Alabama Medicaid DUR Board Meeting Minutes Summary
April 27, 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, Alex Jenkins, LaQwanda Eddings-Haygood, ACHN Pharmacists

Members Absent: Nina Ford Johnson, Amber Clark

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

Review and Adoption of Minutes: The minutes of the January 26, 2022 meeting were presented, and M. Bulloch made a motion to approve the minutes. D. McConaghy seconded the motion, and the motion was approved unanimously.

Prior Authorization and Overrides Update: L. Thomas began the Prior Authorization and Overrides Update with the Monthly Manual Prior Authorizations and Overrides Report for the month of October 2021. She reported 13,907 total manual requests and reminded the Board members that Synagis season officially began on October 1. There were 16,607 total electronic requests for the month of October 2021. From the Prior Authorization and Override Response Time Ratio report for October 2021, L. Thomas reported that approximately 36% of all manual PAs and 38% of all overrides were completed in less than two hours. Seventy-three percent of all manual PAs and 74% of all overrides were completed in less than four hours. Ninety percent of all manual PAs and overrides were completed in less than eight hours. For the month of November 2021, L. Thomas reported 12,904 manual PA requests and 15,550 electronic PA requests were received. She reported that 35% of all manual PAs and overrides were completed in less than two hours. Seventy-six percent of all manual PAs and overrides were completed in less than four hours. Eighty-nine percent of all manual PAs and overrides were completed in less than eight hours. For the month of December 2021, L. Thomas reported 12,422 manual PA requests and 14,520 electronic PA requests. L. Thomas reported that approximately 41% of all manual PAs and 43% of all overrides were completed in less than two hours. Sixty-nine percent of all manual PA requests and 72% of all overrides were completed in less than four hours. Eighty-six percent of all manual PA requests and 89% of all overrides were completed in less than eight hours.

Program Summary Review: L. Thomas briefly reviewed the Alabama Medicaid Program Summary for the months of July 2021 through December 2021. She reported 3,863,685 total prescriptions, 237,126 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 $136.21 for December 2021 and compared previous months contained in the table. From the 4th Quarter 2021 Drug Analysis, L.Thomas reported 82% generic utilization, 9% brand single-source, 5% brand multi-source (those requests which required a DAW override), and 3% OTC and "other". From the Top 25 Drugs Based on Number of Claims from 10/01/2021-12/31/2021, L.Thomas reported the top five drugs: amoxicillin, cetirizine, albuterol sulfate HFA, azithromycin, and fluticasone propionate. She reported that this report was similar to the 3rd Quarter 2021 with the exception of the Pfizer Covid-19 vaccine no longer being in the top five. L. Thomas then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 10/01/2021-12/31/2021: Vyvanse®, Humira® Citrate-free, Trikafta®, Invega® Sustenna®, and Suboxone®. From the Top 15 Therapeutic Classes by Total Cost of Claims for the same time frame, L.Thomas reported the top five classes: Antipsychotic Agents, Disease-modifying Antirheumatic Agents, Respiratory and CNS Stimulants, Miscellaneous Anticonvulsants, and Insulins.

RDUR Intervention Report: L. Thomas presented the RDUR Activity Report for January 2021. She reported 503 profiles reviewed and 542 letters sent with 36 responses received as of the date of the report. She reported 46 of 67 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); Appropriate Use (concurrent use of buprenorphine and pure opiate agonists).

Proposed Criteria: L.Thomas presented the proposed set of 41 criteria to the Board and instructed the Board members to mark their ballots. Of the 41 proposed criteria, results from the criteria vote returned 41 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 briefly reviewed the CMS Federal Report, the Fiscal Year 2023 PDMP reports, and the Yellow Card campaign for the anticipated unwinding of the national PHE.

P & T Committee Update: C. Hurst began the P & T Update by informing the Board that the last P & T meeting was held on February 9, 2022 and covered the oral anticoagulants, cardiac agents, antihyperlipidemic agents, and antidepressants. The next P & T Committee meeting will be held on May 4, 2022 and will cover the remaining cardiac agents and the alzheimers agents.

Next Meeting Date: B. Olin reminded the Board that the next DUR meeting will be held on July 20, 2022. A motion to adjourn the meeting was made by C. Stanley. D. Powell seconded the motion and the meeting was adjourned at 1:50 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. Selpercatinib / Overuse	√		

Alert Message: Retevmo (selpercatinib) may be over-utilized. The recommended daily dosage of selpercatinib is based on body weight. Patients weighing 50 kg or greater should receive 160 mg twice daily. Patients weighing less than 50 kg should receive 120 mg twice daily.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Selpercatinib		Cirrhosis
		Hepatic Failure

Max Dose: 320 mg/day

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

2. Selpercatinib / Overuse – Severe Hepatic Impairment	√		

Alert Message: The dose of Retevmo (selpercatinib) should be reduced in patients with severe hepatic impairment [total bilirubin greater than 3 to 10 times the upper limit of normal (ULN) and any AST]. The daily dose of selpercatinib should not exceed 80 mg twice daily in patients with severe hepatic impairment.

Drugs/Diseases

Util A	Util B	Util C (Include)
Selpercatinib		Cirrhosis
		Hepatic Failure

Max Dose: 160 mg/day

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

3. Selpercatinib / Therapeutic Appropriateness	√		

Alert Message: The safety and effectiveness of Retevmo (selpercatinib) for the treatment of non-small cell lung cancer have not been established in pediatric patients.

Drugs/Diseases

Util A	Util B	Util C (Include)
Selpercatinib		Malignant Neoplasm of Bronchus and Lung

Age Range: 0 – 17 yoa

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

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

4. Selpercatinib / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: The safety and effectiveness of Retevmo (selpercatinib) have not been established in pediatric patients less than 12 years of age.

Drugs/Diseases

Util A	Util B	Util C
Selpercatinib		

Age Range: 0 – 11 yoa

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

5. Selpercatinib / Hypertension ___√___ _____ _____

Alert Message: In clinical studies, hypertension occurred in 35% of patients receiving Retevmo (selpercatinib). Treatment-emergent hypertension was most commonly managed with anti-hypertension medications. Do not initiate selpercatinib in patients with uncontrolled hypertension. Optimize blood pressure prior to initiating selpercatinib. Monitor blood pressure after 1 week, at least monthly thereafter, and as clinically indicated. Initiate or adjust anti-hypertensive therapy as appropriate. Based on the severity of hypertension, withhold, reduce dose, or permanently discontinue selpercatinib.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Selpercatinib	Hypertension	Antihypertensive Medications

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

6. Selpercatinib / Hemorrhage ___√___ _____ _____

Alert Message: Serious including fatal hemorrhagic events can occur with Retevmo (selpercatinib). Grade ≥ 3 hemorrhagic events occurred in 2.3% of patients treated with selpercatinib, including 3 (0.4%) patients with fatal hemorrhagic events, including one case each of cerebral hemorrhage, tracheostomy site hemorrhage, and hemoptysis. Permanently discontinue selpercatinib in patients with severe or life-threatening hemorrhage.

Drugs/Diseases

Util A	Util B	Util C
Selpercatinib	Intracranial Hemorrhage Gastrointestinal Bleeding Hematuria	

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

7. Selpercatinib / Drugs That Prolong QT Interval ___√_____ _____ _____

Alert Message: Retevmo (selpercatinib) is associated with QTc interval prolongation. The concurrent use of selpercatinib with a drug that also increases the QT interval may have an additive effect. Monitor the QT interval with ECGs more frequently in patients who require treatment with concomitant medications known to prolong the QT interval.

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

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

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

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

8. Selpercatinib / QT Prolongation ___√___ _____ _____

Alert Message: Retevmo (selpercatinib) can cause concentration-dependent QT interval prolongation. Monitor patients who are at significant risk of developing QTc prolongation, including patients with known long QT syndromes, clinically significant bradyarrhythmias, and severe or uncontrolled heart failure. Assess QT interval, electrolytes, and TSH at baseline and periodically during treatment, adjusting frequency based upon risk factors including diarrhea. Correct hypokalemia, hypomagnesemia, and hypocalcemia prior to initiating selpercatinib and during treatment. Base on the severity of QT prolongation, withhold and dose reduce or permanently discontinue selpercatinib.

Drugs/Diseases

Util A	Util B	Util C
Selpercatinib	Long QT Syndrome	
	Bradyarrhythmia	
	Heart Failure	

References:

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

9. Selpercatinib / Proton Pump Inhibitors ___√___ _____ _____

Alert Message: The coadministration of Retevmo (selpercatinib) with a proton pump inhibitor (PPI) should be avoided. Concomitant use of selpercatinib with acid-reducing agents decreases selpercatinib plasma concentrations, which may reduce selpercatinib anti-tumor activity. If concurrent use of selpercatinib and a PPI cannot be avoided, take selpercatinib with food when coadministered with a PPI.

Conflict Code: DD - Drug/Drug Interaction

Drugs/Diseases

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

References:

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

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

10. Selpercatinib / H2 Receptor Antagonists ___√___ _____ _____

Alert Message: The coadministration of Retevmo (selpercatinib) with an H2 receptor antagonist should be avoided. Concomitant use of selpercatinib with acid-reducing agents decreases selpercatinib plasma concentrations, which may reduce selpercatinib anti-tumor activity. If concurrent use of selpercatinib and an H2 receptor antagonist cannot be avoided, take selpercatinib 2 hours before or 10 hours after administration of the H2 receptor antagonist.

Drugs/Diseases

Util A	Util B	Util C
Selpercatinib	Cimetidine	
	Famotidine	
	Nizatidine	
	Ranitidine	

References:

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

11. Selpercatinib / Locally-Acting Antacids ___√___ _____ _____

Alert Message: The coadministration of Retevmo (selpercatinib) with a locally-acting antacid should be avoided. Concomitant use of selpercatinib with acid-reducing agents decreases selpercatinib plasma concentrations, which may reduce selpercatinib anti-tumor activity. If concurrent use of selpercatinib and a locally-acting antacid cannot be avoided, take selpercatinib 2 hours before or 2 hours after administration of the locally-acting antacid.

Drugs/Diseases

Util A	Util B	Util C
Selpercatinib	Aluminum Carbonate	
	Calcium Carbonate	
	Magnesium Oxide	

References:

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

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

12. Selpercatinib / Moderate & Strong CYP3A Inhibitors ___√___ _____ _____

Alert Message: The coadministration of Retevmo (selpercatinib) with a moderate or strong CYP3A inhibitor should be avoided. Selpercatinib is a CYP3A substrate, and concomitant use with a moderate or strong CYP3A inhibitor increases selpercatinib plasma concentrations, which may increase the risk of selpercatinib adverse reactions, including QT interval prolongation. If concurrent use cannot be avoided, reduce the selpercatinib dose according to the approved product labeling, and monitor the QT interval.

Drugs/Diseases

Util A	Util B		Util C
Selpercatinib	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		

References:

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

13. Selpercatinib / Moderate & Strong CYP3A Inducers ___√___ _____ _____

Alert Message: The coadministration of Retevmo (selpercatinib) with a moderate or strong CYP3A inducer should be avoided. Selpercatinib is a CYP3A substrate, and concurrent use with a moderate or strong CYP3A inducer decreases selpercatinib plasma concentrations, which may reduce selpercatinib anti-tumor activity.

Drugs/Diseases

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

References:

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

14. Selpercatinib / CYP 2C8 & CYP3A Substrates ___√___ _____ _____

Alert Message: Retevmo (selpercatinib) is a moderate CYP2C8 inhibitor and a weak CYP3A inhibitor. Concomitant use of selpercatinib with CYP2C8 and CYP3A substrates increases their plasma concentrations, which may increase the risk of adverse reactions related to these substrates. Avoid coadministration of selpercatinib with CYP2C8 and CYP3A substrates where minimal concentration changes may lead to increased adverse reactions. If coadministration cannot be avoided, follow recommendations for CYP2C8 and CYP3A substrates provided in their approved product labeling.

Drugs/Diseases

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

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

15. Selpercatinib / Pregnancy / Pregnancy Negating ___√___ _____ _____

Alert Message: Based on findings from animal studies and its mechanism of action, Retevmo (selpercatinib) can cause fetal harm when administered to a pregnant woman. There are no available data on selpercatinib use in pregnant women to inform of drug-associated risk. Administration of selpercatinib to pregnant rats during the period of organogenesis resulted in embryolethality and malformations at maternal exposures that were approximately equal to the human exposure at the clinical dose of 160 mg twice daily. Advise pregnant women of the potential risk to a fetus.

Drugs/Diseases

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

Gender: Female
Age Range: 11 – 50 yoa

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

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

16. Selpercatinib / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: There are no data on the presence of Retevmo (selpercatinib) or its metabolites in human milk or on 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 selpercatinib and for 1 week after the final dose.

Drugs/Diseases

Util A	Util B	Util C
Selpercatinib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Retevmo Prescribing Information, May 2020, Eli Lilly and Company.

17. Selpercatinib / Therapeutic Appropriateness ___√___ _____ _____

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

Drugs/Disease

Util A	Util B	Util C (Negating)
Selpercatinib		Contraceptives

Gender: Female
Age Rage: 11 – 50 yoa

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

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

18. Selpercatinib / Therapeutic Appropriateness ___√___ _____ _____

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

Drugs/Disease
Util A Util B Util C
Selpercatinib

Gender: Male

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

19. Selpercatinib / Non-adherence ___√___ _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Retevmo (selpercatinib). 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
Selpercatinib

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.

20. Serdexmethylphenidate/Dexmethylphenidate / Overuse ___√___ _____ _____

Alert Message: Azstarys (serdexmethylphenidate/dexmethylphenidate) may be over-utilized. The maximum recommended dosage of serdexmethylphenidate/dexmethylphenidate, in patients 6 to 12 years of age is 52.3 mg serdexmethylphenidate /10.4mg dexmethylphenidate once daily.

Drugs/Diseases

Util A	Util B	Util C
Serdexmethylphenidate/dexmethylphenidate		

Age Range: 6 – 12 yoa
Max Dose: 52.3 mg/10.4mg once daily

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Azstarys Prescribing Information, March 2021, Corium, Inc.

21. Serdexmethylphenidate/Dexmethylphenidate / Overuse ___√___ _____ _____

Alert Message: Azstarys (serdexmethylphenidate/dexmethylphenidate) may be over-utilized. The maximum recommended dosage of serdexmethylphenidate/dexmethylphenidate, in patients 13 years of age and older is 52.3 mg serdexmethylphenidate /10.4mg dexmethylphenidate once daily.

Drugs/Diseases

Util A	Util B	Util C
Serdexmethylphenidate/dexmethylphenidate		

Age Range: ≥13 yoa
Max Dose: 52.3 mg/10.4mg once daily

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Azstarys Prescribing Information, March 2021, Corium, Inc.

22. Serdexmethylphenidate/Dexmethylphenidate / Risperidone ___√___ _____ _____

Alert Message: When Azstarys (serdexmethylphenidate/dexmethylphenidate) is co-administered with risperidone, and there is a change in dosage of either or both medications, whether an increase or decrease, risk of extrapyramidal symptoms (EPS) may occur. Monitor patients for signs of EPS.

Drugs/Diseases

Util A	Util B	Util C
Serdexmethylphenidate/dexmethylphenidate		Risperidone

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Azstarys Prescribing Information, March 2021, Corium, Inc.

23. Serdexmethylphenidate/Dexmethylphenidate / Pregnancy ___√___ _____ _____

Alert Message: There are no available data on Azstarys (serdexmethylphenidate/dexmethylphenidate) use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Serdexmethylphenidate is a prodrug of dexmethylphenidate and dexmethylphenidate is the d-threo enantiomer of racemic methylphenidate. There may be risks to the fetus associated with the use of CNS stimulants use during pregnancy. CNS stimulants, such as serdexmethylphenidate/dexmethylphenidate, can cause vasoconstriction and thereby decrease placental perfusion.

Drugs/Diseases

Util A	Util B	Util C (Negate)	
Serdexmethylphenidate/dexmethylphenidate		Pregnancy	Abortion
		Delivery	
		Miscarriage	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Azstarys Prescribing Information, March 2021, Corium, Inc.

24 Serdexmethylphenidate/Dexmethylphenidate / Lactation ___√___ _____ _____

Alert Message: The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Azstarys (serdexmethylphenidate/dexmethylphenidate) and any potential adverse effects on the breastfed infant from serdexmethylphenidate/dexmethylphenidate or the underlying maternal condition. There are no available data on the presence of serdexmethylphenidate in human milk, effects on the breastfed infant, or effects on milk production. Dexmethylphenidate is the d-threo enantiomer of racemic methylphenidate, and methylphenidate has been shown to be present in human breast milk.

Drugs/Diseases

Util A	Util B	Util C
Serdexmethylphenidate/dexmethylphenidate	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Azstarys Prescribing Information, March 2021, Corium, Inc.

25. Serdexmethylphenidate/Dexmethylphenidate / MAOIs ___√___ _____ _____

Alert Message: The safety and effectiveness of Azstarys (serdexmethylphenidate/dexmethylphenidate) in pediatric patients less than 6 years have not been established.

Drugs/Diseases

Util A	Util B	Util C
Serdexmethylphenidate/dexmethylphenidate		

Age Range: 0 - 5 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Azstarys Prescribing Information, March 2021, Corium, Inc.

26. Exenatide ER / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: The safety and effectiveness of Bydureon Bcise (exenatide extended-release) have not been established in pediatric patients less than 10 years of age.

Drugs/Diseases

Util A	Util B	Util C
Exenatide ER		

Age Range: 0 – 9 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Bydureon Bcise Prescribing Information. July 2021, AstraZeneca.

27. Risperidone SubQ / Overuse ___√___ _____ _____

Alert Message: Perseris (risperidone extended-release subcutaneous injection) may be over-utilized. Initiate subcutaneous risperidone at a dose of 90 mg or 120 mg once monthly. Do not administer more than one dose (90 mg or 120 mg total) per month.

Drugs/Diseases

Util A	Util B	Util C
Risperidone SubQ		

Max Dose: 1 injection/month

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.
Perseris Prescribing Information, December 2019, Indivior, Inc.

28. Risperidone SubQ / Oral Risperidone / Strong 3A4 Inducers (Negating) ___√___ _____ _____

Alert Message: Neither a loading dose nor any supplemental oral risperidone is recommended with Perseris (risperidone extended-release subcutaneous injection).

Drugs/Diseases

Util A	Util B	Util C (Negating)
Risperidone SubQ	Oral Risperidone	Apalutamide
		Carbamazepine
		Enzalutamide
		Mitotane
		Phenobarbital
		Phenytoin
		Primidone
		Rifampin

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.
Perseris Prescribing Information, December 2019, Indivior, Inc.

29. Risperidone SubQ / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: The safety and effectiveness of Perseris (risperidone extended-release subcutaneous injection) have not been established in pediatric patients.

Drugs/Diseases

Util A	Util B	Util C
Risperidone SubQ		

Age Range: 0 – 17 yoa
rences:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.
Perseris Prescribing Information, December 2019, Indivior, Inc.

30. Risperidone SubQ / Strong CYP34A4 Inducers ___√___ _____ _____

Alert Message: Concomitant use of Perseris (risperidone extended-release subcutaneous injection) with a strong CYP3A4 inducer may result in decreased risperidone plasma concentrations, which could lead to decreased risperidone efficacy. A risperidone dosage increase may be considered. Refer to the official prescribing information for risperidone dosage modifications.

Drugs/Diseases

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

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.
Perseris Prescribing Information, December 2019, Indivior, Inc.

31. Risperidone SubQ / Strong CYP2D6 Inhibitors ___√___ _____ _____

Alert Message: Concomitant use of Perseris (risperidone extended-release subcutaneous injection) with a strong CYP2D6 inhibitor may increase risperidone plasma concentrations, increasing the risk of risperidone-related adverse effects. A risperidone dosage adjustment may be considered when a strong CYP2D6 inhibitor is initiated or discontinued. Refer to the official prescribing information for risperidone dosage modifications.

Drugs/Diseases

Util A	Util B	Util C
Risperidone SubQ	Bupropion	
	Dacomitinib	
	Fluoxetine	
	Paroxetine	
	Quinidine	

References:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Facts & Comparisons, 2021 Updates, Wolters Kluwer Health.
Perseris Prescribing Information, December 2019, Indivior, Inc.

32. Risperidone SubQ / Non-adherence ___√___ _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Perseris (risperidone extended-release subcutaneous injection). 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
Risperidone SubQ		

References:

Higashi k, Medic G, Littlewood K, et al., Medication Adherence in Schizophrenia: Factors Influencing Adherence and Consequences of Nonadherence, A Systemic Literature Review. There Adv Psychopharmacol. 2013 2(4):200-218.
Acsher-Svanum H, Zhu B, Faries DE, et al., The Cost of Relapse and the Predictors of Relapse in the Treatment of Schizophrenia. BMC Psychiatry 2010, 10:2.
Berger A, Edelsbery J, Sanders KN, et al., Medication Adherence and Utilization in Patients with Schizophrenia or Bipolar Disorder Receiving Aripiprazole, Quetiapine, or Ziprasidone at Hospital Discharge: A Retrospective Cohort Study. BMC Psychiatry 2012;12:99.
Stephenson JJ, Tuncelli O, Gu T, et al. Adherence to Oral Second-Generation Antipsychotic Medications in Patients with Schizophrenia and Bipolar Disorder: Physicians' Perceptions of Adherence vs. Pharmacy Claims. Int J Clin Pract. June 2012, 66, 6, 565-573.

33. Elexacaftor/Tezacaftor/Ivacaftor / Hepatic Impairment ___√___ _____ _____

Alert Message: In clinical studies, the use of Trikafta (elexacaftor/tezacaftor/ivacaftor) in patients with moderate hepatic impairment (Child-Pugh Class B) resulted in a higher AUC and Cmax for each individual. Treatment is not recommended for patients with moderate hepatic impairment. If use is clinically warranted in patients with moderate hepatic impairment, elexacaftor/tezacaftor/ivacaftor should be used with caution at a reduced dose, according to official prescribing information. Liver function tests should be closely monitored in patients with mild and moderate hepatic impairment. No dose modification is recommended for patients with mild hepatic impairment (Child-Pugh Class A).

Drugs/Diseases

Util A	Util B	Util C
Elexacaftor/Tezacaftor/Ivacaftor	Hepatic Impairment	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Trikafta Prescribing Information, June 2021, Vertex Pharmaceuticals Inc.

34. Elexacaftor/Tezacaftor/Ivacaftor / Severe Hepatic Impairment ___√___ _____ _____

Alert Message: Trikafta (elexacaftor/tezacaftor/ivacaftor) should not be used in patients with severe hepatic impairment (Child-Pugh Class C). Elexacaftor/tezacaftor/ivacaftor has not been studied in this patient population. In clinical studies, patients with moderate hepatic impairment (Child-Pugh Class B) had increased exposure to all three components of the co-packaged product. Drug exposure is expected to be even higher in patients with severe hepatic impairment.

Drugs/Diseases

Util A	Util B	Util C
Elexacaftor/Tezacaftor/Ivacaftor	Cirrhosis	
	Hepatic Failure	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Trikafta Prescribing Information, June 2021, Vertex Pharmaceuticals Inc.

35. Elexacaftor/Tezacaftor/Ivacaftor / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: The safety and effectiveness of Trikafta (elexacaftor/tezacaftor/ivacaftor) in patients with cystic fibrosis (CF) younger than 6 years of age have not been established.

Drugs/Diseases

Util A	Util B	Util C
Elexacaftor/Tezacaftor/Ivacaftor		

Age Range: 0 – 5 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Trikafta Prescribing Information, June 2021, Vertex Pharmaceuticals Inc.

36. Elexacaftor/Tezacaftor/Ivacaftor / CYP3A Inducers ___√___ _____ _____

Alert Message: Exposure to ivacaftor is significantly decreased and exposure to elexacaftor and tezacaftor are expected to decrease by the concomitant use of strong CYP3A inducers, which may reduce the therapeutic effectiveness of Trikafta (elexacaftor/tezacaftor/ivacaftor). Therefore, co-administration with strong CYP3A inducers is not recommended.

Drugs/Diseases

Util A	Util B	Util C
Elexacaftor/Tezacaftor/Ivacaftor	Apalutamide	
	Carbamazepine	
	Enzalutamide	
	Mitotane	
	Phenobarbital	
	Phenytoin	
	Primidone	
	Rifampin	

References:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Trikafta Prescribing Information, June 2021, Vertex Pharmaceuticals Inc.

37. Elexacaftor/Tezacaftor/Ivacaftor / Moderate & Strong CYP3A4 Inhibitors ___√___ _____ _____

Alert Message: Exposure to elexacaftor, tezacaftor, and ivacaftor is increased when co-administered with strong or moderate CYP3A inhibitors. The dose of Trikafta (elexacaftor/tezacaftor/ivacaftor) should be reduced, according to the official prescribing information, when used concomitantly with moderate or strong CYP3A inhibitors.

Drugs/Diseases

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

References:

Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Trikafta Prescribing Information, June 2021, Vertex Pharmaceuticals Inc.

38. Elexacaftor/Tezacaftor/Ivacaftor / Sensitive P-gp Substrates ___√___ _____ _____

Alert Message: Caution and appropriate monitoring should be used when Trikafta (elexacaftor/tezacaftor/ivacaftor) is co-administered with a P-gp substrate with a narrow therapeutic index. The ivacaftor component of the co-packaged combination product is a P-gp inhibitor, and concurrent use with a sensitive P-gp substrate may result in increased substrate exposure. Appropriate monitoring should be used when these agents are co-administered.

Drugs/Diseases

Util A	Util B	Util C
Elexacaftor/Tezacaftor/Ivacaftor	Digoxin	
	Cyclosporine	
	Tacrolimus	
	Sirolimus	
	Everolimus	

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Trikafta Prescribing Information, June 2021, Vertex Pharmaceuticals Inc.

39. Elexacaftor/Tezacaftor/Ivacaftor / Pregnancy / Pregnancy Negating ___√___ _____ _____

Alert Message: There are limited and incomplete human data from clinical trials on the use of Trikafta (elexacaftor/tezacaftor/ivacaftor) or its individual components in pregnant women to inform a drug-associated risk. Although there are no animal reproduction studies with the concomitant administration of elexacaftor, tezacaftor, and ivacaftor, separate reproductive and developmental studies were conducted with each component in pregnant rats and rabbits. Placental transfer in pregnant rats was observed for each component. No component was found to affect fetal survival or to be teratogenic.

Drugs/Diseases

Util A	Util B	Util C (Negate)
Elexacaftor/Tezacaftor/Ivacaftor	Pregnancy	Abortion
		Delivery
		Miscarriage

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Trikafta Prescribing Information, June 2021, Vertex Pharmaceuticals Inc.

40. Elexacaftor/Tezacaftor/Ivacaftor / Lactation ___√___ _____ _____

Alert Message: There is no information regarding the presence of elexacaftor, tezacaftor, or ivacaftor in human milk, the effects on the breastfed infant, or the effects on milk production. In animal studies, elexacaftor, tezacaftor, and ivacaftor are excreted into the milk of lactating rats. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Trikafta (elexacaftor/tezacaftor/ivacaftor) and any potential adverse effects on the breastfed child from (elexacaftor/tezacaftor/ivacaftor) or the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Elexacaftor/Tezacaftor/Ivacaftor	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2021 Elsevier/Gold Standard.
Trikafta Prescribing Information, June 2021, Vertex Pharmaceuticals Inc.

41. Elexacaftor/Tezacaftor/Ivacaftor / Non-adherence ___√___ _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Trikafta (elexacaftor/tezacaftor/ivacaftor). Nonadherence to the prescribed dosing regimen may result in subtherapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs.

Drugs/Diseases

Util A	Util B	Util C
Elexacaftor/Tezacaftor/Ivacaftor		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005;353:487-97.
Eakin MN, Bilderback A, Boyle MP, et al., Longitudinal Association Between Medication Adherence and Lung Health in People with Cystic Fibrosis. Jrnl Cyst Fib. 2011:10(4):258-264.
Bishay LC, Sawicki GS., Strategies to Optimize Adherence in Adolescent Patients with Cystic Fibrosis. Adolesc Health, Med & Ther. 2016 Oct21;7:117-124.

Stephanie McGee Azar, Commissioner — (✓) Approve ( ) Deny — 5/24/2022 Date

Christopher Stanley, MD
Medical Director — (✓) Approve ( ) Deny — 5/23/2022 Date

Ginger Wettingfeld, Deputy Commissioner — (✓) Approve ( ) Deny — 5/23/22 Date