Alabama Medicaid DUR Board Meeting Minutes Summary
July 26, 2023

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

Also Present: Lori Thomas, Julie Jordan, Heather Vega, LaQwanda Eddings-Haygood, Jack Wanschek, Kimberly Graham, ACHN Pharmacists

Members Absent: Rachel Seaman, George Sutton

Call to Order: The DUR meeting was called to order by D. Powell at approximately 1:06 p.m.

Review and Adoption of Minutes: The minutes of the April 26, 2023, meeting were presented, and D. McConaghy 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 January 2023. She reported 14,816 manual PAs and overrides. There were 22,635 total electronic requests for the month of January 2023. L. Thomas compared January 2022 to January 2023 and pointed out the increased volume. From the Prior Authorization and Override Response Time Ratio report for January 2023, L. Thomas reported that approximately 1% of all manual PAs and 1% of all overrides were completed in less than two hours, but a total of 77% of all PAs were completed in under 2 hours (including electronic PA transactions). Nine percent of all manual PAs and overrides were completed in less than four hours. Forty-seven percent of all manual PAs and 48% of all overrides were completed in less than eight hours. L. Thomas reminded the Board Members that 75% of all PAs and overrides must be completed in under 8 hours. For the month of February 2023, L. Thomas reported 14,613 manual PA requests and 20,957 electronic PA requests were received. She reported that 1% of all manual PAs and of all overrides were completed in less than two hours. Seventy-six percent of all prior authorizations were completed in less than two hours. Five percent of all manual PAs and of all overrides were completed in less than four hours. Thirty-eight percent of all manual PAs and of all overrides were completed in less than eight hours. For the month of March 2023, L. Thomas reported 17,144 manual PA requests and 22,309 electronic PA requests. L. Thomas reported that approximately 1% of all manual PAs and of all overrides were completed in less than two hours. Seventy-six percent of all prior authorizations were completed in less than two hours. Eight percent of all manual PA requests and 5% of all overrides were completed in less than four hours. Forty percent of all manual PAs and 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 October 2022 through March 31, 2023. She reported 254,936 average recipients per month using pharmacy benefits, and an average paid per prescription of $141.68.

Cost Management Analysis: L. Thomas reported an average cost per claim of $145.45 for March 2023 and compared previous months contained in the table. From the 1st Quarter Drug Analysis, L. Thomas reported 84% generic utilization, 8% brand single-source, 4% 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 01/01/2023 – 03/31/2023, L. Thomas reported the top five drugs: amoxicillin, albuterol sulfate HFA, cetirizine, azithromycin, and fluticasone propionate. L. Thomas then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 01/01/2023 – 03/31/2023: Humira® Citrate-free Pen, Vyvanse®, Trikafta®, Invega Sustenna®, and Trulicity®. From the Top 15 Therapeutic Classes by Total Cost of Claims for the same time frame, L. Thomas reported the top five classes: Antipsychotic Agents,

Disease-modifying Antirheumatic Agents, Skin and Mucous Membrane Agents, Amphetamines, and Antineoplastic Agents.

RDUR Intervention Report: L. Thomas presented the RDUR Activity Report for July 2022. She reported 500 profiles reviewed and 840 letters sent with 62 responses received as of the date of the report. She reported 30 of 46 physicians indicated that they found the RDUR letters "useful" or "extremely useful". The criteria for the cycle of intervention letters included Drug-Drug Interaction (Support Act criteria – pure opioid agonists and benzodiazepines); Drug-Drug Interaction (Support Act criteria – pure opioid agonists and antipsychotics); Therapeutic Appropriateness (appropriate use of immediate-release opioids).

Proposed Criteria: L. Thomas presented the proposed set of 42 criteria to the Board and instructed the Board members to mark their ballots. Of the 42 proposed criteria, results from the criteria vote returned 38 approved and 4 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. L. Eddings-Haygood reminded the Board members that every July the Board votes on a Vice Chair. Ballots were distributed and members were asked to mark their ballots and pass them to the front. Results of the vote elected D. Powell as Vice Chair. The current Vice Chair, C. Deas, will begin her term as Chairman of the Board beginning with the October 2023 meeting.

P & T Committee Update: K. Newman began the P & T Update by informing the Board that the last P & T meeting was held on May 3, 2023, and covered the wakefulness promoting agents; anti-infectives; and cerebral stimulants. The next meeting is scheduled for August 2, 2023, and will cover the remaining anti-infective agents.

Next Meeting Date: D. Powell reminded the Board that the next DUR meeting will be held on October 25, 2023. A motion to adjourn the meeting was made by C. Deas and M. Bulloch seconded the motion. The meeting was adjourned at 1:58 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. Belumosudil / Overuse Alert Message: Rezurock (belumosudil) may be over-utilized. The recommended dose of belumosudil is 200 mg given orally once daily until the progression of chronic GVHD requires new systemic therapy. Drugs/Diseases Util A: Belumosudil Util B: Util C (Negating): Strong CYP3A4 Inducers; Proton Pump Inhibitors Max Dose: 200 mg/day References: Clinical Pharmacology, 2022 Elsevier/Gold Standard. Rezurock Prescribing Information, Kadmon Pharmaceuticals, LLC.	___√_____	_____	_____
2. Belumosudil / Therapeutic Appropriateness Alert Message: The safety and effectiveness of Rezurock (belumosudil) in pediatric patients less than 12 years old have not been established. Drugs/Diseases Util A: Belumosudil Util B: Util C: Age Range: 0 – 11 yoa References: Clinical Pharmacology, 2021 Elsevier/Gold Standard. Rezurock Prescribing Information, Kadmon Pharmaceuticals, LLC.	____√_____	_____	_____

3. Belumosudil / Strong CYP3A4 Inducers ____√____

Alert Message: Coadministration of Rezurock (belumosudil) with strong CYP3A inducers decreases belumosudil exposure, which may reduce the efficacy of belumosudil. If concurrent therapy is warranted, increase the dosage of belumosudil, a CYP3A4 substrate, to 200 mg twice daily when coadministered with strong CYP3A inducers.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Rezurock Prescribing Information, Kadmon Pharmaceuticals, LLC.

4. Belumosudil / Proton Pump Inhibitors ____√____

Alert Message: Coadministration of Rezurock (belumosudil) with a proton pump inhibitor decreases belumosudil exposure, which may reduce the efficacy of belumosudil. If concurrent therapy is warranted, increase the dosage of belumosudil to 200 mg twice daily when coadministered with a proton pump inhibitor.

Drugs/Diseases

Util A	Util B	Util C
Belumosudil	Dexlansoprazole	
	Esomeprazole	
	Lansoprazole	
	Omeprazole	
	Pantoprazole	
	Rabeprazole	

Minimum Dose: 400 mg/day

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Rezurock Prescribing Information, Kadmon Pharmaceuticals, LLC.

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

5. Belumosudil / Pregnancy / Pregnancy Negating ___√___ _____ _____

Alert Message: Based on findings in animals and its mechanism of action, Rezurock (belumosudil) can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of belumosudil to pregnant rats and rabbits during the period of organogenesis caused adverse developmental outcomes including embryofetal mortality and malformations at maternal exposures (AUC) less than those in patients at the recommended dose. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with belumosudil and for at least one week after the last dose.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Rezurock Prescribing Information, Kadmon Pharmaceuticals, LLC.

6. Belumosudil / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: There are no data available on the presence of Rezurock (belumosudil) or its metabolites in human milk, or the effects on the breastfed child, or milk production. Because of the potential for serious, adverse reactions from belumosudil in the breastfed child, advise lactating women not to breastfeed during treatment with belumosudil and for at least one week after the last dose.

Drugs/Diseases

Util A	Util B	Util C
Belumosudil	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Rezurock Prescribing Information, Kadmon Pharmaceuticals, LLC.

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

7. Belumosudil / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: Advise females of reproductive potential to use effective contraception during treatment with Rezurock (belumosudil) and for at least one week after the last dose of belumosudil. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be informed of the potential hazard to a fetus.

Drugs/Diseases
Util A Util B Util C
Belumosudil

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Rezurock Prescribing Information, Kadmon Pharmaceuticals, LLC.

8. Belumosudil / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: Advise males with partners of reproductive potential to use effective contraception during treatment with Rezurock (belumosudil) and for at least one week after the last dose of belumosudil.

Drugs/Diseases
Util A Util B Util C
Belumosudil

Gender: Male

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Rezurock Prescribing Information, Kadmon Pharmaceuticals, LLC.

9. Belumosudil / Non-adherence ___√___ _____ _____

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

Drugs/Diseases
Util A Util B Util C
Belumosudil

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med. 2005;353:487-97.
Ruddy K, Mayer E, Partridge A. Patient Adherence and Persistence With Oral Anticancer Treatment. CA Cancer J Clin 2009;59:56-66.
Greer JA, Amoyal N, Nisotel L, et al. Systemic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist. 2016;21:354-376.
Barillet M, Prevost V, Joly F, Clarisse B. Oral Antineoplastic Agents: How do We Care About Adherence? Br J Clin Pharmacol. 2015;80(6):1289-1302. doi:10.1111/bcp.1273

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

10. Benralizumab / Therapeutic Appropriateness ____√____ _____ _____

Alert Message: The safety and efficacy of Fasenra (benralizumab) in pediatric patients less than 12 years of age have not been established.

Drugs/Diseases

Util A	Util B	Util C
Benralizumab		

Age Range: 0 – 11 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Fasenra Prescribing Information, June 2022, AstraZeneca.

11. Benralizumab / Helminth Infections _____ ____√____ _____

Alert Message: Treat patients with pre-existing helminth infections before initiating therapy with Fasenra (benralizumab). If patients become infected while receiving treatment with benralizumab and do not respond to anti-helminth treatment, discontinue treatment with benralizumab until the infection resolves.

Drugs/Diseases

Util A	Util B	Util C
Tezepelumab-ekko	Helminth Infection	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Fasenra Prescribing Information, June 2022, AstraZeneca.

12. Benralizumab / Pregnancy / Pregnancy Negating _____ ____√____ _____

Alert Message: The data on pregnancy exposure from the clinical trials for Fasenra (benralizumab) are insufficient to inform on drug-associated risk. Monoclonal antibodies such as benralizumab are transported across the placenta during the third trimester of pregnancy; therefore, potential effects on a fetus are likely to be greater during the third trimester of pregnancy.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Tezepelumab-ekko	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Fasenra Prescribing Information, June 2022, AstraZeneca.

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

13. Benralizumab / Lactation ____ √ ____

Alert Message: There is no information regarding the presence of Fasenra (benralizumab) in human or animal milk, and the effects of benralizumab on the breastfed infant and milk production are not known. However, benralizumab is a humanized monoclonal antibody (IgG1/κ-class), and immunoglobulin G (IgG) is present in human milk in small amounts. If benralizumab is transferred into human milk, the effects of local exposure in the gastrointestinal tract and potential limited systemic exposure in the infant to benralizumab are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for benralizumab and any potential adverse effects on the breast-fed child from benralizumab or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Tezepelumab-ekko	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Fasenra Prescribing Information, June 2022, AstraZeneca.

14. Afatinib / Overuse ____ √ ____

Alert Message: Gilotrif (afatinib) may be over-utilized. The recommended dosage of afatinib is 40 mg orally once daily until disease progression or no longer tolerated by the patient.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Afatinib		CKD Stage 4, 5, & ESRD

Max Dose: 40 mg/day

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gilotrif Prescribing Information, April 2022, Boehringer Ingelheim Pharmaceuticals, Inc.

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

15. Afatinib / Therapeutic Appropriateness ___√___ _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Afatinib		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gilotrif Prescribing Information, April 2022, Boehringer Ingelheim Pharmaceuticals, Inc.

16. Afatinib / Overuse – Severe Renal Impairment ___√___ _____ _____

Alert Message: Gilotrif (afatinib) may be over-utilized. The recommended dosage of afatinib in patients with pre-existing severe renal impairment (estimated glomerular filtration rate [eGFR] 15 to 29 mL/min /1.73 m2) is 30 mg orally once daily. The eGFR should be determined by Modification of Diet in Renal Disease formula.

Drugs/Diseases

Util A	Util B	Util C (Include)
Afatinib		CKD Stage 4

Max Dose: 30 mg/day

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gilotrif Prescribing Information, April 2022, Boehringer Ingelheim Pharmaceuticals, Inc.

17. Afatinib / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: Gilotrif (afatinib) has not been studied in patients with eGFR < 15 mL/min/1.73m2 or on dialysis. Patients with severe renal impairment have a higher exposure to afatinib than patients with normal renal function.

Drugs/Diseases

Util A	Util B	Util C
Afatinib	CKD Stage 5 ESRD Dialysis	

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gilotrif Prescribing Information, April 2022, Boehringer Ingelheim Pharmaceuticals, Inc.

18. Afatinib / Hepatic Impairment ____√____

Alert Message: Hepatotoxicity has occurred in patients treated with Gilotrif (afatinib). Obtain periodic liver testing in patients during treatment with afatinib. Withhold afatinib in patients who develop worsening of liver function. In patients who develop severe hepatic impairment while taking afatinib, discontinue treatment.

Drugs/Diseases

Util A	Util B	Util C
Afatinib	Hepatic Impairment	

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gilotrif Prescribing Information, April 2022, Boehringer Ingelheim Pharmaceuticals, Inc.

19. Afatinib / Interstitial Lung Disease ____√____

Alert Message: Gilotrif (afatinib) can cause interstitial lung disease (ILD) or ILD-like adverse reactions. Monitor the patient for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, fever). Withhold afatinib during evaluation of patients with suspected ILD and discontinue afatinib in patients with confirmed ILD and discontinue afatinib in patients with confirmed ILD.

Drugs/Diseases

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

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gilotrif Prescribing Information, April 2022, Boehringer Ingelheim Pharmaceuticals, Inc.

20. Afatinib / Gastrointestinal Perforation ___√____

Alert Message: Gastrointestinal perforation, including fatal cases, has occurred with Gilotrif (afatinib). Patients receiving concomitant corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs) or anti-angiogenic agents, or patients with increasing age or who have an underlying history of gastrointestinal ulceration, underlying diverticular disease or bowel metastases may be at increased risk of perforation. Permanently discontinue afatinib in patients who develop gastrointestinal perforation.

Drugs/Diseases

Util A	Util B	Util C
Afatinib	Diverticulitis	
	GI Perforation	
	Anti-Angiogenic Agents	
	NSAIDS	

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gilotrif Prescribing Information, April 2022, Boehringer Ingelheim Pharmaceuticals, Inc.

21. Afatinib / Keratitis ___√_____ _____ _____

Alert Message: Keratitis has occurred in patients treated with Gilotrif (afatinib). Advise patients to immediately report eye problems (e.g., eye pain, swelling, redness, blurred vision, or other vision changes). Withhold afatinib during evaluation of patients with suspected keratitis, and if diagnosis of ulcerative keratitis is confirmed, interrupt or discontinue afatinib. If keratitis is diagnosed, the benefits and risks of continuing treatment should be carefully considered. Afatinib should be used with caution in patients with a history of keratitis, ulcerative keratitis, or severe dry eye. Contact lens use is also a risk factor for keratitis and ulceration.

Drugs/Diseases

Util A	Util B	Util C
Afatinib	Keratitis	
	Visual Disturbances	

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gilotrif Prescribing Information, April 2022, Boehringer Ingelheim Pharmaceuticals, Inc.

22. Afatinib / P-gp Inhibitors ___√_____ _____ _____

Alert Message: The concurrent use of Gilotrif (afatinib), a P-gp substrate, with a P-gp inhibitor can result in increased afatinib exposure. Reduce the afatinib daily dose by 10 mg if not tolerated for patients who require therapy with a P-gp inhibitor. Resume the previous afatinib dose after discontinuation of the P-gp inhibitor as tolerated.

Drugs/Diseases

Util A	Util B	Util C
Afatinib	Amiodarone	
	Cyclosporine	
	Erythromycin	
	Itraconazole	
	Ketoconazole	
	Nelfinavir	
	Quinidine	
	Ritonavir	
	Saquinavir	
	Tacrolimus	
	Verapamil	

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gilotrif Prescribing Information, April 2022, Boehringer Ingelheim Pharmaceuticals, Inc.

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

23. Afatinib / P-gp Inducers ____√____ _____ _____

Alert Message: The concurrent use of Gilotrif (afatinib), a P-gp substrate, with a P-gp inducer can result in decreased afatinib exposure. Increase the afatinib daily dose by 10 mg as tolerated for patients who require chronic therapy with a P-gp inducer. Resume the previous afatinib dose 2 to 3 days after discontinuation of the P-gp inducer.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gilotrif Prescribing Information, April 2022, Boehringer Ingelheim Pharmaceuticals, Inc.

24. Afatinib / Pregnancy / Pregnancy Negating ____√____ _____ _____

Alert Message: There are no available data on the use of Gilotrif (afatinib) in pregnant women. Based on findings from animal studies and its mechanism of action, afatinib can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gilotrif Prescribing Information, April 2022, Boehringer Ingelheim Pharmaceuticals, Inc.

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

25. Afatinib / Therapeutic Appropriateness ____√____ _____ _____

Alert Message: There are no data on the presence of Gilotrif (afatinib) in human milk or its effects on the breastfed infant or milk production. Afatinib was present in the milk of lactating rats. Because of the potential for serious adverse reactions in breastfed infants from afatinib, advise women not to breastfeed during treatment with afatinib and for 2 weeks after the final dose..

Drugs/Diseases

Util A	Util B	Util C
Afatinib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Facts & Comparisons, 2022 Updates, Wolters Kluwer Health.

26. Afatinib / Therapeutic Appropriateness ____√____ _____ _____

Alert Message: Advise females of reproductive potential to use effective contraception during treatment and for at least 2 weeks after the last dose of Gilotrif (afatinib). Based on findings from animal studies and its mechanism of action, afatinib can cause fetal harm when administered to a pregnant woman.

Drugs/Diseases

Util A	Util B	Util C (Include)
Afatinib		Contraceptives

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Gilotrif Prescribing Information, April 2022, Boehringer Ingelheim Pharmaceuticals, Inc.

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

27. Afatinib / Non-adherence ___√___ _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Gilotrif (afatinib). 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
Afatinib		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Ruddy K, Mayer E, Partridge A. Patient Adherence and Persistence With Oral Anticancer Treatment. CA Cancer J Clin 2009;59:56-66.
Barillet M, Prevost V, Joly F, Clarisse B. Oral Antineoplastic Agents: How do We Care About Adherence? Br J Clin Pharmacol. 2015;80(6):1289-1302. doi:10.1111/bcp.1273
Greer JA, Amoyal N, Nisotel L, et al. Systemic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist. 2016;21:354-376.

28. Mobocertinib / Overuse ____√____ _____ _____

Alert Message: Exkivity (mobocertinib) may be over-utilized. The recommended dosage of mobocertinib is 160 mg orally once daily until disease progression or unacceptable toxicity.

Drugs/Diseases

Util A	Util B	Util C
Mobocertinib		

Max Dose: 160 mg/day

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Exkivity Prescribing Information, September 2021, Takeda Pharmaceuticals America.

29. Mobocertinib / Therapeutic Appropriateness ____√____ _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Mobocertinib		

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Exkivity Prescribing Information, September 2021, Takeda Pharmaceuticals America.

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

30. Mobocertinib / Therapeutic Appropriateness (Black Box) ___√_____ _____ _____

Alert Message: Exkivity (mobocertinib) can cause life-threatening heart rate-corrected QT (QTc) prolongation, including Torsades de Pointes, which can be fatal, and requires monitoring of QTc and electrolytes at baseline and periodically during treatment. Assess QTc and electrolytes at baseline and correct abnormalities in sodium, potassium, calcium, and magnesium before initiating mobocertinib. Monitor QTc and electrolytes periodically during treatment. Increase monitoring frequency in patients with risk factors for QTc prolongation, such as patients with congenital long QT syndrome, heart disease, or electrolyte abnormalities. Withhold, reduce the dose, or permanently discontinue mobocertinib based on the severity of QTc prolongation.

Drugs/Diseases

Util A	Util B	Util C
Mobocertinib	QT Prolongation	

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Exkivity Prescribing Information, September 2021, Takeda Pharmaceuticals America.

31. Mobocertinib / Strong CYP3A4 Inhibitors (Black Box) ___√_____ _____ _____

Alert Message: Coadministration of Exkivity (mobocertinib) with a strong CYP3A4 inhibitor should be avoided. Mobocertinib is a CYP3A4 substrate, and concurrent use with a strong CYP3A4 inhibitor may significantly increase mobocertinib exposure and the risk of mobocertinib-related QT (QTc) prolongation.

Drugs/Diseases

Util A	Util B		Util C
Mobocertinib	Clarithromycin	Nelfinavir	
	Cobicistat	Posaconazole	
	Darunavir	Ritonavir	
	Indinavir	Saquinavir	
	Itraconazole	Voriconazole	
	Ketoconazole		
	Nefazodone		

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Exkivity Prescribing Information, September 2021, Takeda Pharmaceuticals America.

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

32. Mobocertinib / QT Prolonging Drugs (Black Box) ____√____ _____ _____

Alert Message: Exkivity (mobocertinib) can cause life-threatening heart rate-corrected QT (QTc) prolongation, including Torsades de Pointes, which can be fatal and requires monitoring of QTc and electrolytes at baseline and periodically during treatment. Avoid the use of concomitant drugs, which are known to prolong the QTc interval.

Drugs/Diseases

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

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Exkivity Prescribing Information, September 2021, Takeda Pharmaceuticals America.

33. Mobocertinib / Moderate CYP3A4 Inhibitors (Black Box) ___√_____ _____ _____

Alert Message: Coadministration of Exkivity (mobocertinib) with a moderate CYP3A4 inhibitor should be avoided. Mobocertinib is a CYP3A4 substrate, and concurrent use with a CYP3A4 inhibitor may increase mobocertinib exposure and the risk of mobocertinib-related QT (QTc) prolongation. If concomitant use with a moderate CYP3A inhibitor cannot be avoided, reduce the mobocertinib dose by approximately 50% and monitor the QTc interval more frequently with ECGs. After the moderate CYP3A inhibitor has been discontinued for 3 to 5 elimination half-lives, resume mobocertinib at the dose taken before initiating the moderate CYP3A inhibitor.

Drugs/Diseases

Util A	Util B		Util C
Mobocertinib	Atazanavir	Diltiazem	Verapamil
	Aprepitant	Dronedarone	
	Cimetidine	Erythromycin	
	Ciprofloxacin	Fluconazole	
	Crizotinib	Fluvoxamine	
	Cyclosporine	Imatinib	

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Exkivity Prescribing Information, September 2021, Takeda Pharmaceuticals America.

34. Mobocertinib / Interstitial Lung Disease ____√_____ _____ _____

Alert Message: Exkivity (mobocertinib) can cause ILD/pneumonitis, which can be fatal. Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis. Immediately withhold mobocertinib in patients with suspected ILD/pneumonitis (any grade) and permanently discontinue mobocertinib if ILD/pneumonitis is confirmed.

Drugs/Diseases

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

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Exkivity Prescribing Information, September 2021, Takeda Pharmaceuticals America.

35. Mobocertinib / Cardiac Toxicity ____√____ _____ _____

Alert Message: Exkivity (mobocertinib) can cause cardiac toxicity (including decreased ejection fraction, cardiomyopathy, and congestive heart failure) resulting in heart failure, which can be fatal. Monitor cardiac function, including assessment of left ventricular ejection fraction at baseline and during treatment. Withhold, reduce the dose, or permanently discontinue mobocertinib based on the severity.

Drugs/Diseases

Util A	Util B	Util C
Mobocertinib	Cardiomyopathy	
	Heart Failure	

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Exkivity Prescribing Information, September 2021, Takeda Pharmaceuticals America.

36. Mobocertinib / Diarrhea ____√____ _____ _____

Alert Message: Exkivity (mobocertinib) can cause diarrhea, which can be severe. In the pooled mobocertinib safety population, diarrhea occurred in 93% of patients. Diarrhea may lead to dehydration or electrolyte imbalance, with or without renal impairment. Treat diarrhea promptly. Advise patients to start an antidiarrheal agent (e.g., loperamide) at the first sign of diarrhea or increased bowel movement frequency and to increase fluid and electrolyte intake. Monitor electrolytes and withhold mobocertinib, reduce the dose or permanently discontinue mobocertinib based on the severity.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Mobocertinib	Diarrhea	Loperamide

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Exkivity Prescribing Information, September 2021, Takeda Pharmaceuticals America.

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

37. Mobocertinib / Pregnancy / Pregnancy Negating ___√___ _____ _____

Alert Message: Based on findings from animal studies and its mechanism of action, Exkivity (mobocertinib) can cause fetal harm when administered to a pregnant woman. There are no available data on mobocertinib use in pregnant women. Oral administration of mobocertinib to pregnant rodents during the period of organogenesis resulted in embryolethality (embryo-fetal death) and maternal toxicity at plasma exposures approximately 1.7 times the human exposure based on AUC at the 160 mg once daily clinical dose. Advise pregnant women of the potential risk to a fetus.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Exkivity Prescribing Information, September 2021, Takeda Pharmaceuticals America.

38. Mobocertinib / Lactation ___√___ _____ _____

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

Drugs/Diseases

Util A	Util B	Util C
Mobocertinib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Exkivity Prescribing Information, September 2021, Takeda Pharmaceuticals America.

39. Mobocertinib / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: Advise females of reproductive potential to use effective non-hormonal contraception during treatment with Exkivity (mobocertinib) and for 1 month after the last dose. Mobocertinib may render hormonal contraceptives ineffective.

Drugs/Diseases

Util A	Util B	Util C
Mobocertinib	Hormonal Contraceptives	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Exkivity Prescribing Information, September 2021, Takeda Pharmaceuticals America.

40. Mobocertinib / Sensitive CYP3A4 Substrates ___√___ _____ _____

Alert Message: Coadministration of Exkivity (mobocertinib) with a CYP3A4 substrate may result in decreased plasma concentrations of the CYP3A4 substrate. Avoid concomitant use of mobocertinib with other CYP3A substrates where minimal concentration changes may lead to serious therapeutic failures. If concomitant use is unavoidable, increase the CYP3A substrate dosage in accordance with the approved product prescribing information.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Exkivity Prescribing Information, September 2021, Takeda Pharmaceuticals America.

41. Mobocertinib / Strong & Moderate CYP3A4 Inducers ___√___ _____ _____

Alert Message: Coadministration of Exkivity (mobocertinib) with a strong or moderate CYP3A4 inducer should be avoided. Mobocertinib is a CYP3A4 substrate, and concurrent use with a strong or moderate CYP3A4 inducer may decrease mobocertinib exposure and reduce mobocertinib anti-tumor activity.

Drugs/Diseases

Util A	Util B	Util C
Mobocertinib	Apalutamide	
	Bosentan	
	Carbamazepine	
	Efavirenz	
	Etravirine	
	Phenobarbital	
	Phenytoin	
	Primidone	
	Rifabutin	
	Rifampin	
	Rifapentine	

References:

Clinical Pharmacology, 2022 Elsevier/Gold Standard.
Exkivity Prescribing Information, September 2021, Takeda Pharmaceuticals America.

42. Mobocertinib / Non-adherence ____√____ _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Exkivity (mobocertinib). 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
Mobocertinib		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Ruddy K, Mayer E, Partridge A. Patient Adherence and Persistence With Oral Anticancer Treatment. CA Cancer J Clin 2009;59:56-66.
Barillet M, Prevost V, Joly F, Clarisse B. Oral Antineoplastic Agents: How do We Care About Adherence? Br J Clin Pharmacol. 2015;80(6):1289-1302. doi:10.1111/bcp.1273
Greer JA, Amoyal N, Nisotel L, et al. Systemic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist. 2016;21:354-376.

Stephanie McGee Azar, Commissioner (√) Approve ( ) Deny 8/24/23 Date

M J Rowe, MD (√) Approve ( ) Deny 8/23/2023 Date
Melinda Rowe, MD,
Medical Director

Ginger Carmack, Deputy Commissioner (√) Approve ( ) Deny 8-24-23 Date