Alabama Medicaid DUR Board Meeting Minutes
October 25, 2017

Members Present: Robert Moon, Chris Phung, Paula Thompson, Denyse Thornley-Brown, Rachel Seaman, P.J. Hughes, Dan McConaghy

Also Present: Kelli Littlejohn Newman, Tiffany Minnifield, Lori Thomas, Clemice Hurst, Heather Vega, Whitney Hughley

Present via Conference Call: Kristian Testerman, Lauren Ward, Tammy Dubac, Amy Donaldson, Joshua Lee

Members Absent: Marilyn Bulloch

Call to Order: The DUR meeting was called to order by D. Thornley-Brown at approximately 1:05p.m.

Review and Adoption of Minutes: The minutes of the July 26, 2017 meeting were presented and P. Thompson made a motion to approve the minutes. P.J. Hughes 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 April 2017. She reported 10,004 total manual requests and 22,455 total electronic requests. From the Prior Authorization and Override Response Time Ratio report for April 2017, L. Thomas reported that approximately 68% of all manual PAs and 61% of all overrides were completed in less than two hours. Eighty-three percent of all manual PAs and all overrides were completed in less than four hours. Eighty-seven percent of all manual PAs and all overrides were completed in less than eight hours. For the month of May 2017, L. Thomas reported 11,210 manual PA requests and 22,424 electronic PA requests were received. She reported that 70% of all manual PAs and 66% of all overrides were completed in less than two hours. Eighty-five percent of all manual PAs and 84% of all overrides were completed in less than four hours. Eighty-nine percent of all manual PAs and 88% of all overrides were completed in less than eight hours. For the month of June 2017, L. Thomas reported 10,934 manual PA requests and 21,990 electronic PA requests. L. Thomas reported that approximately 72% of all manual PAs and 70% of all overrides were completed in less than two hours. Eighty-five percent of all manual PA requests and all overrides were completed in less than four hours. Ninety-one percent of all manual PA requests 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 January 2017 through June 2017. She reported 3,684,864 total prescriptions, 223,342 average recipients per month using pharmacy benefits, and an average paid per prescription of $102.80.

Cost Management Analysis: L.Thomas reported an average cost per claim of $107.27 for June 2017 and emphasized that the table contained the average cost per claim over the past two years. From the 1st Quarter 2017 Drug Analysis, L.Thomas reported 79.6% generic utilization, 9.2% brand single-source, 7.1% brand multi-source (those requests which required a DAW override), and 4.1% OTC and "other". From the Top 25 Drugs Based on Number of Claims from 04/01/2017 – 06/30/2017, L.Thomas reported the top five drugs: amoxicillin, cetirizine, hydrocodone-acetaminophen, ProAir® HFA, and montelukast sodium. L. Thomas then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 04/01/2017 – 06/30/2017: Vyvanse®, Focalin XR®, Invega® Sustenna®, Lyrica®, and Adderall XR®. She reminded the Board that Vyvanse® and Focalin XR® are preferred agents. 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, Amphetamines, Miscellaneous Anticonvulsants, Respiratory and CNS Stimulants, and Insulins.

RDUR Intervention Report: L. Thomas presented the RDUR Activity Report for April 2017. She reported 526 profiles reviewed and 551 letters sent with 99 responses received as of the date of the report. She reported 42 of 76 physicians indicated that they found the RDUR letters "useful" or "extremely useful". The criteria for the cycle of intervention letters included Drug-Disease Precaution (use of pregabalin in patients with Heart Failure); Pregabalin Overutilization; Hepatitis C SVR Response Rates; Appropriate Use (concurrent use of immediate-release opioids); Appropriate Use (concurrent use of buprenorphine and pure opiate agonists).

Proposed Criteria: L.Thomas presented the proposed set of 49 criteria to the Board. T.Minnifield instructed the Board members to mark their ballots. Of the 49 criteria, results from the criteria vote returned 43 approved and 6 approved as amended.

Medicaid Update: T. Minnifield reminded the Board members that all updated Medicaid drug lists provided are also available online and that the next DUR Meeting would be January 24th.

P & T Committee Update: C. Hurst began the P & T Update by informing the Board that the last meeting was held on August 9, 2017, and covered the Cardiac Agents, Anticoagulants, and Antihyperlipidemic Agents. The next P & T meeting is scheduled for November 8, 2017, at 9 a.m. and will cover the Antihypertensives and the remaining Hepatitis C Antivirals.

Next Meeting Date: D. Thornley-Brown notified the Board that the next DUR meeting will be held on January 24, 2017. A motion to adjourn the meeting was made by D. Thornley-Brown. P. Thompson seconded the motion and 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. Venetoclax / Overutilization	___√____	_____	_____

Alert Message: Venclexta (venetoclax) may be over-utilized. The manufacturer's recommended maximum daily dose is 400 mg.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C
Venetoclax		

Max Dose: 400 mg/day

References:
Venclexta Prescribing Information, April 2016, AbbVie Inc.
Clinical Pharmacology, 2017 Elsevier/Gold Standard.

2. Venetoclax / Strong CYP3A4 Inhibitors	_____	___√____	_____

Alert Message: Avoid concomitant use of strong CYP3A4 inhibitors with the CYP3A4 substrate Venclexta (venetoclax) in patients who have completed the ramp-up phase and are on a steady daily dose of venetoclax. If a strong CYP3A4 inhibitor must be used, reduce the venetoclax dose by 75%. Resume the venetoclax dose that was used prior to initiating the CYP3A4 inhibitor 2 to 3 days after discontinuation of the inhibitor. Concurrent use of a strong CYP3A4 inhibitor with venetoclax is contraindicated at initiation and during ramp-up phase of venetoclax therapy.

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

Util A	Util B	Util C **(Include)**	
Venetoclax		Boceprevir	Ketoconazole
		Cobicistat	Itraconazole
		Saquinavir	Voriconazole
		Ritonavir	Posaconazole
		Indinavir	Conivaptan
		Nelfinavir	Clarithromycin
		Idelalisib	Telithromycin

Max Dose: > 100 mg/day
Day Supply: > 35 days

References:
Venclexta Prescribing Information, April 2016, AbbVie Inc.
Clinical Pharmacology, 2017 Elsevier/Gold Standard.

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

3. Venetoclax / Moderate & Strong CYP3A4 Inducers ___√____ _____ _____

Alert Message: Avoid concomitant use of Venclexta (venetoclax), a CYP3A4 substrate, with moderate to strong CYP3A4 inducers. Consider alternative treatments with less CYP3A4 induction.

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

Util A	Util B				Util C
Venetoclax	Carbamazepine	Primidone	Rifapentine	Efavirenz	
	Phenytoin	Rifabutin	Bosentan	Etravirine	
	Phenobarbital	Rifampin	Modafinil		

References:
Venclexta Prescribing Information, April 2016, AbbVie Inc.
Clinical Pharmacology, 2017 Elsevier/Gold Standard.

4. Venetoclax / Moderate CYP3A4 Inhibitors & P-gp Inhibitors _____ ___√____ _____

Alert Message: Avoid concomitant use of moderate CYP3A4 inhibitors or P-gp inhibitors with the CYP3A4 substrate Venclexta (venetoclax). Consider alternative treatment options. If a moderate CYP3A4 or P-gp inhibitor must be used, reduce the venetoclax dose by 50% and monitor the patient closely for signs of venetoclax toxicities. Resume the venetoclax dose that was used prior to initiating the CYP3A4 inhibitor 2 to 3 days after discontinuation of the inhibitor.

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

Util A	Util B		Util C
Venetoclax	Erythromycin	Cyclosporine	
	Ciprofloxacin	Felodipine	
	Diltiazem	Quinidine	
	Dronedarone	Ranolazine	
	Fluconazole	Ticagrelor	
	Verapamil	Amiodarone	
	Aprepitant	Azithromycin	
	Cimetidine	Captopril	
	Crizotinib	Carvedilol	
	Imatinib		

References:
Venclexta Prescribing Information, April 2016, AbbVie Inc.
Clinical Pharmacology, 2017 Elsevier/Gold Standard.

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

5. Venetoclax / P-gp Substrates w/ Narrow Therapeutic Indexes ___√___ _____ _____

Alert Message: Avoid concomitant use of a drug that is a P-gp substrate that has a narrow therapeutic index with the P-gp inhibitor Venclexta (venetoclax). If the concurrent use is warranted, the P-gp substrate should be taken at least 6 hours before venetoclax.

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

Util A	Util B	Util C
Venetoclax	Digoxin	
	Everolimus	
	Sirolimus	
	Tacrolimus	

References:
Venclexta Prescribing Information, April 2016, AbbVie Inc.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

6. Venetoclax / Therapeutic Appropriateness – Pediatric Patients ___√___ _____ _____

Alert Message: Safety and effectiveness of Venclexta (venetoclax) have not been established in pediatric patients.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Venetoclax		

Age Range: 0 – 17 yoa

References:
Venclexta Prescribing Information, April 2016, AbbVie Inc.
Clinical Pharmacology, 2017 Elsevier/Gold Standard.

7. Venetoclax / Therapeutic Appropriateness ____√____ _____ _____

Alert Message: Based on its mechanism of action and findings in animals, Venclexta (venetoclax) may cause fetal harm when administered to a pregnant woman. Females of reproductive potential should undergo pregnancy testing before initiation of venetoclax and should be advised to use effective contraception during treatment with venetoclax and for at least 30 days after the last dose.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Venetoclax		Oral Contraceptives
		Injectable Contraceptives
		Transdermal Contraceptives
		Implantable Contraceptives

Gender: Female
Age Range: 11 – 50 yoa

References:
Venclexta Prescribing Information, April 2016, AbbVie Inc.
Clinical Pharmacology, 2017 Elsevier/Gold Standard.

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

8. Idelalisib / Overutilization ___√___ _____ _____

Alert Message: The manufacturer's recommended maximum daily dose of Zydelig (idelalisib) is 150 mg twice daily.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Idelalisib		

Max Dose: 300 mg/day

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Zydelig Prescribing Information, September 2016. Gilead Sciences.

9. Idelalisib / Hepatic Impairment ___√____ _____ _____

Alert Message: Fatal and/or serious hepatotoxicity occurred in 18% of patients treated with Zydelig (idelalisib) monotherapy and 11% of patients treated with idelalisib in combination trials. Monitor ALT and AST in all patients receiving idelalisib every 2 weeks for the first 3 months of treatment, every 4 weeks for the next 3 months, then every 1 to 3 months thereafter. Withhold idelalisib if the ALT and AST is greater than 5 times the upper limit of normal, and continue to monitor AST, ALT, and total bilirubin weekly until the abnormality is resolved.

Conflict Code: MC – Drug (Actual) Disease Precaution/Warning (Black Box Warning)
Drugs/Diseases

Util A	Util B	Util C
Idelalisib	Hepatic Impairment	

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Zydelig Prescribing Information, September 2016. Gilead Sciences.

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

10. Idelalisib / Diarrhea & Colitis ___√___ _____ _____

Alert Message: Fatal and/or severe diarrhea or colitis occurred in 14% of patients treated with Zydelig (idelalisib) monotherapy and 19% of patients treated with idelalisib in combination trials. Diarrhea can occur at any time during idelalisib treatment. In case of severe diarrhea or colitis interrupt idelalisib therapy until problem is resolved then reinitiate therapy at a reduced dose of 100 mg twice a day. Discontinue idelalisib permanently in patients with life-threatening diarrhea.

Conflict Code: MC – Drug (Actual) Disease Precaution/Warning (Black Box Warning) Drugs/Diseases

Util A	Util B	Util C
Idelalisib	Diarrhea	
	Colitis	

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Zydelig Prescribing Information, September 2016. Gilead Sciences.

11. Idelalisib / Pneumonitis ___√___ _____ _____

Alert Message: Fatal and/or serious pneumonitis occurred in 4% of patients treated with Zydelig (idelalisib) in clinical trials. Monitor patient for pulmonary symptoms and bilateral interstitial infiltrates. If pneumonitis is suspected, interrupt idelalisib until etiology of pulmonary symptoms has been determined. Patients with pneumonitis thought to be caused by idelalisib have been treated with discontinuation of idelalisib and administration of corticosteroids.

Conflict Code: MC – Drug (Actual) Disease Precaution/Warning (Black Box Warning) Drugs/Diseases

Util A	Util B	Util C
Idelalisib	Pneumonitis	

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Zydelig Prescribing Information, September 2016. Gilead Sciences.

12. Idelalisib / GI Perforation ___√___ _____ _____

Alert Message: Fatal and/or serious intestinal perforation can occur in patients receiving Zydelig (idelalisib). At the time of perforation, some patients had moderate to severe diarrhea. Advise patients to promptly report any new or worsening abdominal pain, chills, fever, nausea, or vomiting. Discontinue idelalisib permanently in patients who experience intestinal perforation.

Conflict Code: MC – Drug (Actual) Disease Precaution/Warning (Black Box Warning) Drugs/Diseases

Util A	Util B	Util C
Idelalisib	GI Perforation	

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Zydelig Prescribing Information, September 2016. Gilead Sciences.

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

13. Idelalisib / Neutropenia ___√___ _____ _____

Alert Message: Treatment-emergent Grade 3 or 4 neutropenia occurred in 25% of patients treated with Zydelig (idelalisib) monotherapy and 46% of patients treated with idelalisib in combination trials. Monitor blood counts at least every 2 weeks for the first 6 months of therapy, and at least weekly in patients while neutrophil counts are less than 1.0 Gi/L.

Conflict Code: MC – Drug (Actual) Disease Precaution/Warning
Drugs/Diseases

Util A	Util B	Util C
Idelalisib	Neutropenia	

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Zydelig Prescribing Information, September 2016. Gilead Sciences.

14. Idelalisib / Therapeutic Appropriateness ____√____ _____ _____

Alert Message: Based on findings in animals, Zydelig (idelalisib) may cause fetal harm when administered to a pregnant woman. If the drug is used during pregnancy, or if the patient becomes pregnant while taking the drugs, apprise the patient of the potential hazard to the fetus. Advise females of reproductive potential to avoid becoming pregnant while taking idelalisib and for 1 month after the last dose of idelalisib.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Idelalisib		

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Zydelig Prescribing Information, September 2016. Gilead Sciences.

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

15. Idelalisib / Strong CYP3A4 Inducers ___√____ _____ _____

Alert Message: The concurrent use of Zydelig (idelalisib) with a strong CYP3A4 inducer should be avoided. Idelalisib is a CYP3A4 substrate and co-administration with a strong CYP3A4 inducer may result in a significant decrease in idelalisib exposure and loss of therapeutic effect.

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

Util A	Util B	Util C
Idelalisib	Phenytoin	
	Phenobarbital	
	Primidone	
	Carbamazepine	
	Rifampin	
	Rifapentine	
	Rifabutin	

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Zydelig Prescribing Information, September 2016. Gilead Sciences.

16. Idelalisib / Strong CYP3A4 Inhibitors _____ ___√____ _____

Alert Message: The concurrent use of Zydelig (idelalisib), a CYP3A4 substrate, with a strong CYP3A4 inhibitor may result in increased idelalisib exposure and should be avoided. If concomitant use is warranted, monitor the patient for signs of idelalisib toxicity. Follow manufacturer recommended dose modifications for adverse reactions.

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

Util A	Util B		Util C
Idelalisib	Ketoconazole	Clarithromycin	
	Itraconazole	Atazanavir	
	Nefazodone	Saquinavir	
	Telithromycin	Ritonavir	
	Indinavir	Nelfinavir	
	Voriconazole	Boceprevir	
	Posaconazole	Cobicistat	

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Zydelig Prescribing Information, September 2016. Gilead Sciences.

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

17. Cobicistat / Irinotecan / Atazanavir __✓_____ _____ _____

Alert Message: A review of recent pharmacy claims shows that the patient is receiving concurrent therapy with Tybost (cobicistat) and a drug that is contraindicated. Co-administration of cobicistat and the identified agent may result in serious and/or life-threatening events.

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

Util A	Util B	Util C **(Include)**
Cobicistat	Irinotecan	Atazanavir

References:
Tybost Prescribing Information, June 2016, Gilead Sciences, Inc.
Clinical Pharmacology, 2017, Elsevier/Gold Standard.

18. Cobicistat / Nevirapine / Atazanavir ___✓_____ _____ _____

Alert Message: A review of recent pharmacy claims shows that the patient is receiving concurrent therapy with Tybost (cobicistat) and a drug that is contraindicated. Co-administration of cobicistat and the identified agent may result in serious and/or life-threatening events.

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

Util A	Util B	Util C **(Include)**
Cobicistat	Nevirapine	Atazanavir

References:
Tybost Prescribing Information, June 2016, Gilead Sciences, Inc.
Clinical Pharmacology, 2017, Elsevier/Gold Standard.

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

19. Cobicistat / Indinavir / Atazanavir __√____ _____ _____

Alert Message: A review of recent pharmacy claims shows that the patient is receiving concurrent therapy with Tybost (cobicistat) and a drug that is contraindicated. Co-administration of cobicistat and the identified agent may result in serious and/or life-threatening events.

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

Util A	Util B	Util C **(Include)**
Cobicistat	Indinavir	Atazanavir

References:
Tybost Prescribing Information, June 2016, Gilead Sciences, Inc.
Clinical Pharmacology, 2017, Elsevier/Gold Standard.

20. Elvitegravir / Other Antiretrovirals ___√____ _____ _____

Alert Message: The patient appears to be receiving an INSTI-based ART regimen that is not recommended in treatment-naive patients. The recommended INSTI-based regimens for non-pregnant, adolescent and adults involving elvitegravir include: elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine or elvitegravir/cobicistat/tenofovir disoproxil/emtricitabine.

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

Util A	Util B		Util C
Elvitegravir	Maraviroc	Atazanavir	
	Enfuvirtide	Darunavir	
	Delavirdine	Fosamprenavir	
	Efavirenz	Indinavir	
	Nevirapine	Nelfinavir	
	Rilpivirine	Ritonavir	
	Abacavir	Saquinavir	
	Didanosine	Tipranavir	
	Lamivudine		
	Stavudine		
	Zidovudine		

Age Range: ≥ 12 yoa

References:
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents. Department of Health and Human Services. July 14, 2016.
Available at: http://www.aidsinfo.nih.gov/contentfiles/adultand adolescentgl.pdf.
Panel on Treatment of HIV-infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-Infected Women for Maternal Health and Interventions to Reduce Perinatal\HIV Transmission in the United States. March 28, 2014.
Available at: http://aidsinfor.nih.gov/contentfiels/PerinatalGL.pdf
Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. March 1, 2016.
Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/pediatricguidelines.pdf

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

21. Dabigatran / Lovastatin & Simvastatin ___√___ _____ _____

Alert Message: Concurrent use of Pradaxa (dabigatran), a P-gp substrate, with simvastatin or lovastatin, strong P-gp inhibitors, may result in increased dabigatran systemic exposure and risk of hemorrhage. Separating the timing of administration of the agents by at least 2 hours may mitigate this interaction. Another consideration is switching the patient to a statin that is not a strong P-gp inhibitor (e.g., atorvastatin, pravastatin, and rosuvastatin) to avoid the increased risk of hemorrhage.

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

Util A	Util B	Util C
Dabigatran	Lovastatin Simvastatin	

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Antoniou T, Macdonald EM, Yao Z, et al. Association Between Statin Use and Ischemic Stroke or Major Hemorrhage in Patients Taking Dabigatran for Atrial Fibrillation. *CMAJ* 2016; DOI:10.1503/cmaj.160303
Pradaxa Prescribing Information, Nov. 2015, Boehringer Ingelheim Pharmaceuticals, Inc.

22. Ivacaftor / Overutilization (≥ 6 yoa) ___√___ _____ _____

Alert Message: The recommended daily dose of Kalydeco (ivacaftor) for patients 6 years of age and older is 150 mg taken every 12 hours (300 mg total daily dose).

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Ivacaftor		Hepatic Impairment

Age Range: ≥ 6 yoa
Max Dose: 300 mg/day

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Kalydeco Prescribing Information, Feb. 2017, Vertex Pharmaceuticals Inc.

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

23. Ivacaftor / Overutilization- (2 – 5 yoa) ___√___ _____ _____

Alert Message: The recommended daily dose of Kalydeco (ivacaftor) for patients ages 2 to less than 6 years of age is weight-based. Patients weighing less than 14 kg should receive one 50 mg ivacaftor packet every 12 hours (100 mg total daily dose). Patients weighing 14 kg or more should receive one 75 mg ivacaftor packet every 12 hours (150 mg total daily dose).

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Ivacaftor		Hepatic Impairment

Age Range: 2 - 5 yoa
Max Dose: 150 mg/day

References:
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Kalydeco Prescribing Information, Feb. 2017, Vertex Pharmaceuticals Inc.

24. Ivacaftor / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: The safety and efficacy of Kalydeco (ivacaftor) in patients with cystic fibrosis younger than 2 years of age have not been studied and use is not recommended in this patient population.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Ivacaftor		

Age Range: 0 - 1 yoa

References:
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Kalydeco Prescribing Information, Feb. 2017, Vertex Pharmaceuticals Inc.

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

25. Ivacaftor / Overutilization – Hepatic Impairment (≥ 6 yoa) ___√___ _____ _____

Alert Message: Kalydeco (ivacaftor) may be over-utilized. The daily dose of ivacaftor should be reduced to one tablet or one packet once daily for patients with moderate hepatic impairment. Ivacaftor should be used with caution in patients with severe hepatic impairment at a dose of one tablet or one packet once daily or less frequently. No dose adjustment is necessary in mild hepatic impairment.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Ivacaftor		Hepatic Impairment

Age Range: ≥ 6 yoa
Max Dose: 150 mg/day

References:
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Kalydeco Prescribing Information, Feb. 2017, Vertex Pharmaceuticals Inc.

26. Ivacaftor / Overutilization – Hepatic Impairment (2 - 5 yoa) ___√___ _____ _____

Alert Message: Kalydeco (ivacaftor) may be over-utilized. The daily dose of ivacaftor for patients 2 to less than 6 years of age with moderate hepatic impairment is as follows: one 50 mg packet once daily for patients weighing less than 14 kg or one 75 mg packet once daily for patients weighing 14 kg or more. For patients with severe hepatic impairment use the same dose reduction according to weight once daily or less frequently than once daily. No dose adjustment is necessary in mild hepatic impairment.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Ivacaftor		Hepatic Impairment

Age Range: 2 - 5 yoa
Max Dose: 75 mg/day

References:
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Kalydeco Prescribing Information, Feb. 2017, Vertex Pharmaceuticals Inc.

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

27. Ivacaftor / Strong CYP3A4 Inducers ___√____ _____ _____

Alert Message: Concurrent use of Kalydeco (ivacaftor) with strong CYP3A4 inducers is not recommended. Ivacaftor is a sensitive CYP3A4 substrate and concomitant administration with a strong inducer may substantially decrease ivacaftor exposure, reducing its therapeutic effectiveness.

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

Util A	Util B		Util C
Ivacaftor	Phenytoin	Rifabutin	
	Phenobarbital	Rifapentine	
	Primidone	Rifampin	
	Carbamazepine		

References:
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Kalydeco Prescribing Information, Feb. 2017, Vertex Pharmaceuticals Inc.

28. Ivacaftor / Strong CYP3A4 Inhibitors (≥ 6 yoa) _____ ___√_____ _____

Alert Message: Concurrent use of Kalydeco (ivacaftor), a sensitive CYP3A4 substrate, with a strong CYP3A4 inhibitor may result in significantly elevated ivacaftor exposure. In patients 6 years and older it is recommended that the daily dose of ivacaftor be reduced to one 150 mg tablet twice a week during concomitant therapy with a strong CYP3A4 inhibitor.

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

Util A	Util B	Util C **(Include)**	
Ivacaftor		Nefazodone	Saquinavir
		Clarithromycin	Ritonavir
		Telithromycin	Nelfinavir
		Ketoconazole	Indinavir
		Itraconazole	Cobicistat
		Voriconazole	Boceprevir
		Posaconazole	Idelalisib

Age Range: 6 – 999 yoa
Max Dose: 300 mg/week

References:
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Kalydeco Prescribing Information, Feb. 2017, Vertex Pharmaceuticals Inc.

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

29. Ivacaftor / Strong CYP3A4 Inhibitors (2 – 5 yoa) _____ ___√____ _____

Alert Message: Concurrent use of Kalydeco (ivacaftor), a sensitive CYP3A4 substrate, with a strong CYP3A4 inhibitor may result in significantly elevated ivacaftor exposure. In patients 2 to less than 6 years of age it is recommended that the daily dose of ivacaftor be reduced as follows: 2 to less than 6 years of age weighing < 14 kg reduce the dose to one 50 mg packet twice a week and for patients 2 to less than 6 years of age weighing 14 kg or more, reduce the dose to one 75 mg packet twice a week.

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

Util A	Util B	Util C **(Include)**	
Ivacaftor		Nefazodone	Saquinavir
		Clarithromycin	Ritonavir
		Telithromycin	Nelfinavir
		Ketoconazole	Indinavir
		Itraconazole	Cobicistat
		Voriconazole	Boceprevir
		Posaconazole	Idelalisib

Age Range: 2 - 5 yoa
Max Dose: 150 mg/week

References:
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Kalydeco Prescribing Information, Feb. 2017, Vertex Pharmaceuticals Inc.

30. Ivacaftor / Moderate CYP3A4 Inhibitors (≥ 6 yoa) ___√____ _____ _____

Alert Message: Concurrent use of Kalydeco (ivacaftor), a sensitive CYP3A4 substrate, with a moderate CYP3A4 inhibitor may result in elevated ivacaftor exposure. In patients 6 years and older it is recommended that the dose of ivacaftor be reduced to one 150 mg tablet once daily during concomitant therapy.

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

Util A	Util B	Util C **(Include)**	
Ivacaftor		Aprepitant	Erythromycin
		Cimetidine	Fluconazole
		Ciprofloxacin	Fluvoxamine
		Crizotinib	Imatinib
		Cyclosporine	Verapamil
		Diltiazem	Dronedarone

Age Range: ≥ 6 yoa
Max Dose: 150 mg/day

References:
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Kalydeco Prescribing Information, Feb. 2017, Vertex Pharmaceuticals Inc.

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

31. Ivacaftor / Moderate CYP3A4 Inhibitors (2 – 5 yoa) ___√___ _____ _____

Alert Message: Concurrent use of Kalydeco (ivacaftor), a sensitive CYP3A4 substrate, with a moderate CYP3A4 inhibitor may result in significantly elevated ivacaftor exposure. In patients 2 to less than 6 years of age it is recommended that the dose of ivacaftor be reduced as follows: one 50 mg packet once daily in patients weighing less than 14 kg and for patients weighing 14 kg or more, reduce dose to one 75 mg packet once daily.

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

Util A	Util B	Util C **(Include)**	
Ivacaftor		Aprepitant	Erythromycin
		Cimetidine	Fluconazole
		Ciprofloxacin	Fluvoxamine
		Crizotinib	Imatinib
		Cyclosporine	Verapamil
		Diltiazem	Dronedarone

Age Range: 2 - 5 yoa
Max Dose: 300 mg/week

References:
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Kalydeco Prescribing Information, Feb. 2017, Vertex Pharmaceuticals Inc.

32. Ivacaftor / Sensitive CYP3A4 or P-gp Substrate ___√___ _____ _____

Alert Message: Concurrent use of Kalydeco (ivacaftor), a CYP3A4 and P-gp inhibitor, with a sensitive CYP3A4 and/or P-gp substrate may result in increased substrate exposure which may potentiate or prolong the therapeutic effect and adverse events. Appropriate monitoring is recommended when co-administering these agents.

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

Util A	Util B	Util C
Ivacaftor	Cyclosporine	
	Digoxin	
	Tacrolimus	

References:
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Kalydeco Prescribing Information, Feb. 2017, Vertex Pharmaceuticals Inc.

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

33. Ivacaftor / Nonadherence ___√___ _____ _____

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

Conflict Code: LR - Nonadherence
Drugs/Diseases

Util A	Util B	Util C
Ivacaftor		

References:
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Eakin MN, Bilderback A, Boyle MP, Mogayzel PJ, Riekert KA. Longitudinal Association Between Medication Adherence and Lung Health in People with Cystic Fibrosis. Jrnl Cyst Fib. 2011;10(4):258-264.
Bishay LC, Sawicki. Strategies to Optimize Treatment Adherence in Adolescent Patients with Cystic Fibrosis. Adolesc
Health, Med & Ther. 2016 Oct 21;7:117-124.
Bishay LC, Sawicki GS., Strategies to Optimize Adherence in Adolescent Patients with Cystic Fibrosis. Adolesc Health, Med & Ther. 2016 Oct 21;7:117-124.

34. Lisdexamfetamine / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: The safety and effectiveness of Vyvanse (lisdexamfetamine) for the treatment of moderate to severe Binge Eating Disorder (BED) in patients less than 18 years of age have not been established.

Conflict Code: TA – therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C **(Negate)**
Lisdexamfetamine	Binge Eating Disorder	ADHD

Age Range: < 18 years of age

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Facts & Comparisons, 2017 Wolters Kluwer Health.

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

35. Evotaz / Overutilization ___√___ _____ _____

Alert Message: Evotaz (atazanavir/cobicistat) is not recommended for use in treatment-experienced patients with end-stage renal disease managed with hemodialysis.

Conflict Code: TA – therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Atazanavir/Cobicistat	CKD Stage 4 & 5 ESRD Hemodialysis	

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Evotaz Prescribing Information, Jan 2017, Bristol-Myers Squibb.

36. Olaparib / Overutilization ___√___ _____ _____

Alert Message: The manufacturer's recommended daily dose of Lynparza (olaparib) in patients with moderate renal impairment (CLcr 31 - 50 mL/min) is 300 mg (six 50 mg capsules) taken twice daily, for a total daily dose of 600 mg. No dosage adjustment is recommended in mild renal impairment (CLcr 51 - 80 mL/min). The pharmacokinetics of olaparib have not been evaluated in patients with severe renal impairment or end-stage renal disease (CLcr </= 30 mL/min).

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Olaparib		CKD 3, 4 & 5 ESRD

Max Dose: 600 mg/day

References:
Lynparza Prescribing Information, Dec. 2017, AstraZeneca.
Clinical Pharmacology, 2017 Elsevier/Gold Standard.

37. Terbinafine / Hepatic Impairment ___√___ _____ _____

Alert Message: Oral terbinafine is contraindicated in patients with chronic or active hepatic disease. Cases of liver failure, some leading to liver transplant or death, have occurred with the use of terbinafine in individuals with and without preexisting liver disease. Perform liver function test prior to initiation of therapy and periodically thereafter. Discontinue terbinafine if liver injury develops.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Terbinafine		Hepatic Impairment

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Facts & Comparisons, 2017 Wolters Kluwer Health.

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

38. Lurasidone / Overutilization Bipolar Depression __√_____ _____ _____

Alert Message: Latuda (lurasidone) may be over-utilized. The manufacturer's recommended maximum dose, for the treatment of bipolar depression in adults, is 120 mg once daily. Exceeding the recommended dose may increase the risk of adverse effects (e.g., akathisia, somnolence, and dystonia).

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Lurasidone		CKD 3, 4 & 5
		Hepatic Impairment
		Mod CYP3A4 Inhibitors
		Schizophrenia

Age Range: ≥ 18 years of age
Max Dose: 120 mg/day

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Facts & Comparisons, 2017 Wolters Kluwer Health.
Latuda Prescribing Information, Feb. 2017, Sunovion Pharma, Inc.

39. Lurasidone / Overutilization (13 – 17 yoa) ___√_____ _____ _____

Alert Message: Latuda (lurasidone) may be over-utilized. The manufacturer's recommended maximum dose, for the treatment of schizophrenia in adolescents 13 to 17 years of age, is 80 mg once daily. Exceeding the recommended dose may increase the risk of adverse effects (e.g., akathisia, somnolence, and dystonia).

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Lurasidone		

Age Range: 13 - 17 years of age
Max Dose: 80 mg/day

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Facts & Comparisons, 2017 Wolters Kluwer Health.
Latuda Prescribing Information, Feb. 2017, Sunovion Pharma, Inc.

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

40. Hydroxychloroquine / Digoxin ___√___ _____ _____

Alert Message: Concurrent use of hydroxychloroquine with digoxin may result in increased serum digoxin levels. Serum digoxin levels should be closely monitored in patients receiving combination therapy.

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

Util A	Util B	Util C
Hydroxychloroquine	Digoxin	

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Plaquenil Prescribing Information, Jan. 2017, Concordia Pharmaceuticals Inc.

41. Hydroxychloroquine / Antidiabetic Medications ___√___ _____ _____

Alert Message: Hydroxychloroquine can cause hypoglycemia and concurrent use with insulin or antidiabetic agents may enhance the effects of the hypoglycemic therapy. A decrease in the doses of insulin or antidiabetic agent may be required.

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

Util A	Util B	Util C
Hydroxychloroquine	Antidiabetic Agents	

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Plaquenil Prescribing Information, Jan. 2017, Concordia Pharmaceuticals Inc.

42. Metronidazole / Disulfiram ___√___ _____ _____

Alert Message: The use of disulfiram with or within 2 weeks of metronidazole-containing agent is contraindicated due to the risk of CNS toxicity (e.g., acute psychosis and confusion).

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

Util A	Util B	Util C
Metronidazole	Disulfiram	

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Facts & Comparisons, 2017 Wolters Kluwer Health.

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

43. Pylera / Severe Renal Disease ___√___ _____ _____

Alert Message: The use of Pylera (bismuth/metronidazole/tetracycline) is contraindicated in patients with severe renal impairment. The antianabolic action of the tetracycline component of the combination product may cause an increase in blood urea nitrogen (BUN). In patients with significant impaired renal function, higher serum concentrations of tetracycline may lead to azotemia, hyperphosphatemia, and acidosis.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C (Include)
Pylera		CKD Stage 4 & 5

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Pylera Prescribing Information, Jan. 2017, Apralis Pharm US, Inc.

44. Repaglinide / Cyclosporine ___√___ _____ _____

Alert Message: Concurrent use of repaglinide with cyclosporine may significantly increase repaglinide exposure. The repaglinide total daily dose should not exceed 6 mg if these agents are co-administered. Repaglinide is a substrate of enzyme CYP3A4 and OATP1B1 transport protein and cyclosporine inhibits CYP3A4 and OATP1B1.

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

Util A	Util B	Util C **(Include)**
Repaglinide		Cyclosporine

Max Dose: 6 mg

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Prandin Prescribing Information, Feb. 2017, Novo Nordisk.

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

45. Repaglinide / Clopidogrel ___√____ _____ _____

Alert Message: Concurrent use of repaglinide with clopidogrel may significantly increase repaglinide exposure and should be avoided. If co-administration cannot be avoided the total daily dose of repaglinide should not exceed 4 mg. Repaglinide is a substrate of enzyme CYP2C8 and clopidogrel is a strong CYP2C8 inhibitor.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Repaglinide		Clopidogrel

Max Dose: 4mg/day

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Prandin Prescribing Information, Feb. 2017, Novo Nordisk.
Micromedex Solutions, DrugDex Drug Evaluations, 2017 Truven Health Analytics.

46. Repaglinide - All / CYP3A4 & CYP2C8 Inhibitors _____ ____√____ _____

Alert Message: Concurrent use of a repaglinide-containing agent with a strong CYP3A4 or CYP2C8 inhibitor may significantly increase repaglinide exposure. Repaglinide is a substrate of CYP3A4 and CYP2C8. Dosage reduction of the repaglinide-containing agent may be required as well as increased frequency of glucose monitoring.

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

Util A	Util B			Util C
Repaglinide - all	Montelukast	Saquinavir	Voriconazole	
	Phenelzine	Ritonavir	Posaconazole	
	Nefazodone	Indinavir	Itraconazole	
	Clarithromycin	Nelfinavir	Boceprevir	
	Telithromycin	Ketoconazole	Cobicistat	

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Facts & Comparisons, 2017 Wolters Kluwer Health.

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

47. Osimertinib / BCRP Substrates ___√___ _____ _____

Alert Message: Concurrent use of the BCRP inhibitor, Tagrisso (osimertinib), with a BCRP substrate may result in increased exposure to the BCRP substrate and risk of exposure-related toxicity. Monitor patient for adverse reactions associated with the BCRP substrate.

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

Util A	Util B	Util C
Osimertinib	Rosuvastatin	
	Sulfasalazine	
	Topotecan	
	Tenofovir	
	Prazosin	
	Dantrolene	

References:
Clinical Pharmacology, 2017 Elsevier/Gold Standard.
Tagrisso Prescribing Information, Sept. 2016, AstraZeneca.

48. Tiotropium / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: The safety and effectiveness of Spiriva Handihaler (tiotropium inhalation powder) have not been established in children.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Tiotropium		

Age Range: 0-17 yoa

References:
Spiriva Prescribing Information, Dec. 2015, Boehringer Ingelheim Pharmaceuticals, Inc.
Clinical Pharmacology, 2017 Elsevier/Gold Standard.

49. Tiotropium / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: The safety and effectiveness of Spiriva Respimat (tiotropium inhalation spray) for the treatment of asthma in children less than 6 years of age have not been established.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Tiotropium		

Age Range: 0-5 yoa

References:
Spiriva Respimat Prescribing Information, Feb. 2017, Boehringer Ingelheim Pharmaceuticals, Inc.
Clinical Pharmacology, 2017 Elsevier/Gold Standard.

Stephanie McGee Azar, Commissioner — (X) Approve ( ) Deny — 1-12-18 Date

R Moon MD
Robert Moon, M.D., Deputy Commissioner and Medical Director — (X) Approve ( ) Deny — 1-5-18 Date

Kathy Hall
Kathy Hall, Deputy Commissioner — (X) Approve ( ) Deny — 1/3/18 Date