

Alabama Medicaid DUR Board Meeting Minutes Summary
January 27, 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: Clinton Martin

Call to Order: The DUR meeting was called to order by R. Seaman at approximately 9:04 a.m.

Review and Adoption of Minutes: The minutes of the October 28, 2020 meeting were presented, and B. Olin 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 July 2020. She reported 12,157 total manual requests and 12,890 total electronic requests. From the Prior Authorization and Override Response Time Ratio report for July 2020, L. Thomas reported that approximately 84% of all manual PAs and all overrides were completed in less than two hours. Ninety-three percent of all manual PAs and all overrides were completed in less than four hours. Ninety-three percent of all manual PAs and all overrides were completed in less than eight hours. For the month of August 2020, L. Thomas reported 12,357 manual PA requests and 13,303 electronic PA requests were received. She reported that 76% of all manual PAs and 75% of all overrides were completed in less than two hours. Ninety-two percent of all manual PAs and 91% of all overrides were completed in less than four hours. Ninety-three percent of all manual PAs and 92% of all overrides were completed in less than eight hours. For the month of September 2020, L. Thomas reported 12,811 manual PA requests and 12,801 electronic PA requests. L. Thomas reported that approximately 68% of all manual PAs and 69% of all overrides were completed in less than two hours. Eighty-six percent of all manual PA requests and 88% of all overrides were completed in less than four hours. Ninety-one percent of all manual PA requests and 92% 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 April 2020 through September 2020. She reported 3,166,678 total prescriptions, 186,140 average recipients per month using pharmacy benefits, and an average paid per prescription of \$136.27.

Cost Management Analysis: L. Thomas reported an average cost per claim of \$131.40 for September 2020 and emphasized that the table contained the average cost per claim over the past two years. From the 3rd Quarter 2020 Drug Analysis, L. Thomas reported 82% generic utilization, 9% brand single-source, 5% 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 07/01/2020 – 09/30/2020, L. Thomas reported the top five drugs: cetirizine, albuterol sulfate HFA, amoxicillin, montelukast sodium, and gabapentin. L. Thomas mentioned that hydrocodone-APAP was previously reported as being fourth, but had moved to sixth for this reported quarter. L. Thomas then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 07/01/2020 – 09/30/2020: Vyvanse[®], Invega[®] Sustenna[®], Focalin XR[®], Suboxone[®], and Humira[®] Citrate-free and this was identical to 2nd Quarter 2020. 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, Insulins, Respiratory and CNS Stimulants, and Miscellaneous Anticonvulsants.

Therapeutic Drug Class Review: L. Thomas reviewed the Calcitonin Gene-Related Peptide medication class that was approved by the P & T Committee for PDL implementation in July 2019. She reviewed the six medications in this drug class and briefly went over the Prior Authorization criteria. A chart was provided to the DUR Board Members with each medication and the number of PA approvals and denials.

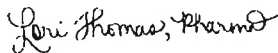
Proposed Criteria: L. Thomas presented the proposed set of 34 criteria to the Board and instructed the Board members to mark their ballots. Of the 34 proposed criteria, results from the criteria vote returned 34 approved.

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 November 4, 2020, and covered the Cerebral Stimulants; Wakefulness Promoting Agents; Alzheimer's Agents; Sedatives/Anxiolytics/Hypnotics; Antidepressants; Genitourinary Smooth Muscle Relaxants; and Disease-Modifying Antirheumatic Agents. The next P & T Committee meeting will be held on February 3, 2021, and will cover the Skin and Mucous Membrane Agents and Disease-Modifying Antirheumatic Agents.

Next Meeting Date: A motion to adjourn the meeting was made by B. Olin. C. Deas seconded the motion and the meeting was adjourned at 10:12 a.m.

Respectfully submitted,



Lori Thomas, PharmD.

ALABAMA MEDICAID RETROSPECTIVE DRUG UTILIZATION REVIEW CRITERIA RECOMMENDATIONS

Criteria Recommendations

Accepted Approved Rejected
As
Amended

1. Darolutamide / Overutilization

Alert Message: Nubeqa (darolutamide) may be over-utilized. The recommended dose of darolutamide is 600 mg (two 300 mg film-coated tablets) taken orally, twice daily, equivalent to a total daily dose of 1200 mg. Patients receiving darolutamide should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had a bilateral orchiectomy.

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Drugs/Diseases

<u>Util A</u> Darolutamide	<u>Util B</u>	<u>Util C (Negate)</u> CKD 4, 5, & ESRD Hepatic Impairment
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Max Dose: 1200 mg/day

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Nubeqa Prescribing Information, August 2019, Bayer Healthcare Pharma.

2. Darolutamide / Overutilization - Renal Impairment

Alert Message: For patients with severe renal impairment (eGFR 15–29 mL/min/1.73 m²) not receiving hemodialysis, the recommended dose of Nubeqa (darolutamide) is 300 mg twice daily. No dose reduction is needed for patients with mild or moderate renal impairment (eGFR 30-89 mL/min/1.73 m²). The effect of end-stage renal disease (eGFR ≤15 mL/min/1.73 m²) on darolutamide pharmacokinetics is unknown.

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Drugs/Diseases

<u>Util A</u> Darolutamide	<u>Util B</u>	<u>Util C (Include)</u> CKD 4, 5, & ESRD
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Max Dose: 600 mg/day

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Nubeqa Prescribing Information, August 2019, Bayer Healthcare Pharma.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

3. Darolutamide / Overutilization – Hepatic Impairment

 v _____ _____

Alert Message: For patients with moderate hepatic impairment (Child-Pugh Class B), the recommended dose of Nubeqa (darolutamide) is 300 mg twice daily. Darolutamide undergoes hepatic metabolism, and moderate hepatic impairment will result in higher exposure to darolutamide. No dose reduction is needed for patients with mild hepatic impairment. The effect of severe hepatic impairment (Child-Pugh C) on darolutamide pharmacokinetics is unknown.

Drugs/Diseases

Util A

Util B

Util C (Include)

Darolutamide

Hepatic Impairment

Max Dose: 600 mg/day

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.

Nubeqa Prescribing Information, August 2019, Bayer Healthcare Pharma.

4. Darolutamide / Embryo-Fetal Toxicity

 v _____ _____

Alert Message: Based on the mechanism of action, advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 1 week after the last dose of Nubeqa (darolutamide).

Drugs/Diseases

Util A

Util B

Util C

Darolutamide

Gender: Male

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.

Nubeqa Prescribing Information, August 2019, Bayer Healthcare Pharma.

5. Darolutamide / Therapeutic Appropriateness (0- 17 yoa)

 v _____ _____

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

Drugs/Diseases

Util A

Util B

Util C

Darolutamide

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.

Nubeqa Prescribing Information, August 2019, Bayer Healthcare Pharma.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

6. Darolutamide / Combined P-gp and Strong or Moderate 3A4 Inducers

v _____

Alert Message: Concomitant use of Nubeqa (darolutamide), a P-gp and CYP3A4 substrate, with a combined P-gp and strong or moderate CYP3A4 inducer decreases darolutamide exposure, which may decrease darolutamide activity. Avoid concomitant use of darolutamide with combined P-gp and strong or moderate CYP3A4 inducers.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Darolutamide	Apalutamide Phenobarbital Primidone Carbamazepine Phenytoin Rifampin Lumacaftor	

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Nubeqa Prescribing Information, August 2019, Bayer Healthcare Pharma.

7. Darolutamide / Combined P-gp and Strong or Moderate 3A4 Inhibitors

v _____

Alert Message: Concomitant use of Nubeqa (darolutamide), a P-gp and CYP3A4 substrate, with a combined P-gp and strong or moderate CYP3A4 inhibitor increases darolutamide exposure, which may increase the risk of darolutamide-related adverse reactions. Monitor patients more frequently for darolutamide adverse reactions and modify darolutamide dosage as needed.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Darolutamide	Clarithromycin Cobicistat Ritonavir Nelfinavir Saquinavir Itraconazole Ketoconazole Posaconazole Mifepristone	

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Nubeqa Prescribing Information, August 2019, Bayer Healthcare Pharma.

8. Darolutamide / BCRP Substrates

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Alert Message: Nubeqa (darolutamide) is an inhibitor of BCRP transporter. Concomitant use of darolutamide increases the AUC and Cmax of BCRP substrates which may increase the risk of BCRP substrate-related toxicities. Avoid concomitant use of darolutamide with drugs that are BCRP substrates where possible. If used together, monitor patients more frequently for adverse reactions, and consider a dose reduction of the BCRP substrate drug. Consult the approved product labeling of the BCRP substrate when used concomitantly with darolutamide.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Darolutamide	Dolutegravir Dantrolene Alpelisib Pibrentasvir Methotrexate Pazopanib Prazosin Rosuvastatin Talazoparib Tenofovir Sulfasalazine Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir	

References:

Clinical Pharmacology, 2019 Elsevier/Gold Standard.
 Nubeqa Prescribing Information, August 2019, Bayer Healthcare Pharma.
 FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at:
<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Drug\InteractionalLabeling/ucm093664.htm>

9. Darolutamide / Nonadherence

_____v_____

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

Drugs/Diseases

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

References:

Osterberg L, Blaschke T. Adherence to Medication. *N Engl J Med* 2005; 353:487- 497.
 Paoella GA, Boyd AD, Wirth SM, Cuellar S, Venepalli NK, Crawford SY. Adherence to Oral Anticancer Medications: Evolving Interprofessional Roles and Pharmacist Workforce Considerations. *Pharmacy (Basel)*. 2018;6(1):23. Published 2018 Mar 8. doi:10.3390/pharmacy6010023.
 Greer JA, Amoyal N, Nisotel L, Fishbein JN, et al., A Systematic Review of Adherence to Oral Antineoplastic Therapies. *The Oncologist*. 2016;21:354–376.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

10. Amlodipine/Celecoxib / Overutilization

Alert Message: The recommended dose of Consensi (amlodipine/celecoxib) is 10 mg amlodipine/200 mg celecoxib per day. Use the lowest effective dosage of the celecoxib-containing product for the shortest duration consistent with individual treatment goals. If analgesic therapy is no longer indicated, discontinue amlodipine/celecoxib and initiate patient on alternative antihypertensive therapy, such as amlodipine monotherapy.

 v _____

Drugs/Diseases

Util A Util B Util C
Amlodipine/Celecoxib

Max Dose: 10 mg amlodipine/200 mg celecoxib

References:

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

11. Amlodipine/Celecoxib / Advanced Renal Disease

Alert Message: The use of Consensi (amlodipine/celecoxib) should be avoided in patients with advanced renal disease unless the benefits are expected to outweigh the risk of worsening renal function. The celecoxib component of the combination product may hasten the progression of renal dysfunction in patients with preexisting renal disease. If use of the celecoxib-containing product cannot be avoided in patients with advanced renal disease, monitor patients for signs of worsening renal function.

 v _____

Drugs/Diseases

Util A Util B Util C (Include)
Amlodipine/Celecoxib CKD Stage 3, 4, & 5

References:

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

12. Amlodipine/Celecoxib / Heart Failure

Alert Message: Avoid the use of Consensi (amlodipine/celecoxib) in patients with severe heart failure unless the benefits are expected to outweigh the risk of worsening heart failure. If a celecoxib-containing product is used in patients with severe heart failure, monitor the patients for signs of worsening heart failure.

 v _____

Drugs/Diseases

Util A Util B Util C (Include)
Amlodipine/Celecoxib Heart Failure Edema

References:

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

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

13. Amlodipine/Celecoxib / Recent Myocardial Infarction

 v

Alert Message: Avoid the use of Consensi (amlodipine/celecoxib) in patients with a recent myocardial infarction unless the benefits are expected to outweigh the risk of recurrent CV thrombotic events. If use of a celecoxib-containing product cannot be avoided in patients with a recent myocardial infarction, monitor the patients for signs of cardiac ischemia.

Drugs/Diseases

Util A Util B Util C
Amlodipine/Celecoxib Myocardial Infarction

References:

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

14. Amlodipine/Celecoxib / Therapeutic Appropriateness

 v

Alert Message: The safety and efficacy of Consensi (amlodipine/celecoxib) in pediatric patients have not been established.

Drugs/Diseases

Util A Util B Util C
Amlodipine/Celecoxib

Age Range: 0 – 17 yoa

References:

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

15. Empagliflozin/Linagliptin/Metformin XR / Nonadherence

 v

Alert Message: Based on refill history, your patient may be under-utilizing Trijardy XR (empagliflozin/linagliptin/metformin extended-release). 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
Empagliflozin/Linagliptin/Metformin

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005;353:487-97.
Ho PM, Rumsfeld JS, Masoudi FA, et al., Effect of Medication Nonadherence in Diabetes Mellitus. Cardiology Review, April 2007.
Currie CJ, Peyrot M, Morgan CL, et al. The Impact of Treatment Noncompliance on Mortality in People With Type 2 Diabetes. Diabetes Care 35:1279-1284, June 2012.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

16. Empagliflozin/Linagliptin/Metformin XR / Overutilization

 v

Alert Message: Trijardy XR (empagliflozin/linagliptin/metformin extended-release) may be over-utilized. The recommended maximum dose of the combination agent is empagliflozin 25 mg/linagliptin 5mg/metformin 2000 mg once daily with a meal in the morning.

Drugs/Diseases

Util A

Util B

Util C

Empagliflozin/Linagliptin/Metformin

Max Dose: 25mg/5mg/2000mg per day

References:

Trijardy Prescribing Information, Jan. 2020, Boehringer Ingelheim Pharmaceuticals, Inc. Clinical Pharmacology, 2020 Elsevier/Gold Standard.

17. Empagliflozin/Linagliptin/Metformin XR / Therapeutic Appropriateness

 v

Alert Message: The safety and effectiveness of Trijardy XR (empagliflozin/linagliptin/metformin extended-release) in pediatric patients under 18 years of age have not been established.

Drugs/Diseases

Util A

Util B

Util C

Empagliflozin/Linagliptin/Metformin

Age Range: 0-17 yoa

References:

Trijardy Prescribing Information, Jan. 2020, Boehringer Ingelheim Pharmaceuticals, Inc. Clinical Pharmacology, 2020 Elsevier/Gold Standard.

18. Empagliflozin/Linagliptin/Metformin XR / Mild to Mod. Renal Impairment

 v

Alert Message: Assessment of renal function is recommended prior to initiation of Trijardy XR (empagliflozin/linagliptin/metformin extended-release) and periodically thereafter. No dosage adjustment is needed in patients with an eGFR greater than or equal to 45 mL/min/1.73m². Empagliflozin/linagliptin/metformin ER should not be initiated in patients with an eGFR less than 45 mL/min/1.73m² or continued in patients with an eGFR less than 45 mL/min/1.73m².

Drugs/Diseases

Util A

Util B

Util C (Include)

Empagliflozin/Linagliptin/Metformin

CKD Stage 1

CKD Stage 2

CKD Stage 3

References:

Trijardy Prescribing Information, Jan. 2020, Boehringer Ingelheim Pharmaceuticals, Inc. Clinical Pharmacology, 2020 Elsevier/Gold Standard.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

19. Empagliflozin/Linagliptin/Metformin XR / CKD 4, 5, ESRD, & Dialysis

 v _____ _____

Alert Message: Trijardy XR (empagliflozin/linagliptin/metformin extended-release) use is contraindicated in patients with severe renal impairment (eGFR less than 30 mL/min/1.73m²), end-stage renal disease, or receiving dialysis. The empagliflozin component of the combination product causes intravascular volume contraction and can cause acute kidney injury. The metformin component of the combination product is associated with the occurrence of lactic acidosis. The risk of metformin accumulation and metformin-associated lactic acidosis increases with the severity of renal impairment.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Empagliflozin/Linagliptin/Metformin		CKD Stage 4 & 5 ESRD Dialysis

References:

Trijardy Prescribing Information, Jan. 2020, Boehringer Ingelheim Pharmaceuticals, Inc. Clinical Pharmacology, 2020 Elsevier/Gold Standard.

20. Empagliflozin/Linagliptin/Metformin XR / Ketoacidosis

 v _____ _____

Alert Message: Trijardy XR (empagliflozin/linagliptin/metformin) use is contraindicated in patients with ketoacidosis. Fatal cases of ketoacidosis have been reported in patients receiving SGLT2 inhibitors, including empagliflozin, a component of the combination product. In patients treated with empagliflozin/linagliptin/metformin ER, consider monitoring for ketoacidosis and temporarily discontinuing empagliflozin/linagliptin/metformin ER in clinical situations known to predispose to ketoacidosis (e.g., prolonged fasting due to acute illness or surgery).

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Empagliflozin/Linagliptin/Metformin	Ketoacidosis	

References:

Trijardy Prescribing Information, Jan. 2020, Boehringer Ingelheim Pharmaceuticals, Inc. Clinical Pharmacology, 2020 Elsevier/Gold Standard.

21. Empagliflozin/Linagliptin/Metformin XR / Insulin & Sulfonylureas

 v _____ _____

Alert Message: The concurrent use of Trijardy XR (empagliflozin/linagliptin/metformin extended-release) with insulin or an insulin secretagogue can increase the risk of hypoglycemia. A lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with empagliflozin/linagliptin/metformin ER.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Empagliflozin/Linagliptin/Metformin	Insulins Chlorpropamide Glimepiride Glipizide Glyburide Tolazamide Tolbutamide	

References:

Trijardy Prescribing Information, Jan. 2020, Boehringer Ingelheim Pharmaceuticals, Inc. Clinical Pharmacology, 2020 Elsevier/Gold Standard.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

22. Empagliflozin/Linagliptin/Metformin XR / Pregnancy / Negating

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Alert Message: Based on animal data showing adverse renal effects from empagliflozin, Trijardy XR (empagliflozin/linagliptin/metformin extended-release) is not recommended during the second and third trimesters of pregnancy.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negate)</u>
Empagliflozin/Linagliptin/Metformin	Pregnancy	Abortion Delivery Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Trijardy Prescribing Information, Jan. 2020, Boehringer Ingelheim Pharmaceuticals, Inc.
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

23. Empagliflozin/Linagliptin/Metformin XR / Lactation

___^v___

Alert Message: Because of the potential for serious adverse reactions in a breastfed infant, including the potential for empagliflozin to affect postnatal renal development, advise patients that the use of Trijardy XR (empagliflozin/linagliptin/metformin extended-release) is not recommended while breastfeeding.

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Empagliflozin/Linagliptin/Metformin	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Trijardy Prescribing Information, Jan. 2020, Boehringer Ingelheim Pharmaceuticals, Inc.
Clinical Pharmacology, 2020 Elsevier/Gold Standard.

24. Ubrogepant / Overuse

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Alert Message: Ubrogepant (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

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negate)</u>
Ubrogepant		Cirrhosis CKD 4 CKD 5

Max Dose: 200 mg/day

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

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

25. Ubrogapant / Overuse

Alert Message: Ubrovelvy (ubrogapant) may be over-utilized. The recommended initial dose of ubrogapant 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 ubrogapant 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.

_____v_____

Conflict Code: ER - Overutilization

Drugs/Diseases

Util A

Util B

Util C (Include)

Ubrogapant

Cirrhosis

CKD 4

CKD 5

Max Dose: 100 mg/day

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.

Ubrovelvy Prescribing Information, Dec. 2019, Allergan.

26. Ubrogapant / ESRD

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

_____v_____

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C (Include)

Ubrogapant

ESRD

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.

Ubrovelvy Prescribing Information, Dec. 2019, Allergan.

27. Ubrogapant / Therapeutic Appropriateness

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

_____v_____

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C

Ubrogapant

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.

Ubrovelvy Prescribing Information, Dec. 2019, Allergan.

28. Ubrogepant / Strong CYP3A4 Inhibitors

Alert Message: The co-administration of Ubrogepant (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 AUC_{inf} and C_{max} of ubrogepant, respectively.

_____v_____

Conflict Code: DD - Drug/Drug Interaction

Drugs/Diseases

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

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrogepant Prescribing Information, Dec. 2019, Allergan.

29. Ubrogepant 100 mg / Moderate CYP3A4 Inhibitors

Alert Message: When Ubrogepant (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 AUC_{inf} and C_{max} of ubrogepant, respectively.

_____v_____

Conflict Code: DD - Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
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.
Ubrogepant Prescribing Information, Dec. 2019, Allergan.

30. Ubrogepant 100 mg / Weak CYP3A4 Inhibitors

_____v_____

Alert Message: When Ubrovelvy (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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Ubrogepant 100 mg	Amiodarone	Lapatinib
	Chlorzoxazone	Lomitapide
	Cilostazol	Ranitidine
	Fosaprepitant	Ranolazine
	Istradefylline	Tacrolimus
	Ivacaftor	Ticagrelor

References:

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

31. Ubrogepant / Strong CYP3A4 Inducers

_____v_____

Alert Message: The concurrent use of Ubrovelvy (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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Ubrogepant	Carbamazepine	
	Enzalutamide	
	Mitotane	
	Phenobarbital	
	Phenytoin	
	Primidone	
	Rifampin	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrovelvy Prescribing Information, Dec. 2019, Allergan.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

32. Ubrogepant 100 mg / BCRP and/or P-gp Only Inhibitors

 v _____ _____

Alert Message: When Ubrogepant (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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Ubrogepant 100 mg	Carvedilol Eltrombopag Quinidine	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Ubrogepant Prescribing Information, Dec. 2019, Allergan.

33. Ubrogepant / Lactation

 v _____ _____

Alert Message: There are no data on the presence of Ubrogepant (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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Ubrogepant	Lactation	

Gender: Female

Age Range: 11 – 50 yoa

References:

Ubrogepant Prescribing Information, Dec. 2019, Allergan.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

34. Ubrogepant / Pregnancy / Pregnancy Negating

Alert Message: There are no adequate data on the developmental risk associated with the use of Ubrogepant (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.

_____v_____

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.

Ubrogepant Prescribing Information, Dec. 2019, Allergan.


Stephanie McGee Azar, Commissioner

Approve () Deny

2-23-2021
Date


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

Approve () Deny

2/19/2021
Date


Kathy Hall, Deputy Commissioner

Approve () Deny

2/19/21
Date