

## **Alabama Medicaid DUR Board Meeting Minutes January 28, 2015**

**Members Present:** Denyse Thornley-Brown, Kelli Littlejohn, Bernie Olin, Frank Pettyjohn, Richard Glaze, Marilyn Bulloch, P.J. Hughes, Dan McConaghy

**Also Present:** Tiffany Minnifield, Clemice Hurst, Lori Thomas, Heather Vega, Allison Scott

**Present via Conference Call:** Kristian Testerman, Nichelle Wilson

**Members Absent:** Robert Moon, Donald Kern, Jared Johnson, Paula Thompson, and Sandra Parker

**Call to Order:** The DUR meeting was called to order by D. Thornley-Brown at approximately 1:03 p.m.

**Review and Adoption of Minutes:** The minutes of the October 22, 2014 meeting were presented and reviewed. B. Olin made a motion to approve the minutes as presented and F. Pettyjohn seconded the motion. The motion was approved unanimously.

**Prior Authorization and Overrides Update:** L. Thomas began the Prior Authorization and Overrides Update with the Monthly Manual Prior Authorizations and Overrides Report for the month of July 2014. She reported 9,151 total PA and override requests. She then reported 21,671 electronic PA requests for the same time frame. From the Prior Authorization and Override Response Time Ratio report for July 2014, L. Thomas reported that approximately 35% of all manual PAs and overrides were responded to in less than two hours, about 75-76% in less than four hours, and 98% in less than eight hours. L. Thomas reminded the Board Members that 75% of PAs and overrides must be completed in less than 8 hours to meet contractual requirements. For the month of August 2014, L. Thomas reported 8,574 manual requests and 20,566 electronic PA requests. She reported that 27% of manual PAs and 25% of overrides were responded to in less than two hours, approximately 66% in less than four hours, and 98% in less than eight hours. For the month of September 2014, L. Thomas reported 8,940 manual requests and 20,902 electronic PA requests for the same time frame. B. Olin inquired about the high denial rate for electronic PAs. L. Thomas explained that all criteria must be met through pharmacy and medical claims to meet the criteria and result in an approval. For September 2014, L. Thomas reported that 33% of PAs and 26% of overrides were completed in less than two hours and 65% of PAs and 59% of overrides were completed in less than four hours. Approximately 94% of PAs and 96% of overrides were completed in less than eight hours.

**Program Summary Review:** L. Thomas briefly reviewed the Alabama Medicaid Program Summary. She reported 3,526,034 total prescriptions, 215,241 average recipients per month using pharmacy benefits, and an average paid per prescription of \$84.17 for the second and third quarter of 2014.

**Cost Management Analysis:** L. Thomas reported an average cost per claim of \$83.48 for September 2014. L. Thomas explained the maintenance supply to the new members. K. Littlejohn described how the average cost per claim increased while overall spending flatlined. From the 3<sup>rd</sup> Quarter 2014 Drug Analysis, L. Thomas reported 79.09% generic utilization, 11.17% brand single-source, 6.08% brand multi-source (those requests which required a DAW override) and 3.66% OTC and "other". L. Thomas mentioned that OTC products have not been covered by Alabama Medicaid since October 2013. From the Top 25 Drugs Based on Number of Claims from 07/01/2014– 09/30/2014, L. Thomas reported the top five drugs: hydrocodone-acetaminophen, amoxicillin, ProAir HFA, cetirizine, and montelukast sodium. She then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 007/01/2014-09/30/2014: Abilify®, Vyvanse®, Invega Sustenna®, Sovaldi®, and Adderall XR®. L. Thomas pointed out that 151 recipients used Sovaldi during 2014, which represented 427 Sovaldi claims. 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, Hemostatics, Anticonvulsants, and Corticosteroids (Respiratory Tract). L. Thomas reminded the Board that this list was identical to what was last reported.

**RDUR Intervention Report:** L. Thomas presented the RDUR Activity Report for July 2014. She reported 674 profiles reviewed and 588 letters sent with 136 responses received. She reported 77 of 110 physicians indicated that they found the RDUR letters “useful” or “extremely useful”. The criteria for the cycle of intervention letters was the underutilization of lipid-lowering agents. For August 2014, there were 690 profiles reviewed and 608 letters sent. There were 117 responses received with 61 out of 95 physicians indicating that they found the RDUR letters “useful or extremely useful”. The criteria for the cycle of intervention letters included drug-drug interaction (potassium-sparing diuretics or ACE inhibitors with potassium supplements); drug-disease interaction (beta-blockers and Peripheral Vascular Disease; potassium-sparing diuretics in renal failure); and appropriate use (concurrent use of buprenorphine and pure opiate agonist). At this time, L. Thomas explained the Lock In Program to the new members. P. Hughes asked if patients could be locked in based on a particular disease state, such as diabetes, to allow for standard of care. K. Littlejohn responded that one of the roles of the RCOs will be to standardize care. M. Bulloch asked if children and adults could be locked in. K. Littlejohn explained that both children and adults could be locked in. For September 2014, there were 675 profiles reviewed and 694 letters sent. There were 146 responses received with 72 out of 102 physicians indicating that they found the RDUR letters “useful or extremely useful”. The criteria for the cycle of intervention letters included drug-disease interaction (thiazides may lead to glucose intolerance and hyperglycemia; oxybutynin use in hepatic or renal impairment; oxybutynin use in patients with GERD or taking drugs that may cause esophagitis); and appropriate use (concurrent use of buprenorphine and pure opiate agonist).

**Proposed Criteria:** L. Thomas presented the proposed set of 46 criteria to the Board. T. Minnifield instructed the Board members to mark their ballots. Of the 46 criteria, results from the criteria vote returned 45 approved and 1 approved as amended.

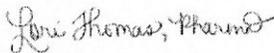
**Medicaid Update:** T. Minnifield began the Medicaid Update by reminding the Board members that all updated Medicaid information discussed is available online, as well as any new Medicaid ALERTs. T. Minnifield provided the upcoming DUR meeting dates.

**P & T Committee Update:** C. Hurst began the P & T Update by informing the Board that the last meeting was held on November 12, 2014, and covered the remaining Anti-Infectives. The next P & T meeting is scheduled for February 11, 2015, at 9am and will cover First-Generation Antihistamines; Estrogens; and Diabetic agents.

**New Business:** K. Littlejohn informed the Board that the State Pharmacy Association announced in December that pharmacy was carved-out of the RCOs and referred to the APA release. T. Minnifield notified the Board that the next DUR meeting will be held on April 22, 2015. F. Pettyjohn made a motion to adjourn the meeting. The motion was seconded by P. Hughes. A voice vote to adjourn was unanimous. The meeting was adjourned at 2:20 p.m.

**Next Meeting Date:** The next DUR Board meeting will be held on April 22, 2015.

Respectfully submitted,



Lori Thomas, PharmD



**4. Tasimelteon / Tobacco Use Disorder**

\_\_\_\_\_ ✓ \_\_\_\_\_

Alert Message: The diagnostic history suggests that the patient may be a smoker. Hetlioz (tasimelteon) exposure is decreased by 40% in smokers compared to non-smokers due to induction, by tobacco smoke, of tasimelteon CYP1A2-mediated metabolism. Patients should be advised of the potential for reduced efficacy of tasimelteon during tobacco smoking.

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

Util A                      Util B                      Util C  
Tasimelteon              Tobacco Use Disorder

References:  
Hetlioz Prescribing Information, Jan. 2014, Vanda Pharmaceuticals Inc.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**5. Tasimelteon / Therapeutic Appropriateness**

\_\_\_\_\_ ✓ \_\_\_\_\_

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

Conflict Code: TA - Therapeutic Appropriateness  
Drugs/Diseases

Util A                      Util B                      Util C  
Tasimelteon

Age Range: 0 -18 yoa

References:  
Hetlioz Prescribing Information, Jan. 2014, Vanda Pharmaceuticals Inc.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**6. Tasimelteon / Therapeutic Appropriateness**

\_\_\_\_\_ ✓ \_\_\_\_\_

Alert Message: Caution should be exercised when prescribing Hetlioz (tasimelteon) in elderly patients (> 65 years of age) as they may experience an increased risk of adverse effects. In clinical studies tasimelteon exposure increased by approximately two-fold in elderly patients compared with non-elderly adults.

Conflict Code: TA - Therapeutic Appropriateness  
Drugs/Diseases

Util A                      Util B                      Util C  
Tasimelteon

Age Range: ≥ 66 yoa

References:  
Hetlioz Prescribing Information, Jan. 2014, Vanda Pharmaceuticals Inc.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**7. Dolutegravir / Non-recommended NRTI's**

\_\_\_\_\_✓\_\_\_\_\_

Alert Message: The NRTIs didanosine, stavudine, and zidovudine are not recommended as part of an initial ART regimen for ART treatment-naïve patients, primarily because of their toxicities. The fixed dose combination of tenofovir/emtricitabine is recommended for most initial ART regimens. Abacavir/emtricitabine is a recommended dual NRTI option when combined with dolutegravir in patient who are HLA-B\*5701 negative or when combined with efavirenz in patients with pre-treatment HIV RNA level < 100,000 copies/ml.

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Didanosine	Efavirenz	
Stavudine	Atazanavir	
Zidovudine	Darunavir	
	Dolutegravir	

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. May 1, 2014. Available at: <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>.

**8. Oxycodone-All / CYP3A4 Inducers**

\_\_\_\_\_✓\_\_\_\_\_

Alert Message: Concomitant use of an oxycodone-containing agent with a CYP3A4 inducer may lead to increased oxycodone clearance resulting in lack of efficacy or possibly development of an abstinence syndrome in a patient who had developed physical dependence to oxycodone. Caution is advised when initiating oxycodone in patients currently taking or discontinuing CYP3A4 inducers. Frequently evaluate the patient and consider oxycodone dose adjustments until stable drug effects are achieved.

Conflict Code: DD - Therapeutic Duplication of Long-Acting Opioids

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Oxycodone- All	Carbamazepine	
	Phenytoin	
	Phenobarbital	
	Primidone	
	Rifampin	
	Rifabutin	
	Rifapentine	
	Efavirenz	
	Etravirine	
	Bosentan	

References:

Clinical Pharmacology, 2014 Elsevier/Gold Standard.  
Facts & Comparisons, 2014 Updates, Wolters Kluwer Health.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**9. Vorapaxar / Overutilization**

\_\_\_\_\_✓\_\_\_\_\_

Alert Message: The manufacturer's recommended dose of Zontivity (vorapaxar) is one 2.08 mg tablet once daily.

Conflict Code: ER - Overutilization

Drugs/Diseases

Util A

Util B

Util C

Vorapaxar

Max Dose: 2.08 mg /day

References:

Zontivity Prescribing Information, May 2014, Merck Sharp & Dohme Corp.

Clinical Pharmacology, 2014 Elsevier/Gold Standard.

Facts & Comparisons, 2014 Updates, Wolters Kluwer Health.

**10. Vorapaxar / Therapeutic Appropriateness (Black Box Warning)**

\_\_\_\_\_✓\_\_\_\_\_

Alert Message: Zontivity (vorapaxar) use is contraindicated in patients with a history of stroke, transient ischemic attack (TIA), intracranial hemorrhage (ICH), or active pathological bleeding. Vorapaxar is an antiplatelet agent which increases the risk of bleeding including ICH and fatal bleeding. Discontinue vorapaxar in patients who experience a stroke, TIA, or ICH.

Conflict Code: TA – Therapeutic Appropriateness (Black Box – Contraindication)

Drugs/Diseases

Util A

Util B

Util C (Include)

Vorapaxar

Stroke

Transient Ischemic Attack

Intracranial Hemorrhage

Peptic Ulcer Bleeding

References:

Zontivity Prescribing Information, May 2014, Merck Sharp & Dohme Corp.

Clinical Pharmacology, 2014 Elsevier/Gold Standard.

Facts & Comparisons, 2014 Updates, Wolters Kluwer Health.

**11. Vorapaxar / Other Antiplatelet Agents Negating**

\_\_\_\_\_✓\_\_\_\_\_

Alert Message: A review of recent pharmacy claims for the patient does not show the use of Zontivity (vorapaxar) with aspirin and/or clopidogrel according to their indications and standard of care. There is no experience with the use of vorapaxar alone as the only administered antiplatelet agent.

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C (Negating)

Vorapaxar

Aspirin

Clopidogrel

References:

Zontivity Prescribing Information, May 2014, Merck Sharp & Dohme Corp.

Clinical Pharmacology, 2014 Elsevier/Gold Standard.

Facts & Comparisons, 2014 Updates, Wolters Kluwer Health.

**12. Vorapaxar / Other Antiplatelet Agents Negating** \_\_\_\_\_√\_\_\_\_\_

Alert Message: The concurrent use of Zontivity (vorapaxar) with other antiplatelet drugs may result in a potential additive effect for bleeding. Vorapaxar is indicated for combination therapy with aspirin and/or clopidogrel but there is limited clinical experience with the use of vorapaxar with other antiplatelet drugs.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vorapaxar	Dipyridamole Ticlopidine Cilostazol Prasugrel Ticagrelor Anagrelide	

References:

Zontivity Prescribing Information, May 2014, Merck Sharp & Dohme Corp.

Clinical Pharmacology, 2014 Elsevier/Gold Standard.

Facts & Comparisons, 2014 Updates, Wolters Kluwer Health.

**13. Vorapaxar / Anticoagulants** \_\_\_\_\_√\_\_\_\_\_

Alert Message: The concurrent use of Zontivity (vorapaxar) with warfarin or other anticoagulants should be avoided. Vorapaxar is a platelet aggregation inhibitor and concomitant use with an anticoagulant may have an additive effect, increasing the risk of bleeding.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vorapaxar	Warfarin Dabigatran Apixaban Rivaroxaban Enoxaparin	

References:

Zontivity Prescribing Information, May 2014, Merck Sharp & Dohme Corp.

Clinical Pharmacology, 2014 Elsevier/Gold Standard.

Facts & Comparisons, 2014 Updates, Wolters Kluwer Health.

**14. Vorapaxar / Agents Affecting Hemostasis** \_\_\_\_\_√\_\_\_\_\_

Alert Message: Caution should be exercised when Zontivity (vorapaxar) is prescribed with drugs that affect hemostasis (e.g., chronic NSAIDs, SSRIs, and SNRIs) as concomitant use of these agents may increase the risk of bleeding. Patients should be instructed to monitor for signs and symptoms of bleeding during concurrent use and promptly report any bleeding events.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vorapaxar	NSAIDs SSRIs SNRI's	

References:

Zontivity Prescribing Information, May 2014, Merck Sharp & Dohme Corp.

Clinical Pharmacology, 2014 Elsevier/Gold Standard.

Facts & Comparisons, 2014 Updates, Wolters Kluwer Health.

**15. Vorapaxar / Strong CYP3A4 Inhibitors** \_\_\_√\_\_\_

Alert Message: Concurrent use of Zontivity (vorapaxar) with strong CYP3A4 inhibitors should be avoided. Vorapaxar is a CYP3A4 substrate and use with a strong inhibitor of CYP3A4-mediated metabolism may result in increased vorapaxar exposure and risk of bleeding.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vorapaxar	Nefazodone	Ketoconazole
	Clarithromycin	Itraconazole
	Telithromycin	Posaconazole
	Saquinavir	Voriconazole
	Ritonavir	Boceprevir
	Indinavir	Telaprevir
	Nelfinavir	

References:

Zontivity Prescribing Information, May 2014, Merck Sharp & Dohme Corp.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.  
Facts & Comparisons, 2014 Updates, Wolters Kluwer Health.

**16. Vorapaxar / Strong CYP3A4 Inducers** \_\_\_√\_\_\_

Alert Message: Concurrent use of Zontivity (vorapaxar) with strong CYP3A4 inducers should be avoided. Vorapaxar is a CYP3A4 substrate and use with a strong inducer of CYP3A4-mediated metabolism may result in decreased vorapaxar exposure and loss of efficacy.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vorapaxar	Carbamazepine	
	Phenytoin	
	Phenobarbital	
	Primidone	
	Rifampin	
	Rifabutin	
	Rifapentine	

References:

Zontivity Prescribing Information, May 2014, Merck Sharp & Dohme Corp.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.  
Facts & Comparisons, 2014 Updates, Wolters Kluwer Health.

**17. Vorapaxar / Hepatic Impairment** \_\_\_√\_\_\_

Alert Message: Based on the inherent risk of bleeding in patients with severe hepatic impairment, Zontivity (vorapaxar) is not recommended in such patients. No dosage adjustment is required in patients with mild and moderate hepatic impairment.

Conflict Code: TA - Therapeutic Appropriateness  
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Vorapaxar		Hepatic Impairment

References:

Zontivity Prescribing Information, May 2014, Merck Sharp & Dohme Corp.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.  
Facts & Comparisons, 2014 Updates, Wolters Kluwer Health.

**18. Vorapaxar / Non-adherence**

\_\_\_\_\_✓\_\_\_\_\_

Alert Message: Based on refill history, your patient may be under-utilizing Zontivity (vorapaxar). Non-adherence 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

Vorapaxar

References:

Zontivity Prescribing Information, May 2014, Merck Sharp & Dohme Corp.  
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.  
Kumbhani DJ, Steg PG, Cannon CP, et al. Adherence to Secondary Prevention Medications and Four-year Outcomes in Outpatients With Atherosclerosis. Am J Med. 2013 Aug;126(8):693-700.  
<http://dx.doi.org/10.1016/j.amjmed.2013.01.033>.  
Kneeland PP, Fang MC. Current Issues in Patient Adherence and Persistence: Focus on Anticoagulants for the Treatment and Prevention of Thromboembolism. Pat Pref Adher 2010;4:51-60.  
Ferguson C, Inglis SC, Newton PJ, et al. Atrial Fibrillation and Thromboprophylaxis in Heart Failure: The Need for Patient-centered Approaches to Address Adherence. Vascular Health and Risk Management 2013;9:3-11.

**19. Vorapaxar / Therapeutic Appropriateness**

\_\_\_\_\_✓\_\_\_\_\_

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

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C

Vorapaxar

Age Range: 0-18 yoa

References:

Zontivity Prescribing Information, May 2014, Merck Sharp & Dohme Corp.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.  
Facts & Comparisons, 2014 Updates, Wolters Kluwer Health.

**20. Empagliflozin / Overutilization**

\_\_\_\_\_✓\_\_\_\_\_

Alert Message: Jardiance (empagliflozin) may be over-utilized. The manufacturer's recommended dose of empagliflozin is 10 mg once daily in the morning, taken with or without food. In patients tolerating empagliflozin, the dose may be increased to 25 mg once daily.

Conflict Code: ER - Overutilization

Drugs/Diseases

Util A

Util B

Util C

Empagliflozin

Max Dose: 25mg/day

References:

Jardiance Prescribing Information, Aug. 2014, Boehringer Ingelheim Pharmaceuticals, Inc.

**21. Empagliflozin / Mild to Moderate Renal Impairment**

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Alert Message: Assessment of renal function is recommended prior to initiation of Jardiance (empagliflozin) and periodically thereafter. No dosage adjustment is needed in patients with an eGFR greater than or equal to 45 mL/min/1.73m<sup>2</sup>. Empagliflozin should not be initiated in patients with an eGFR less than 45 mL/min/1.73m<sup>2</sup> and should be discontinued if eGFR is persistently less than 45 mL/min/1.73m<sup>2</sup>.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Empagliflozin		CKD Stage 1 CKD Stage 2 CKD Stage 3

References:

Jardiance Prescribing Information, Aug. 2014, Boehringer Ingelheim Pharmaceuticals, Inc.

**22. Empagliflozin / Severe Renal Impairment, ESRD & Dialysis**

\_\_\_\_\_√\_\_\_\_\_

Alert Message: Jardiance (empagliflozin) use is contraindicated in patients with severe renal impairment, end-stage renal disease, or receiving dialysis. Based on its mechanism of action, inhibition of SGLT2 in the proximal renal tubules, empagliflozin is not expected to be effective in these patients.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

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

References:

Jardiance Prescribing Information, Aug. 2014, Boehringer Ingelheim Pharmaceuticals, Inc.

**23. Empagliflozin / Non-adherence**

\_\_\_\_\_√\_\_\_\_\_

Alert Message: Based on refill history, your patient may be under-utilizing Jardiance (empagliflozin). Non-adherence 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 – Non-adherence

Drugs/Diseases

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

References:

Jardiance Prescribing Information, Aug. 2014, Boehringer Ingelheim Pharmaceuticals, Inc.  
 Osterberg L, Blaschke T. Adherence to medication. N Engl J Med 2005;353:487-97.  
 Ho PM, Rumsfeld JS, Masoudi FA, et al., Effect of Medication Nonadherence in Diabetes Mellitus. Cardiology Review, April 2007.  
 Currie CJ, Peyrot M, Morgan CL, et al. The Impact of Treatment Noncompliance on Mortality in People With Type 2 Diabetes. Diabetes Care 35:1279-1284, June 2012.  
 Butler RJ, Davis TK, Johnson WL, et al. Effects of Nonadherence with Prescription Drugs Among Older Adults. Am J Manag Care. 2011 Feb; 17(2):153-60.

**24. Empagliflozin / Hypotension, Hypovolemia CKD Stage 3 & Dehydration**   

Alert Message: Jardiance (empagliflozin) causes osmotic diuresis which can lead to volume depletion and hypotension, particularly in patients with impaired renal function, elderly patients, or patients on diuretics. Monitor patients for signs and symptoms during therapy. Before initiating empagliflozin in patients with one or more of these characteristics, volume status should be assessed and corrected.

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

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Empagliflozin	Hypotension Hypovolemia CKD Stage 3 Dehydration	

References:

Jardiance Prescribing Information, Aug. 2014, Boehringer Ingelheim Pharmaceuticals, Inc.

**25. Empagliflozin / Diuretics**   

Alert Message: Jardiance (empagliflozin) causes osmotic diuresis which can lead to volume depletion and hypotension, particularly in patients with impaired renal function, elderly patients, or patients on diuretics. Monitor patients for signs and symptoms during therapy. Before initiating empagliflozin in patients with one or more of these characteristics, volume status should be assessed and corrected.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Empagliflozin	Loop Diuretics Thiazide Diuretics Potassium Sparing Diuretics	

References:

Jardiance Prescribing Information, Aug. 2014, Boehringer Ingelheim Pharmaceuticals, Inc.

**26. Empagliflozin / Insulin & Sulfonylureas**   

Alert Message: The concurrent use of Jardiance (empagliflozin) with insulin or an insulin secretagogue can increase the risk of hypoglycemia. A lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with empagliflozin.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Empagliflozin	Insulin Chlorpropamide Glimepiride Glipizide Glyburide Tolazamide Tolbutamide	

References:

Jardiance Prescribing Information, Aug. 2014, Boehringer Ingelheim Pharmaceuticals, Inc.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**27. Empagliflozin / LDL-Increases**

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Alert Message: The use of Jardiance (empagliflozin) can cause dose-related increases in LDL-C levels. Patients receiving empagliflozin should have their LDL-C levels monitored and treated per standard of care.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C (Include)

Empagliflozin

Hypercholesterolemia

References:

Jardiance Prescribing Information, Aug. 2014, Boehringer Ingelheim Pharmaceuticals, Inc.

**28. Empagliflozin / Pediatric Use**

\_\_\_\_\_\_    \_\_\_    \_\_\_

Alert Message: The safety and effectiveness of Jardiance (empagliflozin) in pediatric patients under 18 years of age have not been established.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C

Empagliflozin

Age Range: 0-17 yoa

References:

Jardiance Prescribing Information, Aug. 2014, Boehringer Ingelheim Pharmaceuticals, Inc.

**29. Dofetilide / Chronic Kidney Disease**

\_\_\_\_\_\_    \_\_\_    \_\_\_

Alert Message: Tikosyn (dofetilide) is contraindicated in patients with severe renal impairment (calculated creatinine clearance < 20mL/min). Overall systemic clearance of dofetilide is decreased and plasma concentration increased with decreasing creatinine clearance. Appropriate dosing recommendations for dialysis patients are unknown.

Conflict Code: MC – Drug/Disease Precaution/Warning

Drugs/Diseases

Util A

Util B

Util C

Dofetilide

Chronic Kidney Disease

References:

Tikosyn Prescribing Information, 2013, Pfizer Labs.

Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**30. Dofetilide / Long QT Syndrome**

\_\_\_\_\_✓\_\_\_\_\_

Alert Message: Tikosyn (dofetilide) is contraindicated in patients with congenital or acquired long QT syndromes and should not be used in patients with a baseline QT interval or QTc > 440 msec. Dofetilide can cause serious ventricular arrhythmias, primarily torsade de pointes type ventricular tachycardia.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Dofetilide	Long QT Syndrome	

References:

Tikosyn Prescribing Information, 2013, Pfizer Labs.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**31. Dofetilide / Contraindicated Drugs**

\_\_\_\_\_✓\_\_\_\_\_

Alert Message: Concurrent use of Tikosyn (dofetilide) and HCTZ, cimetidine, verapamil, ketoconazole, itraconazole, trimethoprim, prochlorperazine, megestrol, and dolutegravir are contraindicated. Co-administration with these agents has been shown to significantly increase dofetilide plasma concentrations and QT interval prolongation.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Dofetilide	Hydrochlorothiazide Verapamil Cimetidine Ketoconazole Itraconazole Trimethoprim Prochlorperazine Megestrol Dolutegravir	

References:

Tikosyn Prescribing Information, 2013, Pfizer Labs.  
Clinical Pharmacology, 2010 Gold Standard.  
Facts & Comparisons, 2014 Updates, Wolters Kluwer Health.

**32. Dofetilide / Drugs Cautioned w/ Dofetilide**

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Alert Message: Caution should be exercised when Tikosyn (dofetilide) is co-administered with a drug that is actively secreted via renal cationic secretion or a CYP3A4 inhibitor. Concurrent use of these agents may increase dofetilide plasma concentrations resulting in QT interval prolongation.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Dofetilide	Procainamide Diltiazem Metformin Memantine Fluvoxamine Nefazodone Triamterene Indinavir Nelfinavir Fosamprenavir Entecavir Lamivudine Zafirlukast	

References:

Tikosyn Prescribing Information, 2013, Pfizer Labs.  
Facts & Comparisons, 2014 Updates, Wolters Kluwer Health.

**33. Dofetilide / Potassium-Depleting Diuretics**

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Alert Message: Caution should be exercised when co-administering Tikosyn (dofetilide) and a potassium-depleting diuretic (e.g., thiazide and loop). Hypokalemia and hypomagnesemia may occur with administration of these diuretics increasing the potential for dofetilide-induced torsade de pointes. The use of the thiazide diuretic hydrochlorothiazide is contraindicated due to substantial increases in dofetilide concentrations.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Dofetilide	Furosemide Bumetanide Torsemide Ethacrynate	Chlorothiazide Chlorthalidone Methyclothiazide Metolazone

References:

Tikosyn Prescribing Information, 2013, Pfizer Labs.  
Facts & Comparisons, 2014 Updates, Wolters Kluwer Health.

**34. Dofetilide / Digoxin**

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Alert Message: Caution should be exercised when co-administering Tikosyn (dofetilide) and digoxin. The concurrent use of these agents has been associated with a higher occurrence of torsade de pointes.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Dofetilide	Digoxin	

References:

Tikosyn Prescribing Information, Nov. 2013, Pfizer Labs.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.  
Facts & Comparisons, 2014 Updates, Wolters Kluwer Health.

**35. Dofetilide / Drugs that Prolong QT Interval**

Alert Message: Tikosyn (dofetilide) can cause QT prolongation and concurrent use with other drugs that prolong the QT interval is not recommended due to the potential risk of life-threatening arrhythmias, including torsade de pointes.

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

<u>Util A</u>	<u>Util B*</u>		<u>Util C</u>
Dofetilide	Albuterol	Galantamine	Moexipril/HCTZ
	Alfuzosin	Gemifloxacin	Quinidine
	Amiodarone	Granisetron	Quinine
	Amitriptyline	Haloperidol	Ranolazine
	Amantadine	Iloperidone	Risperidone
	Amoxapine	Imipramine	Ritonavir
	Anagrelide	Indacaterol	Salmeterol
	Arformoterol	Indapamide	Saquinavir
	Aripiprazole	Isradipine	Sertraline
	Asenapine	Lapatinib	Solifenacin
	Atomoxetine	Levalbuterol	Sorafenib
	Azithromycin	Levofloxacin	Sotalol
	Bedaquiline	Maprotiline	SMZ/TMP
	Buprenorphine	Mefloquine	Sumatriptan
	Chloroquine	Memantine	Sunitinib
	Chlorpromazine	Metaproterenol	Tacrolimus
	Ciprofloxacin	Methadone	Tamoxifen
	Citalopram	Moxifloxacin	Telithromycin
	Clarithromycin	Naratriptan	Terbutaline
	Clomipramine	Ketoconazole	Tetrabenazine
	Clozapine	Itraconazole	Thioridazine
	Crizotinib	Posaconazole	Tizanidine
	Dasatinib	Voriconazole	Tolterodine
	Disopyramide	Nilotinib	Toremifene
	Dofetilide	Norfloxacin	Trazodone
	Dolasetron	Nortriptyline	Trimipramine
	Doxepin	Octreotide	Umeclidinium/Vilanterol
	Dronedarone	Ofloxacin	Vandetanib
	Erythromycin	Olanzapine	Vardenafil
	Escitalopram	Ondansetron	Vemurafenib
	Ezogabine	Paliperidone	Venlafaxine
	Famotidine	Pasireotide	Vorinostat
	Fesoterodine	Pazopanib	Ziprasidone
	Fexofenadine	Perphenazine	Zolmitriptan
	Felbamate	Pimozide	
	Flecainide	Pirbuterol	
	Fluconazole	Prochlorperazine	
	Fluoxetine	Protriptyline	
	Fluphenazine	Quetiapine	
	Formoterol		

**\* Contraindicated drugs taken out of Util B list.**

References:

Tikosyn Prescribing Information, 2013, Pfizer Labs.

Clinical Pharmacology, 2014 Gold Standard.

ArizonaCERT: **Drugs That Prolong the QT Interval and/or Induce Torsades de Pointes**

Available at: <http://www.azcert.org/consumers/interaction-advisory.cfm>

**36. Dofetilide / Chronic Kidney Disease**

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Alert Message: The dose of Tikosyn (dofetilide) should be adjusted based on creatinine clearance and QTc. Therapy should be re-evaluated every 3 months or as medically warranted. If renal function deteriorates after initiation of therapy, reduce the dose based on calculated CrCl: 40 to 60 mL/min dose 250 mcg BID, 20 to < 40 mL/min dose 125 mcg BID and < 20 mL/min dofetilide is contraindicated. If QTc is increased further, dosage adjustment must be made.

Conflict Code: MC – Drug/Disease Precaution/Warning

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Dofetilide		Chronic Kidney Disease

References:

Tikosyn Prescribing Information, 2013, Pfizer Labs.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**37. Dofetilide / Non-adherence**

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

Conflict Code: LR – Non-adherence

Drugs/Diseases

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

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005;353:487-97.  
Iuga AO, McGuire MJ. Adherence and Health Care Costs. Risk Manag Health Policy. 2014 Feb 20;7:35-44.  
Ho MP, Bryson CL, Rumsfeld JS. Medication Adherence: Its Importance in Cardiovascular Outcomes. Circulation. 2009 Jun 16;119(23):3028-3035.

**38. Canagliflozin/Metformin / Overutilization**

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Alert Message: Invokamet (canagliflozin/metformin) may be over-utilized. The manufacturer's recommended total daily dose of canagliflozin/metformin is 300mg/2000mg in patients with an eGFR of 60 mL/min/1.73m2 or greater.

Conflict Code: ER - Overutilization

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>
Canagliflozin/Metformin		CKD Stage 3, 4 & 5 ESRD Dialysis

Max Dose: 300mg/2000mg per day

References:

Invokamet Prescribing Information, Aug. 2014, Janssen Pharmaceuticals, Inc.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.



**42. Canagliflozin/Metformin 150mg / UGT Inducers**

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Alert Message: Concurrent use of Invokamet (canagliflozin/metformin) with a UGT (uridine diphosphate glucuronosyltransferase) inducer may result in decreased canagliflozin exposure and loss of efficacy. Monitor patient for loss of canagliflozin effectiveness.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Canagliflozin/Metformin 150mg/500mg	Rifampin	
Canagliflozin/Metformin 150mg/1000mg	Phenytoin	
	Phenobarbital	
	Ritonavir	

References:

Invokamet Prescribing Information, Aug. 2014, Janssen Pharmaceuticals, Inc.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**43. Canagliflozin/Metformin / Therapeutic Appropriateness**

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Alert Message: Safety and effectiveness of Invokamet (canagliflozin/metformin) in pediatric patients less than 18 years of age have not been established.

Conflict Code: TA – Therapeutic Appropriateness  
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Canagliflozin/Metformin		

Age Range: 0-17 yoa

References:

Invokamet Prescribing Information, Aug. 2014, Janssen Pharmaceuticals, Inc.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**44. Canagliflozin/Metformin / Nonadherence**

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Alert Message: Based on refill history, your patient may be under-utilizing Invokamet (canagliflozin/metformin). Non-adherence 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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Canagliflozin/Metformin		

References:

Osterberg L, Blaschke T. Adherence to medication. N Engl J Med 2005;353:487-97.  
Miller KE, Medication Nonadherence Affects Diabetes Treatment. Am Family Phys. Vol. 75 No. 6, March 15, 2007.  
Ho PM, Rumsfeld JS, Masoudi FA, et al., Effect of Medication Nonadherence in Diabetes Mellitus. Cardiology Review, April 2007.  
Currie CJ, Peyrot M, Morgan CL, et al. The Impact of Treatment Noncompliance on Mortality in People With Type 2 Diabetes. Diabetes Care 35:1279-1284, June 2012.  
Invokamet Prescribing Information, Aug. 2014, Janssen Pharmaceuticals, Inc.

**Criteria Recommendations**

*Accepted Approved Rejected  
As  
Amended*

**45. Canagliflozin/Metformin / Pregnancy / Miscarriage, Delivery & Abortion**    ✓                         

Alert Message: Invokamet (canagliflozin/metformin) should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Canagliflozin/metformin is classified pregnancy category C.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>
Canagliflozin/Metformin	Pregnancy	Delivery Miscarriage Abortion

Age Range: 11-50 yoa

Gender: Female

References:

Invokamet Prescribing Information, Aug. 2014, Janssen Pharmaceuticals, Inc.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**46. Canagliflozin/Metformin / Digoxin**               ✓              

Alert Message: Caution is warranted and monitoring is recommended when Invokamet (canagliflozin/metformin) is coadministered with digoxin. Concurrent use of canagliflozin and digoxin has been shown to increase digoxin exposure. Metformin and digoxin are both cationic drugs and may compete for renal tubular transport resulting in elevated metformin levels.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Canagliflozin/Metformin	Digoxin	

References:

Invokamet Prescribing Information, Aug. 2014, Janssen Pharmaceuticals, Inc.  
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2014 Truven health Analytics.

  
Stephanie McGee Azar, Acting Commissioner

Approve     Deny

4-17-15  
Date

  
Robert Moon, M.D., Deputy Commissioner  
and Medical Director

Approve     Deny

4-16-15  
Date

  
Kathy Hall, Deputy Commissioner

Approve     Deny

4/14/15  
Date