Alabama Medicaid DUR Board Meeting Minutes Summary
July 20, 2022

Members Present: Kelli Littlejohn Newman, Crystal Deas, Dan McConaghy, Marilyn Bulloch, Danielle Powell, Mary Stallworth, Bernie Olin, Kelly Tate, Christopher Stanley

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

Members Absent: Nina Ford Johnson, Amber Clark, Rachel Seaman

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

Review and Adoption of Minutes: The minutes of the April 27, 2022 meeting were presented, and M. Bulloch 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 2022. She reported 12,309 total manual requests and pointed out the number of morphine milligram equivalent overrides and opioid naïve overrides. She reminded the Board members that this edit began in August 2019 and that the MME hard edit is still set at 200MME/day. There were 15,779 total electronic requests for the month of January 2022. From the Prior Authorization and Override Response Time Ratio report for January 2022, L. Thomas reported that approximately 40% of all manual PAs and 42% of all overrides were completed in less than two hours. Seventy-eight percent of all manual PAs and 82% of all overrides were completed in less than four hours. Eighty-seven percent of all manual PAs and 90% of all overrides were completed in less than eight hours. For the month of February 2022, L. Thomas reported 13,376 manual PA requests and 15,739 electronic PA requests were received. She reported that 19% of all manual PAs and 17% of all overrides were completed in less than two hours. L. Thomas also mentioned that during this month there were 6,000 additional PAs submitted. Sixty-two percent of all manual PAs and 63% of all overrides were completed in less than four hours. Eighty-five percent of all manual PAs and 88% of all overrides were completed in less than eight hours. For the month of March 2022, L. Thomas reported 14,883 manual PA requests and 17,273 electronic PA requests. L. Thomas reported that approximately 15% of all manual PAs and 13% of all overrides were completed in less than two hours. Sixty-three percent of all manual PA requests and 60% of all overrides were completed in less than four hours. Eighty-nine percent of all manual PA and all overrides were completed in less than eight hours.

Program Summary Review: L. Thomas briefly reviewed the Alabama Medicaid Program Summary for the months of October 2021 through March 31, 2022. She reported 3,863,685 total prescriptions, 235,545 average recipients per month using pharmacy benefits, and an average paid per prescription of $132.97.

Cost Management Analysis: L. Thomas reported an average cost per claim of $146.35 for March 2022 and compared previous months contained in the table. From the 1st Quarter Drug Analysis, L.Thomas reported 82% generic utilization, 8.6% brand single-source, 5.8% brand multi-source (those requests which required a DAW override), and 3.5% OTC and "other". From the Top 25 Drugs Based on Number of Claims from 01/01/2022-03/31/2022, L.Thomas reported the top five drugs: cetirizine, albuterol sulfate HFA, amoxicillin, azithromycin, and fluticasone propionate. She reported that this report was similar to the 4rd Quarter 2021 and that the number of hydrocodone/APAP claims continue to decrease. L. Thomas then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 01/01/2022-03/31/2022: Vyvanse®, Humira® Citrate-free, Trikafta®, Focalin XR®, and Invega® Sustenna®.

From the Top 15 Therapeutic Classes by Total Cost of Claims for the same time frame, L.Thomas reported the top five classes: Antipsychotic Agents, Disease-modifying Antirheumatic Agents, Respiratory and CNS Stimulants, Miscellaneous Anticonvulsants, and Insulins.

Proposed Criteria: L.Thomas presented the proposed set of 43 criteria to the Board and instructed the Board members to mark their ballots. Of the 43 proposed criteria, results from the criteria vote returned 39 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. K. Newman reminded the Board members that the Agency is still preparing for the unwinding of the national COVID-19 PHE. 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 C. Deas as Vice Chair. The current Vice Chair, D. Powell, will begin her term as Chairman of the Board beginning with the October 2022 meeting.

P & T Committee Update: C. Hurst began the P & T Update by informing the Board that the last P & T meeting was held on May 4, 2022 and covered the remaining cardiac agents, antihypertensives, and alzheimers agents.

Next Meeting Date: B. Olin reminded the Board that the next DUR meeting will be held on October 26, 2022. A motion to adjourn the meeting was made by D. Powell and C. Stanley seconded the motion. The meeting was adjourned at 1:55 p.m.

Respectfully submitted,

Lori Thomas, PharmD

Lori Thomas, PharmD.

ALABAMA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*
1. Monomethyl Fumarate / Overuse Alert Message: Bafiertam (monomethyl fumarate) may be over-utilized. The recommended maintenance dose after 7 days is 190 mg twice a day. Drugs/Diseases Util A: Monomethyl Fumarate Util B: Util C: Max Dose: 380 mg/day References: Clinical Pharmacology, 2021 Elsevier/Gold Standard. Bafiertam Prescribing Information, May 2021, Banner Life Sciences.	√		
2. Monomethyl Fumarate / Therapeutic Appropriateness Alert Message: The safety and effectiveness of Bafiertam (monomethyl fumarate) in pediatric patients have not been established. Drugs/Diseases Util A: Monomethyl Fumarate Util B: Util C: Age Range: 0 – 17 yoa References: Clinical Pharmacology, 2021 Elsevier/Gold Standard. Bafiertam Prescribing Information, May 2021, Banner Life Sciences.	√		
3. Monomethyl Fumarate / Dimethyl Fumarate & Diroximel Fumarate Alert Message: Coadministration of Bafiertam (monomethyl fumarate) with dimethyl fumarate or diroximel fumarate is contraindicated. Both dimethyl fumarate and diroximel fumarate are metabolized to monomethyl fumarate. Concurrent use of monomethyl fumarate with these drugs may lead to toxic adverse effects. Monomethyl fumarate may be initiated the day following discontinuation of either drug. Conflict Code: DD - Drug/Drug Interaction Drugs/Diseases Util A: Monomethyl Fumarate Util B: Dimethyl Fumarate, Diroximel Fumarate Util C: References: Clinical Pharmacology, 2021 Elsevier/Gold Standard. Bafiertam Prescribing Information, May 2021, Banner Life Sciences.	√		

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

4. Monomethyl Fumarate / Progressive Multifocal Leukoencephalopathy ___√___ _____ _____

Alert Message: Progressive multifocal leukoencephalopathy (PML) has occurred in patients with MS treated with dimethyl fumarate, the prodrug of Bafiertam (monomethyl fumarate). At the first sign or symptom suggestive of PML, withhold monomethyl fumarate and perform an appropriate diagnostic evaluation. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes.

Drugs/Diseases

Util A	Util B	Util C
Monomethyl Fumarate	Visual Disturbances	
	Muscle Weakness	
	Disorientation	
	Altered Mental Status	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Bafiertam Prescribing Information, May 2021, Banner Life Sciences.

5. Monomethyl Fumarate / Serious Opportunistic Infections ___√___ _____ _____

Alert Message: Serious opportunistic infections have occurred with dimethyl fumarate, the product of Bafiertam (monomethyl fumarate), including cases of serious viral (herpes simplex virus, West Nile virus, cytomegalovirus), fungal (Candida and Aspergillus), and bacterial (Nocardia, Listeria monocytogenes, Mycobacterium tuberculosis) infections. Patients with symptoms and signs consistent with any of these infections should undergo prompt diagnostic evaluation and receive appropriate treatment. Consider withholding dimethyl fumarate treatment in patients with herpes zoster or other serious infections until the infection has resolved.

Drugs/Diseases

Util A	Util B	Util C
Monomethyl Fumarate	Infections	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Bafiertam Prescribing Information, May 2021, Banner Life Sciences.

6. Monomethyl Fumarate / Flushing / Aspirin ___√___ _____ _____

Alert Message: Bafiertam (monomethyl fumarate) may cause flushing (e.g., warmth, redness, itching, and/or burning sensation). Studies with dimethyl fumarate, the prodrug of monomethyl fumarate, show that administration of non-enteric coated aspirin (up to a dose of 325 mg) 30 minutes prior to dosing may reduce the incidence or severity of flushing.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Dimethyl Fumarate	Flushing	Aspirin

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Bafiertam Prescribing Information, May 2021, Banner Life Sciences.

Criteria Recommendations

	Accepted	***Approved As Amended***	***Rejected***
7. Monomethyl Fumarate / Pregnancy / Pregnancy Negating	___V___	_____	_____

Alert Message: There are no adequate data on the developmental risk associated with the use of Bafiertam (monomethyl fumarate) or dimethyl fumarate (the prodrug of monomethyl fumarate) in pregnant women. Monomethyl fumarate may cause fetal harm. In animal studies, adverse effects on offspring survival, growth, sexual maturation, and neurobehavioral function were observed when dimethyl fumarate was administered during pregnancy and lactation at clinically relevant doses.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Monomethyl Fumarate	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Bafiertam Prescribing Information, May 2021, Banner Life Sciences.

8. Monomethyl Fumarate / Therapeutic Appropriateness	___V___	_____	_____

Alert Message: There are no data on the presence of Bafiertam (monomethyl fumarate) or dimethyl fumarate (the prodrug of monomethyl fumarate) in human milk. The effects on the breastfed infant and milk production are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for monomethyl fumarate and any potential adverse effects on the breastfed infant from the drug or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Monomethyl Fumarate	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Bafiertam Prescribing Information, May 2021, Banner Life Sciences.

9. Monomethyl Fumarate / Abnormal Liver Function Studies	___V___	_____	_____

Alert Message: Clinically significant cases of liver injury have been reported in patients treated with dimethyl fumarate, the prodrug of Bafiertam (monomethyl fumarate, in the postmarketing setting. Obtain serum aminotransferase, alkaline phosphatase (ALP), and total bilirubin levels prior to treatment with monomethyl fumarate and during treatment, as clinically indicated. Discontinue monomethyl fumarate if clinically significant liver injury induced by monomethyl fumarate is suspected.

Drugs/Diseases

Util A	Util B	Util C
Monomethyl Fumarate	Abnormal Results in Liver Function Studies	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Bafiertam Prescribing Information, May 2021, Banner Life Sciences.

Criteria Recommendations

	Accepted	***Approved As Amended***	***Rejected***
10. Monomethyl Fumarate / Non-adherence Alert Message: Based on refill history, your patient may be under-utilizing Bafiertam (monomethyl fumarate). Nonadherence to the prescribed dosing regimen may result in subtherapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs.	___V___	_____	_____

Conflict Code: LR – Non-adherence
Drugs/Diseases

Util A	Util B	Util C
Monomethyl Fumarate		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005;353:487-97.
McKay KA, Tremlett H, Patten SB, et al. Determinants of Non-Adherence to Disease-Modifying Therapies in Multiple Sclerosis: A Cross-Canada Prospective Study. Mult Scler. 2016;23(4):588-596.
Higuera L, Carlin CS, Anderson S. Adherence to Disease-Modifying Therapies for Multiple Sclerosis. J Manag Care Spec Pharm. 2016;22(12):1394-1401.

11. Cyclobenzaprine ER / Therapeutic Appropriateness Alert Message: The safety and effectiveness of Amrix (cyclobenzaprine extended-release) have not been established in pediatric patients.	___V___	_____	_____

Drugs/Diseases

Util A	Util B	Util C
Cyclobenzaprine ER		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Retevmo Prescribing Information, Jan.2021, Eli Lilly and Company.

12. Ibrexafungerp / Overuse Alert Message: Brexafemme (ibrexafungerp) may be over-utilized. The recommended dosage of ibrexafungerp in adult and post-menarchal pediatric females is 300 mg (two 150 mg tablets) administered approximately 12 hours apart (e.g., in the morning and in the evening) for one day, for a total daily dosage of 600 mg (four 150 mg tablets).	_____	___V___	_____

Drugs/Diseases

Util A	Util B	Util C (Negating)	
Ibrexafungerp		Clarithromycin	Nelfinavir
		Cobicistat	Posaconazole
		Indinavir	Ritonavir
		Itraconazole	Saquinavir
		Ketoconazole	Voriconazole
		Nefazodone	

Max Dose: 600 mg/day

References:
Brexafemme Prescribing Information, June 2021, Scynexis, Inc.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

Criteria Recommendations

	Accepted	***Approved As Amended***	***Rejected***

13. Ibrexafungerp / Therapeutic Appropriateness ___V___ _____ _____

Alert Message: The safety and effectiveness of Brexafemme (ibrexafungerp) have not been established in pre-menarchal pediatric females.

Drugs/Diseases

Util A	Util B	Util C
Ibrexafungerp		

Gender: Female
Age Range: 0 – 8 yoa

References:
Brexafemme Prescribing Information, June 2021, Scynexis, Inc.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

14. Ibrexafungerp / Therapeutic Appropriateness ___V___ _____ _____

Alert Message: Advise females of reproductive potential to use effective contraception during treatment with Brexafemme (ibrexafungerp) and for 4 days after the last dose. Based on findings from animal studies, ibrexafungerp use is contraindicated in pregnancy because it may cause fetal harm.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Ibrexafungerp		Contraceptives

Gender: Female
Age Range: 11 – 50 yoa

References:
Brexafemme Prescribing Information, June 2021, Scynexis, Inc.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

15. Ibrexafungerp / Pregnancy / Pregnancy Negating ___V___ _____ _____

Alert Message: Based on findings from animal studies, Brexafemme (ibrexafungerp) use is contraindicated in pregnancy because it may cause fetal harm. In animal reproduction studies, ibrexafungerp administered orally to pregnant rabbits during organogenesis was associated with fetal malformations at dose exposures greater or equal to approximately 5 times the human exposure at the recommended human dose (RHD). Prior to initiating treatment with ibrexafungerp, verify the pregnancy status in females of reproductive potential. Advise females of reproductive potential to use effective contraception during treatment with ibrexafungerp and for 4 days after the last dose.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Ibrexafungerp	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Brexafemme Prescribing Information, June 2021, Scynexis, Inc.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

Criteria Recommendations

	Accepted	***Approved As Amended***	***Rejected***
16. Ibrexafungerp / Lactation			
Alert Message: There are no data on the presence of Brexafemme (ibrexafungerp) in either human or animal 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 ibrexafungerp and any potential adverse effects on the breastfed child from ibrexafungerp or the underlying maternal condition.	___√____	_____	_____

Drugs/Diseases

Util A	Util B	Util C
Ibrexafungerp	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Brexafemme Prescribing Information, June 2021, Scynexis, Inc.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

17. Ibrexafungerp / Strong CYP3A4 Inhibitors			
Alert Message: Brexafemme (ibrexafungerp) is a substrate of CYP3A4. Drugs that inhibit or induce CYP3A may alter the plasma concentrations of ibrexafungerp and affect the safety and efficacy of ibrexafungerp. With concomitant use of a strong CYP3A inhibitor, administer ibrexafungerp 150 mg approximately 12 hours apart (e.g., in the morning and the evening) for one day. No dosage adjustment is warranted in patients with concomitant use of a weak or moderate CYP3A inhibitor.	_____	___√____	_____

Drugs/Diseases

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

References:
Brexafemme Prescribing Information, June 2021, Scynexis, Inc.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

Criteria Recommendations

	Accepted	***Approved As Amended***	***Rejected***

18. Ibrexafungerp / Moderate & Strong CYP3A4 Inducers — ___√___ _____ _____

Alert Message: The concurrent use of Brexafemme (ibrexafungerp) with drugs that are moderate or strong CYP3A inducers should be avoided. Ibrexafungerp is a substrate of CYP3A4, and concomitant use with drugs that induce CYP3A metabolism may significantly reduce the plasma concentrations of ibrexafungerp and decrease ibrexafungerp efficacy.

Drugs/Diseases

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

References:
Brexafemme Prescribing Information, June 2021, Scynexis, Inc.
Clinical Pharmacology, 2021 Elsevier/Gold Standard.

19. Ripretinib / Overuse — ___√___ _____ _____

Alert Message: Qinlock (ripretinib) may be over-utilized. The manufacturer's recommended maximum daily dosage of ripretinib is 150 mg orally once daily.

Drugs/Disease

Util A	Util B	Util C
Ripretinib		

Max Dose: 150 mg/day

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Qinlock Prescribing Information, June 2021, Deciphera Pharmaceuticals, LLC.

20. Ripretinib / Therapeutic Appropriateness — ___√___ _____ _____

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

Drugs/Disease

Util A	Util B	Util C
Ripretinib		

Age Range: 0 – 17 yoa

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Qinlock Prescribing Information, June 2021, Deciphera Pharmaceuticals, LLC.

Criteria Recommendations

	Accepted	***Approved As Amended***	***Rejected***

21. Ripretinib / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: Palmar-plantar erythrodysesthesia syndrome (PPES) has occurred in patients who received Qinlock (ripretinib). In clinical trials, PPES led to dose discontinuation in 1.2% of patients, dose interruption in 2.4% of patients, and dose reduction in 1.2% of patients. Based on severity, withhold ripretinib and then resume at the same or reduced dose.

Drugs/Disease

Util A	Util B	Util C
Ripretinib	Localized skin eruption due to drugs and medications taken internally	

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Qinlock Prescribing Information, June 2021, Deciphera Pharmaceuticals, LLC.

22. Ripretinib / Other Malignancies ___√___ _____ _____

Alert Message: New primary malignancy (e.g., cutaneous squamous-cell carcinoma, keratoacanthoma, and melanoma) has been reported with Qinlock (ripretinib) therapy. Dermatologic evaluations should be performed prior to starting ripretinib therapy and routinely during treatment. Manage suspicious skin lesions with excision and dermatopathologic evaluation. Continue ripretinib at the same dose.

Drugs/Disease

Util A	Util B	Util C
Ripretinib	Squamous Cell Carcinoma Keratoacanthoma Melanoma	

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Qinlock Prescribing Information, June 2021, Deciphera Pharmaceuticals, LLC.

23. Ripretinib / Hypertension ___√___ _____ _____

Alert Message: Hypertension has been reported with Qinlock (ripretinib) therapy. Do not initiate ripretinib in patients with uncontrolled hypertension. Adequately control blood pressure prior to initiating ripretinib. Monitor blood pressure as clinically indicated during treatment with ripretinib, and initiate or adjust antihypertensive therapy as appropriate. Based on severity, withhold ripretinib and then resume at the same or reduced dose or permanently discontinue.

Drugs/Disease

Util A	Util B	Util C (Negating)
Ripretinib	Hypertension	Antihypertensives

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Qinlock Prescribing Information, June 2021, Deciphera Pharmaceuticals, LLC.

Criteria Recommendations

	Accepted	***Approved As Amended***	***Rejected***

24. Ripretinib / Cardiovascular Issues ___V___ _____ _____

Alert Message: Qinlock (ripretinib) should be used with caution in patients with cardiovascular disease. Cardiac dysfunction (including cardiac failure, acute left ventricular failure, diastolic dysfunction, and ventricular hypertrophy) has occurred during ripretinib therapy. Assess ejection fraction by echocardiogram or MUGA scan prior to initiating ripretinib and during treatment, as clinically indicated. Permanently discontinue ripretinib for Grade 3 or 4 left ventricular systolic dysfunction.

Drugs/Disease

Util A	Util B	Util C
Ripretinib	Acute Coronary Syndrome	
	Myocardial Infarction	
	Cardiac Failure	
	Ventricular Hypertrophy	

Reference:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Qinlock Prescribing Information, June 2021, Deciphera Pharmaceuticals, LLC.

25. Ripretinib / Therapeutic Appropriateness _____ ___V___ _____

Alert Message: Qinlock (ripretinib) inhibits the vascular endothelial growth factor (VEGF) signaling pathway and may impaired wound healing. Therefore, ripretinib has the potential to adversely affect wound healing. Withhold ripretinib for at least one week prior to elective surgery. Do not administer ripretinib for at least two weeks following major surgery and until adequate wound healing. The safety of resumption of ripretinib after the resolution of wound healing complications has not been established.

Drugs/Disease

Util A	Util B	Util C
Ripretinib		

Reference:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Qinlock Prescribing Information, June 2021, Deciphera Pharmaceuticals, LLC.

26. Ripretinib / Strong CYP3A Inhibitors _____ ___V___ _____

Alert Message: The concurrent use of Qinlock (ripretinib), a CYP3A substrate, with a strong CYP3A inhibitor can increase the exposure of ripretinib and its active metabolite (DP-5439), which may increase the risk of adverse reactions. If ripretinib is used concomitantly with a strong CYP3A inhibitor, monitor the patient more frequently for ripretinib-related adverse reactions.

Drugs/Disease

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

Reference:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Qinlock Prescribing Information, June 2021, Deciphera Pharmaceuticals, LLC.

Criteria Recommendations

Accepted	*Approved As Amended*	*Rejected*

27. Ripretinib / Strong CYP3A Inducers ___√___ _____ _____

Alert Message: The concurrent use of Qinlock (ripretinib) with a strong CYP3A inducer should be avoided. Ripretinib is a CYP3A substrate, and the use of ripretinib with strong CYP3A inducers may decrease the exposure of ripretinib and its active metabolite (DP-5439), which may decrease ripretinib anti-tumor activity.

Drugs/Disease

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

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Qinlock Prescribing Information, June 2021, Deciphera Pharmaceuticals, LLC.

28. Ripretinib / Moderate CYP3A Inducers ___√___ _____ _____

Alert Message: The concurrent use of Qinlock (ripretinib) with a moderate CYP3A inducer should be avoided. Ripretinib is a CYP3A substrate, and the use of ripretinib with moderate CYP3A inducers may decrease the exposure of ripretinib and its active metabolite (DP-5439), which may decrease ripretinib anti-tumor activity. If a moderate CYP3A inducer cannot be avoided, increase ripretinib dosing frequency from the recommended dose of 150 mg once daily to 150 mg twice daily during the co-administration period. Monitor the patient for clinical response and tolerability.

Drugs/Disease

Util A	Util B		Util C
Ripretinib	Bosentan	Etravirine	
	Butalbital	Rifabutin	
	Efavirenz	Rifapentine	

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Qinlock Prescribing Information, June 2021, Deciphera Pharmaceuticals, LLC.

29. Ripretinib / Pregnancy / Pregnancy Negating ___√___ _____ _____

Alert Message: Based on findings from animal studies and its mechanism of action, Qinlock (ripretinib) can cause fetal harm when administered to a pregnant patient. There are no available data on the use of ripretinib in pregnant patients to inform a drug-associated risk. Administration of ripretinib to pregnant rats and rabbits during the period of organogenesis resulted in malformations primarily associated with the cardiovascular and skeletal systems, anatomic variations, reduced fetal body weight, and increased post-implantation loss at maternal exposures that were approximately equal to the human exposure at the recommended dose of 150 mg. Advise pregnant patients of the potential risk to a fetus.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Ripretinib	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Qinlock Prescribing Information, June 2021, Deciphera Pharmaceuticals, LLC.

Criteria Recommendations

	Accepted	***Approved As Amended***	***Rejected***

30. Ripretinib / Lactation

Alert Message: There are no data regarding the presence of Qinlock (ripretinib) or its metabolites in either human milk or its effects on a breastfed child or milk production. Because of the potential for serious adverse reactions in the breastfed child, advise patients not to breastfeed during treatment with ripretinib and for at least 1 week after the final dose.

√ | | |

Drugs/Diseases

Util A	Util B	Util C
Ripretinib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Qinlock Prescribing Information, June 2021, Deciphera Pharmaceuticals, LLC.

31. Ripretinib / Therapeutic Appropriateness

Alert Message: Advise females of reproductive potential to use effective contraception during Qinlock (ripretinib) treatment and for at least 1 week after the final dose. There are no available data on the use of ripretinib in pregnant women to inform a drug-associated risk.

√ | | |

Drugs/Disease

Util A	Util B	Util C (Negating)
Ripretinib		Contraceptives

Gender: Female
Age Rage: 11 – 50 yoa

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Qinlock Prescribing Information, June 2021, Deciphera Pharmaceuticals, LLC.

32. Ripretinib / Therapeutic Appropriateness

Alert Message: Advise males with female partners of reproductive potential to use effective contraception during treatment with Qinlock (ripretinib) and for at least 1 week after the final ripretinib dose.

√ | | |

Drugs/Disease

Util A	Util B	Util C
Ripretinib		

Gender: Male

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Qinlock Prescribing Information, June 2021, Deciphera Pharmaceuticals, LLC.

Criteria Recommendations

	Accepted	***Approved As Amended***	***Rejected***

33. Ripretinib / Non-adherence ___√___ _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Qinlock (ripretinib). 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
Ripretinib		

References:

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

34. Tazemetostat / Overuse ___√___ _____ _____

Alert Message: Tazverik (tazemetostat) may be over-utilized. The dosage of tazemetostat is 800 mg orally twice daily with or without food until disease progression or unacceptable toxicity.

Drugs/Disease

Util A	Util B	Util C
Tazemetostat		

Max Dose: 1600 mg/day

Reference:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tazverik Prescribing Information, July 2020, Epizyme, Inc.

35. Tazemetostat / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: The safety and effectiveness of Tazverik (tazemetostat) in pediatric patients less than 16 years of age have not been established.

Drugs/Disease

Util A	Util B	Util C
Tazemetostat		

Age Range: 0-15 yoa

Reference:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tazverik Prescribing Information, July 2020, Epizyme, Inc.

Criteria Recommendations

Accepted	*Approved As Amended*	*Rejected*

36. Tazemetostat / Contraceptives

Alert Message: The concurrent use of Tazverik (tazemetostat) with estrogen-containing contraceptives can result in decreased contraceptive plasma concentrations and reduced contraceptive efficacy. Tazemetostat is a weak CYP3 inducer, and estrogens are CYP3A substrates.

___V___ _____ _____

Drugs/Disease

Util A	Util B	Util C
Tazemetostat	Contraceptives	

Reference:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.

Tazverik Prescribing Information, July 2020, Epizyme, Inc.

37. Tazemetostat / Strong or Moderate CYP3A Inhibitors

Alert Message: The coadministration of Tazverik (tazemetostat) with strong or moderate CYP3A inhibitors should be avoided. Tazemetostat is a CYP3A substrate, and concurrent use with a CYP3A4 inhibitor can result in elevated tazemetostat concentrations, which may increase the frequency or severity of tazemetostat-related adverse reactions. If coadministration with a moderate CYP3A inhibitor cannot be avoided, reduce the tazemetostat dose according to the official prescribing information. After discontinuation of the moderate CYP3A inhibitor for 3 elimination half-lives, resume the tazemetostat dose that was taken prior to initiating the inhibitor.

_____ ___V_____ _____

Drugs/Disease

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

Reference:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.

Tazverik Prescribing Information, July 2020, Epizyme, Inc.

Criteria Recommendations

Accepted	***Approved As Amended***	***Rejected***

38. Tazemetostat / Strong or Moderate CYP3A Inducers ___V___ _____ _____

Alert Message: The coadministration of Tazverik (tazemetostat) with strong or moderate CYP3A inducers should be avoided. Tazemetostat is a CYP3A substrate, and concurrent use with a CYP3A4 inducer can result in decreased tazemetostat concentrations and potential loss of tazemetostat efficacy.

Drugs/Disease

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

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tazverik Prescribing Information, July 2020, Epizyme, Inc.

39. Tazemetostat / Pregnancy / Pregnancy Negating ___V___ _____ _____

Alert Message: Based on findings from animal studies and its mechanism of action, Tazverik (tazemetostat) can cause fetal harm when administered to a pregnant patient. There are no available data on tazemetostat use in pregnant patients to inform the drug-associated risk. Administration of tazemetostat to pregnant rats and rabbits during organogenesis resulted in dose-dependent increases in skeletal developmental abnormalities in both species. Advise pregnant patients of the potential risk to a fetus.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Tazemetostat	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tazverik Prescribing Information, July 2020, Epizyme, Inc.

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

40. Tazemetostat / Lactation ___√___ _____ _____

Alert Message: There are no animal or human data on the presence of Tazverik (tazemetostat) in human milk or on its effects on the breastfed child or milk production. Because of the potential risk for serious adverse reactions from tazemetostat in the breastfed child, advise patients not to breastfeed during treatment with tazemetostat and for one week after the final dose.

Drugs/Diseases

Util A	Util B	Util C
Tazemetostat	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tazverik Prescribing Information, July 2020, Epizyme, Inc.

41. Tazemetostat / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: Advise females of reproductive potential to use effective non-hormonal contraception during treatment with Tazverik (tazemetostat) and for 6 months after the final dose. Tazemetostat can cause fetal harm when administered to pregnant women.

Drugs/Disease

Util A	Util B	Util C (Negating)
Tazemetostat		Non-Hormonal Contraceptives

Gender: Female
Age Range: 11 – 50 yoa

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tazverik Prescribing Information, July 2020, Epizyme, Inc.

42. Tazemetostat / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: Advise males with female partners of reproductive potential to use effective contraception during treatment with Tazverik (tazemetostat) and for at least 3 months after the final dose.

Drugs/Disease

Util A	Util B	Util C
Tazemetostat		

Gender: Male

Reference:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Tazverik Prescribing Information, July 2020, Epizyme, Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*
43. Tazemetostat / Non-adherence Alert Message: Based on refill history, your patient may be under-utilizing Tazverik (tazemetostat). 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: Tazemetostat Util B Util C	√		

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.
Barillet M, Prevost V, Joly F, Clarisse B. Oral Antineoplastic Agents: How do We Care About Adherence?. Br J Clin Pharmacol. 2015;80(6):1289–1302. doi:10.1111/bcp.12734
Greer JA, Amoyal N, Nisotel L, et al. Systemic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist. 2016;21:354-376.

Stephanie McGee Azar, Commissioner (✓) Approve ( ) Deny 8/15/22 Date

Ginger Wettingfeld, Deputy Commissioner (✓) Approve ( ) Deny 8.12.22 Date