	

References:

Sympazan Prescribing Information, Nov. 2018, Aquestive Therapeutics.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

35. Itraconazole 65 mg Caps / Overutilization

Alert Message: Tolsura (itraconazole) may be over-utilized. The maximum recommended daily dose is 260 mg/day.

 v _____ _____

Drugs/Diseases

Util A

Util B

Util C

Itraconazole 65 mg Caps

Max Dose: 260 mg/day

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Tolsura Prescribing Information, Dec. 2018, Mayne Pharma.

36. Itraconazole 65 mg Caps / Drugs that Reduce Gastric Acidity

Alert Message: The concurrent use of Tolsura (itraconazole) with a drug that reduces gastric acidity (e.g., aluminum hydroxide, H2-receptor antagonists, and proton pump inhibitors) may result in an increase in the systemic exposure to itraconazole and risk for adverse reactions. Itraconazole dose reduction may be necessary.

 v _____ _____

Drugs/Diseases

Util A

Util B

Util C

Itraconazole 65 mg Caps

Antacids
H-2 Antagonists
Proton Pump Inhibitors

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Tolsura Prescribing Information, Dec. 2018, Mayne Pharma.

37. Galcanezumab-gnlm / Overutilization

Alert Message: Emgality (galcanezumab-gnlm) may be over-utilized. The recommended dosage of galcanezumab-gnlm for the treatment of episodic cluster headaches is 300 mg (three consecutive 100 mg subcutaneous injections) at the onset of the cluster period, then monthly until the end of the cluster period.

 v _____ _____

Drugs/Diseases

Util A

Util B

Util C (Include)

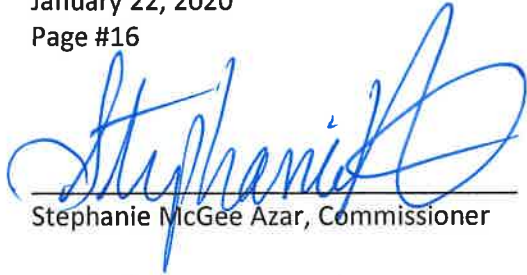
Galcanezumab-gnlm

Cluster Headache

Max Dose: 3 pens per month

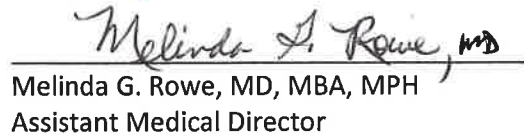
References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Emgality Prescribing Information, June 2019, Eli Lilly and Company.


Stephanie McGee Azar, Commissioner

Approve () Deny

2-19-2020
Date


Melinda G. Rowe, MD, MBA, MPH
Assistant Medical Director

Approve () Deny

2/14/2020
Date


Kathy Hall, Deputy Commissioner

Approve () Deny

2/14/2020
Date