Alabama Medicaid DUR Board Meeting Minutes
July 25, 2013

Members Present: Denyse Thornley-Brown, Paula Thompson, Kelli Littlejohn, Bernie Olin, Rhonda Harden, David Harwood, Dan McConaghy, Jimmy Jackson, Frank Pettyjohn, Robert Moon

Also Present: Tiffany Minnifield, Heather Vega, Lori Thomas, Clemice Hurst, Jacob Parker, Emily McGowan, Jeremy Nolan, Rachel Howorth, Scott Donald, Ariane Casey

Present via Conference Call: Kristian Testerman, Amy Donaldson, Holley Rice

Members Absent: Wendy Gomez, Donald Marks

Call to Order: The DUR meeting was called to order by W. Thornely-Brown at approximately 1:00p.m.

Review and Adoption of Minutes: The minutes of the April 24, 2013 meeting were presented and reviewed. D. Harwood 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 February 2013. She reported 8,673 total requests. She then reported 20,544 electronic requests for the same time frame. From the Prior Authorization and Override Response Time Ratio report for February 2013, L.Thomas reported that approximately 70% of all manual PAs and 68% of all overrides were responded to in less than two hours, about 95% in less than four hours and 99% in less than eight hours. For the month of March, L.Thomas reported 8,387 manual PA requests and 18,958 electronic PA requests. She reported that 76% of all manual PAs and 74% of all overrides were responded to in less than two hours. More than 95% of PAs and overrides were responded to in less than four hours and approximately 99% in less than eight hours. For the month of April 2013, L.Thomas reported 8,960 manual PA requests and 20,499 electronic PA requests for the same time frame. For April, L.Thomas reported over 81% of the manual PAs and over 77% of the overrides were approved in less than two hours, approximately 96% in less than four hours and over 99% approved in less than eight hours.

Program Summary Review: L.Thomas briefly reviewed the Alabama Medicaid Program Summary. She reported 4,697,183 total prescriptions, 246,996 average recipients per month using pharmacy benefits and an average paid per prescription of $59.62 for the months of October 2012 through March 2013.

Cost Management Analysis: L.Thomas reported an average cost per claim of $59.72 for March 2013 and $56.92 for April 2011. She also pointed out the average cost per claim for March 2012, which was $61.17. L. Thomas mentioned that the higher claims cost in January 2013 and February 2013 could be a reflection of those months being at the peak of Synagis® season. From the 1st Quarter 2013 Drug Analysis, L.Thomas reported 76.3% generic utilization, 10.2% brand single-source, 4.1% brand multi-source (those requests which required a DAW override) and 9.3% OTC and "other". From the Top 25 Drugs Based on Number of Claims from 01/01/2013 – 03/31/2013, L.Thomas reported the top five drugs: hydrocodone-acetaminophen, amoxicillin, azithromycin, montelukast sodium, and omeprazole. L. Thomas informed the Board that the top five drugs were the same as last reported in April. D. Thornley-Brown asked if the number of hydrocodone claims had decreased since the Hydrocodone Utilization special letters were given to the top 100 prescribers of hydrocodone. L. Thomas stated that the claims last quarter were fairly similar. K. Littlejohn pointed out that the letters weren't distributed until late February – early March and due to that a decrease may not be seen during the quarter being presented. She then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 01/01/2013 – 03/31/2013: Abilify®, Synagis®, Vyvanse®, Focalin XR® and Adderall XR®. L. Thomas mentioned that the top three were identical to what was reported last quarter. L. Thomas reminded the members that Synagis season ended March 31st. 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, Corticosteroids (Respiratory Tract), Amphetamines, Hemostatics, and Respiratory and CNS Stimulants.

Review of Palivizumab Utilization for the 2012-2013 Season: The 2012-2013 RSV season ended March 31, 2013. L. Thomas provided an update which compared the results of the 2012-13 season to previous seasons. L. Thomas referred to Alabama RSV data from the CDC which supported Alabama Medicaid's policy of limiting the Synagis® timeframe to October 2012 – March 2013. L. Thomas reminded the Board that each recipient could receive a maximum of 5 doses per season and that all policies relating to Synagis® were based on clinical literature

and recommendations. For the 2012-13 season, there were 4,324 claims for 1,024 recipients. The average cost per claim was $2,323 while the average cost per recipient was $9,920. L. Thomas pointed out that the cost per vial has continued to rise over the past few years. There were 2,457 prior authorizations requested over the course of the season, with an approval rate of 71.0%

Proposed Criteria: L.Thomas presented the proposed set of 66 criteria to the Board. T.Minnifield instructed the Board members to mark their ballots. Of the 66 criteria, results from the criteria vote returned 66 approved and 0 rejected.

Medicaid Update: T. Minnifield began the Medicaid Update by reminding the Board members that all Medicaid information discussed is available online. T. Minnifield discussed the copay changes which were effective on July 1, 2013 and the DEA Edit which was effective on July 8, 2013. T. Minnifield notified the Board that every July the Board would vote on a Vice Chair.

P & T Committee Update: C. Hurst began the P & T Update by informing the Board that the last meeting was held on May 15, 2013 and covered the anti-hypertensive agents and diuretics. The next P & T meeting is scheduled for August 14, 2013 at 9am and will cover the Androgens; Respiratory agents; EENT agents; and Intranasal corticosteroids. C. Hurst also discussed the PDL changes that were effective July 1, 2013. C. Hurst mentioned that lansoprazole would now be preferred and azelastine would be non-preferred. C. Hurst also reviewed the July 1 changes that were made to compounding. K. Littlejohn announced some upcoming changes for October 1, 2013: prescription limit for adults; 90-day supply on certain maintenance medications; and discontinuing coverage of OTC products for children and adults (excluding nutritionals and insulins). K. Littlejohn notified the Board that legislation had been changed to allow Alabama Medicaid access to prescription drug monitoring program (PDMP) data.

New Business: T. Minnifield asked members to vote for a new Vice-Chair. The Board voted and returned a majority Vice-Chair vote for Denyse Thornley-Brown. Dr. Thornley-Brown will have her first meeting as Vice-Chair for the 2013-14 term at the October 23, 2013 meeting. D.Thornley-Brown made a motion to adjourn the meeting. The motion was seconded by D. Harwood. A voice vote to adjourn was unanimous. The meeting was adjourned at 2:31p.m.

Next Meeting Date: The next DUR Board meeting will be held on October 23, 2013.

Respectfully submitted,

Lori Thomas, PharmD

Lori Thomas, PharmD

ALABAMA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS

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

1. Pioglitazone / Gemfibrozil ___√___ _____ _____

Alert Message: The maximum recommended dose of a pioglitazone-containing product is 15 mg once daily when used in combination with strong CYP2C8 inhibitors (e.g., gemfibrozil).

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C (Include)
Pioglitazone		Gemfibrozil
Pioglitazone/Metformin IR		
Pioglitazone/Alogliptin		

Max Dose: 15 mg/day of pioglitazone

References:
Facts & Comparison, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Actos Prescribing Information, August 2012, Takeda Pharmaceuticals.
ActoPlus Met Prescribing Information, September 2012, Takeda Pharmaceuticals.
Oseni Prescribing Information, January 2013, Takeda Pharmaceuticals.

2. Actoplus Met XR & Duetact / Gemfibrozil ___√___ _____ _____

Alert Message: The concurrent use of a pioglitazone-containing agent with a CYP2C8 inhibitor (e.g., gemfibrozil) can cause a significant increase in pioglitazone plasma concentrations. If an inhibitor of CYP2C8 is started or stopped during pioglitazone therapy, dosage adjustment of the diabetic treatment may be needed based on clinical response.

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

Util A	Util B	Util C
Pioglitazone/Metformin XR	Gemfibrozil	
Pioglitazone/Glimepiride		

References:
ActoPlus Met XR Prescribing Information, October 2012, Takeda Pharmaceuticals.
Duetact Prescribing Information, October 2012, Takeda Pharmaceuticals.

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

3. Pioglitazone - All / Rifampin ___√___ _____ _____

Alert Message: The concurrent use of a pioglitazone-containing agent with a CYP2C8 inducer (e.g., rifampin) can cause a significant decrease in pioglitazone plasma concentrations. If an inducer of CYP2C8 is started or stopped during pioglitazone therapy, dosage adjustment of the diabetic treatment may be needed based on clinical response, without exceeding the maximum recommended daily dose of 45 mg for pioglitazone.

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

Util A	Util B	Util C
Pioglitazone-All	Rifampin	

References:
Actos Prescribing Information, August 2012, Takeda Pharmaceuticals.
ActoPlus Met Prescribing Information, September 2012, Takeda Pharmaceuticals.
Oseni Prescribing Information, January 2013, Takeda Pharmaceuticals.
ActoPlus Met XR Prescribing Information, October 2012, Takeda Pharmaceuticals.
Duetact Prescribing Information, October 2012, Takeda Pharmaceuticals.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: http://medicine.iupui.edu/clinpharm/ddos/table.asp.

4. Rosiglitazone - All / Rifampin ___√___ _____ _____

Alert Message: The concurrent use of a rosiglitazone-containing agent with a CYP2C8 inducer (e.g., rifampin) can cause a significant decrease in rosiglitazone plasma concentrations. If an inducer of CYP2C8 is started or stopped during rosiglitazone therapy, dosage adjustment of the diabetic treatment may be needed based on clinical response.

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

Util A	Util B	Util C
Rosiglitazone-All	Rifampin	

References:
Avandia Prescribing Information, May 2011, GlaxoSmithKline.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: http://medicine.iupui.edu/clinpharm/ddos/table.asp.

5. Rosiglitazone - All / Gemfibrozil ___√___ _____ _____

Alert Message: The concurrent use of a rosiglitazone-containing agent with a CYP2C8 inhibitor (e.g., gemfibrozil) can cause a significant increase in rosiglitazone plasma concentrations. If an inhibitor of CYP2C8 is started or stopped during pioglitazone therapy, dosage adjustment of the diabetic treatment may be needed based on clinical response.

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

Util A	Util B	Util C
Rosiglitazone- All	Gemfibrozil	

References:
Avandia Prescribing Information, May 2011, GlaxoSmithKline.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: http://medicine.iupui.edu/clinpharm/ddos/table.asp.

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

6. Alogliptin / Overutilization ___√___ _____ _____

Alert Message: The manufacturer's maximum recommended dose of a Nesina (alogliptin) in patients with normal renal function or mild renal impairment is 25 mg once daily.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C (Negate)
Alogliptin		CKD Stage 3-5
		ESRD
		Hypertensive CKD

Max Dose: 25mg/day

References:
Nesina Prescribing Information, January 2013, Takeda Pharmaceuticals.
Facts& Comparisons, 2013 Updates, Wolters Kluwer Health.

7. Alogliptin / Moderate Renal Impairment Dosing ___√___ _____ _____

Alert Message: The maximum recommended dose of Nesina (alogliptin) in patients with moderate renal impairment (CrCl 30 to < 60 mL/min) is 12.5 mg once daily. Patients with severe renal impairment or ESRD should not receive more than 6.25 mg once daily.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C (Include)
Alogliptin		CKD Stage 3
		CKD unspecified
		Hypertensive CKD

Max Dose: 12.5mg/day

References:
Nesina Prescribing Information, January 2013, Takeda Pharmaceuticals.
Facts& Comparisons, 2013 Updates, Wolters Kluwer Health.

8. Alogliptin / Severe Renal Impairment or ESRD Dosing ___√___ _____ _____

Alert Message: The maximum recommended dose of Nesina (alogliptin) in patients with severe renal impairment or ESRD (CrCl< 30 mL/min) is 6.25 mg once daily.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C (Include)
Alogliptin		CKD Stage 3
		CKD unspecified
		Hypertensive CKD

Max Dose: 6.25mg/day

References:
Nesina Prescribing Information, January 2013, Takeda Pharmaceuticals.
Facts& Comparisons, 2013 Updates, Wolters Kluwer Health.

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

9. Alogliptin-All / Pancreatitis ___√___ _____ _____

Alert Message: There have been postmarketing reports of acute pancreatitis in patients taking alogliptin-containing product (Nesina, Kazano and Oseni).
After initiation of any alogliptin-containing product, patients should be observed carefully for signs and symptoms of pancreatitis. If pancreatitis is suspected alogliptin should be promptly discontinued and appropriate management should be initiated.

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

Util A	Util B	Util C
Alogliptin	Pancreatitis	
Alogliptin/Metformin		
Alogliptin/Pioglitazone		

References:
Nesina Prescribing Information, January 2013, Takeda Pharmaceuticals.
Kazano Prescribing Information, January 2013, Takeda Pharmaceuticals.
Oseni Prescribing Information, January 2013, Takeda Pharmaceuticals.

10. Alogliptin-All / Hepatic Effects ___√___ _____ _____

Alert Message: There have been postmarketing reports of fatal and non-fatal hepatic failure in patients taking alogliptin-containing products (Nesina, Kazano and Oseni). If liver injury is detected, promptly interrupt alogliptin-containing therapy and assess patient for probable cause. Do not restart alogliptin-containing product if liver injury is confirmed and no alterative etiology can be found.

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

Util A	Util B	Util C
Alogliptin		
Alogliptin/Metformin		
Alogliptin/Pioglitazone		

References:
Nesina Prescribing Information, January 2013, Takeda Pharmaceuticals.
Kazano Prescribing Information, January 2013, Takeda Pharmaceuticals.
Oseni Prescribing Information, January 2013, Takeda Pharmaceuticals.

11. Alogliptin-All / Insulin & Sulfonylureas ___√___ _____ _____

Alert Message: The concurrent use of an alogliptin-containing product (Nesina, Kazano and Oseni) with insulin or an insulin secretagogue (e.g., sulfonylurea) may result in hypoglycemia. A lower dose of the sulfonylurea or insulin may be required to minimize the risk of hypoglycemia.

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

Util A	Util B	Util C
Alogliptin	Insulin	
Alogliptin/Metformin	Sulfonylureas	
Alogliptin/Pioglitazone		

References:
Nesina Prescribing Information, January 2013, Takeda Pharmaceuticals.
Kazano Prescribing Information, January 2013, Takeda Pharmaceuticals.
Oseni Prescribing Information, January 2013, Takeda Pharmaceuticals.

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

12. Alogliptin-Pioglitazone / Overutilization ___√___ _____ _____

Alert Message: The manufacturer's maximum recommended daily dose of Oseni (alogliptin/pioglitazone) in patients with normal renal function or mild renal impairment is 25 mg alogliptin and 45 mg pioglitazone.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C (Negate)
Alogliptin/Pioglitazone		CKD Stage 3-5
		ESRD
		Hypertensive CKD

Max Dose: 25 mg/day alogliptin

References:
Oseni Prescribing Information, January 2013, Takeda Pharmaceuticals.

13. Alogliptin-Pioglitazone / Moderate Renal Impairment Dosing ___√___ _____ _____

Alert Message: The manufacturer's maximum recommended dose of Oseni (alogliptin/pioglitazone) in patients with moderate renal impairment (CrCl 30 to < 60 mL/min) is 12.5 mg of alogliptin once daily. Alogliptin/pioglitazone use is not recommended for patients with severe renal impairment or ESRD requiring dialysis.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C (Include)
Alogliptin/Pioglitazone		CKD Stage 3
		CKD unspecified
		Hypertensive CKD

Max Dose: 12.5 mg/day

References:
Oseni Prescribing Information, January 2013, Takeda Pharmaceuticals.

14. Alogliptin-Metformin / Overutilization ___√___ _____ _____

Alert Message: The manufacturer's maximum recommended daily dose of Kazano (alogliptin/metformin) is 25 mg alogliptin and 2000 mg metformin.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C (Negate)
Alogliptin/Metformin		Renal Impairment

Max Dose: 25 mg/day alogliptin

References:
Kazano Prescribing Information, January 2013, Takeda Pharmaceuticals.

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

15. Alogliptin-Metformin / Metabolic Acidosis ___√___ _____ _____

Alert Message: Kazano (alogliptin/metformin) use is contraindicated in patients with acute or chronic metabolic acidosis, including diabetic ketoacidosis.

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

Drugs/Diseases		
Util A	Util B	Util C
Alogliptin/Metformin	Acidosis	

References:
Kazano Prescribing Information, January 2013, Takeda Pharmaceuticals.

16. Alogliptin-All / Duplicate Therapy ___√___ _____ _____

Alert Message: Therapeutic duplication of alogliptin-containing products may be occurring.

Conflict Code: TD – Therapeutic Duplication

Drugs/Diseases		
Util A	Util B	Util C
Alogliptin		
Alogliptin/Pioglitazone		
Alogliptin/Metformin		

References:
Nesina Oseni Prescribing Information, January 2013, Takeda Pharmaceuticals.
Oseni Prescribing Information, January 2013, Takeda Pharmaceuticals.
Kazano Prescribing Information, January 2013, Takeda Pharmaceuticals.

17. Alogliptin / Nonadherence ___√___ _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Nesina (alogliptin). 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
Alogliptin		

References:
Nesina Prescribing Information, January 2013, Takeda Pharmaceuticals.
Osterberg L, Blaschke T. Adherence to medication. N Engl J Med 2005;353:487-97.
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.
Ho PM, Rumsfeld JS, Masoudi FA, et al., Effect of Medication Nonadherence in Diabetes Mellitus. Cardiology Review, April 2007.

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

18. Alogliptin-Pioglitazone / Nonadherence ___√___ _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Oseni (alogliptin/pioglitazone). 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
Alogliptin/Pioglitazone		

References:
Oseni Prescribing Information, January 2013, Takeda Pharmaceuticals.
Osterberg L, Blaschke T. Adherence to medication. N Engl J Med 2005;353:487-97.
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.
Ho PM, Rumsfeld JS, Masoudi FA, et al., Effect of Medication Nonadherence in Diabetes Mellitus. Cardiology Review, April 2007.

19. Alogliptin-Metformin / Nonadherence ___√___ _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Kazano (alogliptin/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

Util A	Util B	Util C
Alogliptin/Metformin		

References:
Kazano Prescribing Information, January 2013, Takeda Pharmaceuticals.
Osterberg L, Blaschke T. Adherence to medication. N Engl J Med 2005;353:487-97.
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.
Ho PM, Rumsfeld JS, Masoudi FA, et al., Effect of Medication Nonadherence in Diabetes Mellitus. Cardiology Review, April 2007.

20. Alogliptin-All / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: Safety and effectiveness of alogliptin-containing products (Nesina, Kazano or Oseni) in pediatric patients have not been established.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Alogliptin Alogliptin/Metformin Alogliptin/Pioglitazone		

Age Range: 0-18 yoa

References:
Nesina Prescribing Information, January 2013, Takeda Pharmaceuticals.
Oseni Prescribing Information, January 2013, Takeda Pharmaceuticals.
Kazano Prescribing Information, January 2013, Takeda Pharmaceuticals.

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

21. Metformin – All / Hepatic Impairment ___√___ _____ _____

Alert Message: The use of metformin-containing products should be avoided in patients with clinical or laboratory evidence of hepatic disease. Metformin can, rarely, cause lactic acidosis and impaired hepatic function can significantly limit clearance of lactate. Metformin use in this patient population may increase the risk of lactic acidosis.

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

Drugs/Diseases		
Util A	Util B	Util C
Metformin-All	Hepatic Impairment	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 3013 Elsevier/Gold Standard.

22. Icosapent Ethyl / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: The safety and effectiveness of Vascepa (icosapent ethyl) in pediatric patients have not been established.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases		
Util A	Util B	Util C
Icosapent ethyl		

Age Range: 0 – 18 yoa

References:
Vascepa Prescribing Information, November 2012, Amarin Pharma Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

23. Icosapent Ethyl / Overuse ___√___ _____ _____

Alert Message: Vascepa (icosapent ethyl) may be over-utilized. The manufacturer's maximum recommended dose is 4 grams per day, taken as 2 grams twice daily with food.

Conflict Code: ER - Overutilization

Drugs/Diseases		
Util A	Util B	Util C
Icosapent ethyl		

Max Dose: 4 grams daily

References:
Vascepa Prescribing Information, November 2012, Amarin Pharma Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

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

24. Icosapent Ethyl / Drugs Affecting Coagulation ___√___ _____ _____

Alert Message: Some published studies have demonstrated prolongation of bleeding time when anticoagulants and omega-3 fatty acids are used concurrently. Patients receiving treatment with Vascepa (icosapent ethyl) and drugs affecting coagulation should be monitored periodically.

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

Util A	Util B	Util C
Icosapent Ethyl	Anticoagulants	
	Thrombin Inhibitors	
	Platelet Aggregation Inhibitors	
	Direct Factor Xa Inhibitors	
	Low Molecular Weight Heparins	

References:
Vascepa Prescribing Information, November 2012, Amarin Pharma Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

25. Icosapent Ethyl / Pregnancy / Pregnancy Negating ___√___ _____ _____

Alert Message: Vascepa (icosapent ethyl) is FDA pregnancy category C. There are no adequate and well-controlled studies in pregnant women and it is unknown if icosapent ethyl can cause fetal harm. Icosapent ethyl should be used during pregnancy only if the potential benefit to the patient justifies the potential risk to the fetus.

Conflict Code: MC – Drug/Diagnosis Precaution/Warning/Contraindication
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Icosapent Ethyl	Pregnancy ICD-9s	Delivery
		Miscarriage
		Abortion

References:
Vascepa Prescribing Information, November 2012, Amarin Pharma Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

26. Icosapent Ethyl / Hepatic Impairment ___√___ _____ _____

Alert Message: Patients taking Vascepa (icosapent ethyl) who have hepatic impairment should have ALT and AST levels monitored periodically.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C (Include)
Icosapent Ethyl		Chronic Liver Disease
		Cirrhosis

References:
Vascepa Prescribing Information, November 2012, Amarin Pharma Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

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

27. Icosapent Ethyl / Non-adherence ___J___ _____ _____

Alert Message: Based on refill history, your patients may be under-utilizing Vascepa (icosapent ethyl). 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
Icosapent ethyl		

References:
Schedlbauer A, Davis P, Fahey T. Interventions to Improve Adherence to Lipid Lowering Medication (Review). Cochrane Database System Rev. 2010 Mar 17;(3):CD004371.
Bersot T, Haffner S, Harris WS, et al., Hypertriglyceridemia: Management of Atherogenic Dyslipidemia. Jrnl of Fam Pract. 2006 Jul;55(7):S1-S8.
Osterberg L and Blaschke T. Adherence to Medication. N Engl J Med 2005;353:487-497.

28. Abilify Maintena / Overutilization ___J___ _____ _____

Alert Message: Abilify Maintena (aripiprazole extended-release injection) may be over-utilized. The manufacturer's recommended starting and maintenance dose of extended-release aripiprazole intramuscular injection is 400 mg monthly.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C (Negating)
Aripiprazole Inj.		CYP3A4 Inhibitors & Inducers > 14 day supply CYP2D6 Inhibitors & Inducers > 14 day supply

Max Dose: 400 mg/month

References:
Abilify Maintena Prescribing Information, Feb 2013, Otsuka America Pharmaceuticals, Inc.

29. Abilify Maintena / CYP3A4 Inducers ___J___ _____ _____

Alert Message: Avoid the concomitant use of CYP3A4 inducers with Abilify Maintena (aripiprazole extended-release injection) for greater than 14 days because blood levels of aripiprazole are decreased and may be below the effective levels.

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

Util A	Util B		Util C
Aripiprazole Inj.	Carbamazepine	Modafinil	
	Phenytoin	Armodafinil	
	Phenobarbital	Pioglitazone	
	Oxcarbazepine	Prednisone	
	Efavirenz	Rufinamide	
	Etravirine	Rifampin	
	Bosentan	Rifapentine	
	Nevirapine	Rifabutin	
	Primidone		

References:
Abilify Maintena Prescribing Information, Feb 2013, Otsuka America Pharmaceuticals, Inc.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionLabeling/ucm093664.htm

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

30. Abilify Maintena / Use in Patients < 18 Years of Age ___√___ _____ _____

Alert Message: Safety and effectiveness of Abilify Maintena (aripiprazole extended-release injection) in patients less than 18 years of age have not been evaluated.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

Util A	Util B	Util C
Aripiprazole Inj.		

Age Range: 0-17 yoa

References:

Abilify Maintena Prescribing Information, Feb 2013, Otsuka America Pharmaceuticals, Inc.

31. Abilify Maintena 400mg /Strong CYP3A4 or 2D6 Inh./Negate Other CYP3A4 & 2D6 Inhibitors ___√___ _____ _____

Alert Message: Patients taking 400 mg of Abilify Maintena (aripiprazole extended-release injection) and a strong CYP2D6 or CYP3A4 inhibitor for greater than 14 days should have their Abilify Maintena dose adjusted to 300 mg monthly. Aripiprazole is hepatically metabolized by both CYP2D6 and CYP3A4 isoenzymes and inhibition of metabolism may cause increased aripiprazole levels.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A	Util B	Util C **(Negating)**	
Aripiprazole 400 mg	Ketoconazole	Atazanavir	Tipranavir
	Itraconazole	Darunavir	Zileuton
	Posaconazole	Diltiazem	Celecoxib
	Voriconazole	Verapamil	Oral Contraceptives
	Saquinavir	Imatinib	Desvenlafaxine
	Ritonavir	Aprepitant	Methadone
	Indinavir	Ciprofloxacin	Diphenhydramine
	Nelfinavir	Erythromycin	Escitalopram
	Boceprevir	Alprazolam	Febuxostat
	Telaprevir	Amiodarone	Gefitinib
	Nefazodone	Amlodipine	Hydralazine
	Clarithromycin	Atorvastatin	Hydroxychloroquine
	Telithromycin	Bicalutamide	Imatinib
	Quinidine	Cilostazol	Propafenone
	Cinacalcet	Cimetidine	Sertraline
	Bupropion	Cyclosporine	Mirabegron
	Fluoxetine	Fluvoxamine	Clobazam
	Paroxetine	Isoniazid	Duloxetine
		Ranitidine	Terbinafine
		Ranolazine	

References:

Abilify Maintena Prescribing Information, Feb 2013, Otsuka America Pharmaceuticals, Inc.

FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionLabeling/ucm093664.htm

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

32. Abilify Maintena 400 mg / CYP3A4 inhibitors / CYP2D6 Inhibitors ____/____ _____ _____

Alert Message: Patients taking 400 mg of Abilify Maintena (aripiprazole extended-release injection) and a CYP2D6 plus a CYP3A4 inhibitor for greater than 14 days should have their Abilify Maintena dose adjusted to 200 mg monthly. Aripiprazole is hepatically metabolized by both CYP2D6 and CYP3A4 isoenzymes and inhibition of metabolism may cause increased aripiprazole levels.

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

Util A	Util B		Util C (Include)	
Aripiprazole 400 mg	Ketoconazole	Alprazolam	Quinidine	Sertraline
	Itraconazole	Amiodarone	Cinacalcet	Mirabegron
	Posaconazole	Amlodipine	Bupropion	Clobazam
	Voriconazole	Atorvastatin	Fluoxetine	
	Saquinavir	Cilostazol	Paroxetine	
	Ritonavir	Bicalutamide	Duloxetine	
	Indinavir	Cimetidine	Terbinafine	
	Nelfinavir	Cyclosporine	Amiodarone	
	Atazanavir	Fluoxetine	Celecoxib	
	Darunavir	Fluvoxamine	Oral contraceptives	
	Diltiazem	Isoniazid	Desvenlafaxine	
	Verapamil	Ranitidine	Methadone	
	Imatinib	Ranolazine	Diphenhydramine	
	Aprepitant	Tipranavir	Escitalopram	
	Boceprevir	Zileuton	Febuxostat	
	Telaprevir		Gefitinib	
	Nefazodone		Hydralazine	
	Clarithromycin		Hydroxychloroquine	
	Telithromycin		Imatinib	
	Ciprofloxacin		Propafenone	

References:

Abilify Maintena Prescribing Information, Feb 2013, Otsuka America Pharmaceuticals, Inc.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionLabeling/ucm093664.htm

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

33. Abilify Maintena 300 mg / Strong CYP3A4 & CYP2D6 Inh/Negate Other CYP3A4 & 2D6 Inhibitors ___√_____ _____ _____

Alert Message: Patients taking 300 mg of Abilify Maintena (aripiprazole extended-release injection) and a strong CYP2D6 or CYP3A4 inhibitor for greater than 14 days should have their Abilify Maintena dose adjusted to 200 mg monthly. Aripiprazole is hepatically metabolized by both CYP2D6 and CYP3A4 isoenzymes and inhibition of metabolism may cause increased aripiprazole levels.

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

Util A	Util B	Util C **(Negating)**	
Aripiprazole 300 mg	Ketoconazole	Atazanavir	Tipranavir
	Itraconazole	Darunavir	Zileuton
	Posaconazole	Diltiazem	Celecoxib
	Voriconazole	Verapamil	Oral Contraceptives
	Saquinavir	Imatinib	Desvenlafaxine
	Ritonavir	Aprepitant	Methadone
	Indinavir	Ciprofloxacin	Diphenhydramine
	Nelfinavir	Erythromycin	Escitalopram
	Boceprevir	Alprazolam	Febuxostat
	Telaprevir	Amiodarone	Gefitinib
	Nefazodone	Amlodipine	Hydralazine
	Clarithromycin	Atorvastatin	Hydroxychloroquine
	Telithromycin	Bicalutamide	Imatinib
	Quinidine	Cilostazol	Propafenone
	Cinacalcet	Cimetidine	Sertraline
	Bupropion	Cyclosporine	Mirabegron
	Fluoxetine	Fluvoxamine	Clobazam
	Paroxetine	Isoniazid	Duloxetine
		Ranitidine	Terbinafine
		Ranolazine	

References:
Abilify Maintena Prescribing Information, Feb 2013, Otsuka America Pharmaceuticals, Inc.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at:
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionLabeling/ucm093664.htm

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

34. Abilify Maintena 300 mg / CYP3A4 Inhibitors / CYP2D6 Inhibitors ___√___ _____ _____

Alert Message: Patients taking 300 mg of Abilify Maintena (aripiprazole extended-release injection) and a CYP2D6 inhibitor plus a CYP3A4 inhibitor for greater than 14 days should have their Abilify Maintena dose adjusted to 160 mg monthly. Aripiprazole is hepatically metabolized by both CYP2D6 and CYP3A4 isoenzymes and inhibition of metabolism may cause increased aripiprazole levels.

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

Util A	Util B		Util C (Include)	
Aripiprazole 300 mg	Ketoconazole	Alprazolam	Quinidine	Sertraline
	Itraconazole	Amiodarone	Cinacalcet	Mirabegron
	Posaconazole	Amlodipine	Bupropion	Clobazam
	Voriconazole	Atorvastatin	Fluoxetine	
	Saquinavir	Cilostazol	Paroxetine	
	Ritonavir	Bicalutamide	Duloxetine	
	Indinavir	Cimetidine	Terbinafine	
	Nelfinavir	Cyclosporine	Amiodarone	
	Atazanavir	Fluoxetine	Celecoxib	
	Darunavir	Fluvoxamine	Oral contraceptives	
	Diltiazem	Isoniazid	Desvenlafaxine	
	Verapamil	Ranitidine	Methadone	
	Imatinib	Ranolazine	Diphenhydramine	
	Aprepitant	Tipranavir	Escitalopram	
	Boceprevir	Zileuton	Febuxostat	
	Telaprevir	Ciprofloxacin	Gefitinib	
	Nefazodone		Hydralazine	
	Clarithromycin		Hydroxychloroquine	
	Telithromycin		Imatinib	
	Erythromycin		Propafenone	

References:
Abilify Maintena Prescribing Information, Feb 2013, Otsuka America Pharmaceuticals, Inc.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at:
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionLabeling/ucm093664.htm

35. Voriconazole / Efavirenz Tablets - Single Entity ___√___ _____ _____

Alert Message: If Sustiva (efavirenz) is co-administered with Vfend (voriconazole), the voriconazole maintenance dose should be increased to 400 mg q12h and the efavirenz dose should be decreased to 300 mg q24h using the capsule formulation. Efavirenz tablets should not be broken. Concurrent use of these agents at standard doses poses the risk for voriconazole therapeutic failure and increased efavirenz-related toxicities.

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

Util A	Util B	Util C
Voriconazole	Efavirenz 600 mg Tablet	

References:
Vfend Prescribing Information, Oct. 2011, Pfizer Inc.
Sustiva Prescribing Information, Aug. 2012, Bristol-Myers Squibb.

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

36. Voriconazole / Atripla ___√___ _____ _____

Alert Message: Coadministration of Vfend (voriconazole) with Atripla (efavirenz/ emtricitabine/tenofovir) is contraindicated because Atripla is a fixed-dose combination product and the dose of efavirenz cannot be altered. Concurrent use of these agents at standard doses poses the risk for voriconazole therapeutic failure and increased efavirenz-related toxicities.

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

Util A	Util B	Util C
Voriconazole	Efavirenz/Emtricitabine/Tenofovir	

References:
Vfend Prescribing Information, Oct. 2011, Pfizer Inc.
Atripla Prescribing Information, June 2012, Gilead Science, Inc.
Facts & comparisons, 2013 Updates, Wolters Kluwer Health.

37. Varenicline / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: The safety and effectiveness of Chantix (varenicline) have not been established in patients less than 18 years of age.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Varenicline		

Age Range: 0 – 17 yoa

References:
Chantix Prescribing Information, February 2013, Pfizer Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

38. Varenicline / Overuse ___√___ _____ _____

Alert Message: Chantix (varenicline) may be over-utilized. The manufacturer's maximum recommended dose is 1 mg two times a day for 12 to 24 weeks.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Varenicline		Renal Impairment

Max Dose: 2 mg/day

References:
Chantix Prescribing Information, February 2013, Pfizer Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

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

39. Varenicline / Renal Impairment ___√___ _____ _____

Alert Message: Chantix (varenicline) may be over-utilized. In patients with severe renal impairment (CrCl < 30mL/min), the manufacturer's maximum recommended dose is 0.5 mg two times a day. Patients with end-stage renal disease undergoing hemodialysis may use up to 0.5 mg daily if tolerated.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C (Include)
Varenicline		Renal Impairment

Max Dose: 1 mg/day

References:
Chantix Prescribing Information, February 2013, Pfizer Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

40. Varenicline / Neuropsychiatric Events / Black Box Warning ___√___ _____ _____

Alert Message: Serious neuropsychiatric events have been reported in patients taking Chantix (varenicline). If a patient develops agitation, hostility, depressed mood, changes in behavior or thinking, or if the patient develops suicidal ideation or suicidal behavior while taking or shortly after discontinuing varenicline, the medication should be discontinued and the patient should be monitored and offered supportive care.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Varenicline		

References:
Chantix Prescribing Information, February 2013, Pfizer Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

41. Varenicline / Angioedema and Hypersensitivity Reactions ___√___ _____ _____

Alert Message: In patients treated with Chantix (varenicline), there have been postmarketing reports of hypersensitivity reactions including angioedema. Clinical signs include swelling of the face, mouth, extremities and neck. Patients should discontinue varenicline and immediately seek medical care if they experience these symptoms.

Conflict Code: MC – Drug/Diagnosis Precaution/Warning/Contraindication Drugs/Diseases

Util A	Util B	Util C
Varenicline	Angioedema	
	Hypersensitivity reaction	

References:
Chantix Prescribing Information, February 2013, Pfizer Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

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

42. Varenicline / Skin Reactions ___√___ _____ _____

Alert Message: In patients treated with Chantix (varenicline), there have been postmarketing reports of rare but serious skin reactions, including Stevens-Johnson Syndrome and erythema multiforme. Patients should stop taking varenicline immediately at the first appearance of a skin rash with mucosal lesions or any other signs of hypersensitivity.

Conflict Code: TA – Therapeutic Appropriateness

Util A	Util B	Util C
Varenicline		

References:
Chantix Prescribing Information, February 2013, Pfizer Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

43. Darunavir / Pediatric Patients (0-2 yoa) ___√___ _____ _____

Alert Message: Prezista (darunavir) should not be used in pediatric patients below 3 years of age in view of toxicity and mortality observed in animal trials. In juvenile rats, single doses of darunavir (at ages 5-11 days) or multiple doses of darunavir (at age 12 days) caused mortality. The exposures and toxicity profile in the older animals (day 23 or day 26) were comparable to those observed in adult rats. Due to uncertainties regarding the rate of development of the human blood-brain barrier and liver enzymes, darunavir should not be given to patients below 3 years of age.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Darunavir		

Age Range: 0 – 2 yoa

References:
Prezista Prescribing Information. February 2013. Janssen Products, LP.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

*Clozapine Tabs & Oral Suspension are separated because prescribing information has specific dosing limits for new oral suspension.

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

44. Clozapine Tabs & ODT / CYP1A2, 2D6 & 3A4 Inhibitors ___√___ _____ _____

Alert Message: Caution should be exercised when prescribing a clozapine-containing agent with a CYP1A2, 2D6 or 3A4 inhibitor. Clozapine is primarily metabolized by these 3 isoenzymes and inhibition of clozapine metabolism may lead to increased serum concentrations and risk of clozapine-related adverse effects. Clozapine dose adjustment may be needed when starting or stopping an inhibitor.

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

Util A	Util B		Util C
Clozapine Tabs & ODT	Ciprofloxacin	Nefazodone	Verapamil
	Methoxsalen	Boceprevir	Diltiazem
	Mexiletine	Telaprevir	Nicardipine
	Zileuton	Clarithromycin	Danazol
	Ciprofloxacin	Telithromycin	
	Fluvoxamine	Erythromycin	
	Cimetidine	Ketoconazole	
	Oral Contraceptives	Itraconazole	
	Bupropion	Posaconazole	
	Quinidine	Voriconazole	
	Fluoxetine	Fluconazole	
	Paroxetine	Saquinavir	
	Duloxetine	Ritonavir	
	Citalopram	Indinavir	
	Escitalopram	Nelfinavir	
	Sertraline	Atazanavir	
	Cinacalcet	Fosamprenavir	
	Terbinafine	Imatinib	

References:
Clozaril Prescribing Information, March 2013, Novartis Pharmaceuticals Corporation.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Facts & Comparisons, 2013 Updates Wolters Kluwer Health.
FazaClo Prescribing Information, Nov. 2011, Jazz Pharmaceuticals Commercial Corp.

45. Clozapine Tabs & ODT / CYP1A2, 2D6 & 3A4 Inducers ___√___ _____ _____

Alert Message: Caution should be exercised when prescribing a clozapine-containing agent with a CYP1A2, 2D6 or 3A4 inducer. Clozapine is primarily metabolized by these 3 isoenzymes and induction of clozapine metabolism may lead to decreased serum concentrations and reduced efficacy.

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

Util A	Util B		Util C
Clozapine Tabs & ODT	Carbamazepine	Efavirenz	
	Phenytoin	Etravirine	
	Phenobarbital	Modafinil	
	Rifampin	Ticlopidine	
	Rifabutin	Primidone	
	Rifapentine	Dexamethasone	
	Bosentan	Oxcarbazepine	
	Montelukast		

References:
Clozaril Prescribing Information, March 2013, Novartis Pharmaceuticals Corporation.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
FazaClo Prescribing Information, Nov. 2011, Jazz Pharmaceuticals Commercial Corp.

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

46. Clozapine Oral Suspension / Strong CYP1A2 Inhibitors ___√___ _____ _____

Alert Message: Concurrent use of a strong CYP1A2 inhibitor with Versacloz (clozapine oral suspension) may result in increased serum concentration of clozapine and risk of clozapine-related adverse effects. The manufacturer recommends that the clozapine oral suspension dose should be reduced to one third the original dose during co-administration with a strong CYP1A2 inhibitor.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Versacloz	Fluvoxamine	
	Ciprofloxacin	

References:
Versacloz Prescribing Information, Feb. 2013, Novartis Pharmaceuticals Corporation.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at:
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Drug\InteractionLabeling/ucm093664.htm

47. Clozapine Oral Suspension / Weak or Moderate CYP1A2 Inhibitors ___√___ _____ _____

Alert Message: Concurrent use of a moderate or weak CYP1A2 inhibitor with Versacloz (clozapine oral suspension) may result in increased serum concentrations of clozapine and risk of clozapine-related adverse effects. Monitor patient for adverse reactions and consider reducing the clozapine oral suspension dose if necessary.

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

Util A	Util B	Util C
Versacloz	Methoxsalen	
	Mexiletine	
	Oral Contraceptives	
	Zileuton	

References:
Versacloz Prescribing Information, Feb. 2013, Novartis Pharmaceuticals Corporation.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at:
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Drug\InteractionLabeling/ucm093664.htm

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

48. Clozapine Oral Suspension / CYP2D6 & CYP3A4 Inhibitors ____√____ _____ _____

Alert Message: Concurrent use of CYP2D6 or CYP3A4 inhibitors with Versacloz (clozapine oral suspension) can result in increased serum concentrations of clozapine and risk of clozapine-related adverse effects. Monitor patient for adverse reactions and consider reducing the clozapine oral suspension dose if necessary.

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

Util A	Util B	Util C
Versacloz	Cimetidine	Ketoconazole
	Bupropion	Itraconazole
	Quinidine	Posaconazole
	Fluoxetine	Voriconazole
	Paroxetine	Fluconazole
	Duloxetine	Saquinavir
	Citalopram	Ritonavir
	Escitalopram	Indinavir
	Sertraline	Nelfinavir
	Cinacalcet	Atazanavir
	Terbinafine	Fosamprenavir
	Nefazodone	Imatinib
	Boceprevir	Verapamil
	Telaprevir	Diltiazem
	Clarithromycin	Nicardipine
	Telithromycin	Danazol
	Erythromycin	

References:
Versacloz Prescribing Information, Feb. 2013, Novartis Pharmaceuticals Corporation.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at:
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Drug\InteractionLabeling/ucm093664.htm

49. Clozapine Oral Suspension / CYP1A2 & CYP3A4 Inducers ____√____ _____ _____

Alert Message: Concurrent use of Versacloz (clozapine oral suspension) with a moderate or weak CYP1A2 or CYP3A4 inducer may result in decreased clozapine plasma concentrations and loss of clozapine efficacy. The concomitant use of clozapine suspension and a strong CYP3A4 inducer is not recommended. It may be necessary to increase the clozapine dose during co-administration with an inducer and reduce the clozapine dose if discontinuing the inducer.

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

Util A	Util B	Util C
Versacloz	Carbamazepine	
	Phenytoin	
	Phenobarbital	
	Rifampin	
	Rifapentine	
	Rifabutin	
	Bosentan	
	Efavirenz	
	Etravirine	
	Nevirapine	
	Modafinil	
	Oxcarbazepine	

References:
Versacloz Prescribing Information, Feb. 2013, Novartis Pharmaceuticals Corporation.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at:
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Drug\InteractionLabeling/ucm093664.htm

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

50. Bydureon / Insulins ___√___ _____ _____

Alert Message: The concurrent use of Bydureon (extended-release exenatide) with insulin has not been studied and cannot be recommended.

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

Util A	Util B	Util C
Bydureon	Insulins	

References:
Bydureon Prescribing Information, Jan. 2012, Amylin Pharmaceuticals, Inc.

51. Canagliflozin / CKD Stage 3, 4 & 5, ESRD & Dialysis-Negating ___√___ _____ _____

Alert Message: The recommended starting dose of Invokana (canagliflozin) is 100 mg once daily taken before the first meal of the day. For patients who have an eGFR of 60 mL/min/1.73 m^2 or greater and require additional glycemic control, the dose can be increased to a maximum of 300 mg once daily. Monitor renal function during canagliflozin therapy.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C (Negating)
Canagliflozin		CKD Stage 3, 4 & 5 ESRD Dialysis

Max Dose: 300 mg/day

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

52. Canagliflozin / CKD Stage 3 ___√___ _____ _____

Alert Message: The dose of Invokana (canagliflozin) is limited to 100 mg daily in patients with moderate renal impairment with an eGFR of 45 to less than 60 mL/min/1.73 m^2. Renal function should be monitored frequently during canagliflozin therapy and canagliflozin discontinued when eGFR is persistently less than 45 mL/min/1.73 m^2.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C (Include)
Canagliflozin		CKD Stage 3

Max Dose: 100 mg/day

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

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

53. Canagliflozin / Stage 4 & 5 CKD ___√___ _____ _____

Alert Message: Invokana (canagliflozin) is contraindicated in patients with severe renal impairment (eGFR less than 30 mL/min/1.73 m^2), end stage renal disease or patients on dialysis. Canagliflozin is not expected to be effective in these patient populations.

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

Util A	Util B	Util C
Canagliflozin	CKD Stage 4 & 5	
	ESRD	
	Dialysis	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

54. Canagliflozin / Hypotension, Hypovolemia Dehydration & CKD State 3 ___√___ _____ _____

Alert Message: Invokana (canagliflozin) can cause symptomatic hypotension after initiating therapy. Patients at risk are those with dehydration or hypovolemia, impaired renal function (eGFR < 60mL/min/1.73 m^2), the elderly, patients with low systolic blood pressure or if on diuretics, an ACEI, or ARB. Monitor patient for signs and symptoms after initiating therapy.

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

Util A	Util B	Util C
Canagliflozin	Hypotension	
	Hypovolemia	
	Dehydration	
	CKD Stage 3	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

55. Canagliflozin / Diuretics, ACEIs & ARBs ___√___ _____ _____

Alert Message: Invokana (canagliflozin) can cause symptomatic hypotension after initiating therapy. Patients at risk are those with dehydration or hypovolemia, impaired renal function (eGFR < 60 mL/min/1.73 m^2), the elderly, patients with low systolic blood pressure or if on diuretics, an ACEI, or ARB. Monitor patient for signs and symptoms after initiating therapy.

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

Util A	Util B	Util C
Canagliflozin	ACEIs	
	ARBs	
	Aliskiren	
	Diuretics	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

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

56. Canagliflozin / Hyperkalemia ___√___ _____ _____

Alert Message: Invokana (canagliflozin) can cause hyperkalemia. Monitor serum potassium levels periodically after initiating canagliflozin in patients with impaired renal function and in patients predisposed to hyperkalemia due to medication or other medical conditions.

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

Util A	Util B	Util C
Canagliflozin	Hyperkalemia	
	CKD Stage 3	
	Heart Failure	
	Addison's Disease	
	SLE	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

57. Canagliflozin / Hyperkalemia Inducing Drugs ___√___ _____ _____

Alert Message: Invokana (canagliflozin) can cause hyperkalemia. Monitor serum potassium levels periodically after initiating canagliflozin in patients with impaired renal function and in patients predisposed to hyperkalemia due to medication or other medical conditions.

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

Util A	Util B	Util C
Canagliflozin	Potassium-Sparing Diuretics	
	ACEIs	
	ARBs	
	Aliskiren	
	Eplerenone	
	Drospirenone	
	NSAIDS	
	Cyclosporine	
	Potassium	
	Tacrolimus	
	Trimethoprim	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

58. Canagliflozin / Insulin & Insulin Secretagogues ___√___ _____ _____

Alert Message: The concurrent use of Invokana (canagliflozin) with insulin and insulin secretagogues 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 canagliflozin.

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

Util A	Util B	Util C
Canagliflozin	Insulins	
	Sulfonylureas	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

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

59. Canagliflozin / LDL-C Increases ___√___ _____ _____

Alert Message: The use of Invokana (canagliflozin) can cause dose-related increases in LDL-C levels. Patients receiving canagliflozin 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
Canagliflozin		

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

60. Canagliflozin 100mg / UGT Inducers ___√___ _____ _____

Alert Message: Concurrent use of Invokana (canagliflozin) with a UGT inducer may result in decreased canagliflozin exposure and loss of efficacy. Consider increasing the canagliflozin dose to 300 mg once daily in patients currently taking 100 mg once daily who have an eGFR of 60 mL/min/1.73m^2 or greater and require additional glycemic control. Consider another antihyperglycemic agent in patients with an eGFR of 45 to less than 60 mL/min/1.73m^2 receiving concurrent therapy with a UGT inducer.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A	Util B	Util C
Canagliflozin 100 mg	Rifampin	
	Phenytoin	
	Phenobarbital	
	Ritonavir	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

61. Canagliflozin 300mg / UGT Inducers ___√___ _____ _____

Alert Message: Concurrent use of Invokana (canagliflozin) with a UGT 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

Util A	Util B	Util C
Canagliflozin 300 mg	Rifampin	
	Phenytoin	
	Phenobarbital	
	Ritonavir	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

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

62. Canagliflozin / Digoxin ___√___ _____ _____

Alert Message: The concurrent use of Invokana (canagliflozin) with digoxin may result in increased AUC and Cmax of digoxin. Patients taking canagliflozin with concomitant digoxin should be monitored appropriately.

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

Util A	Util B	Util C
Canagliflozin	Digoxin	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

63. Canagliflozin / Therapeutic Appropriateness ___√___ _____ _____

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

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Canagliflozin		

Age Range: 0-17 yoa

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

64. Canagliflozin / Liver Disease ___√___ _____ _____

Alert Message: The use of Invokana (canagliflozin) has not been studied in patients with severe hepatic impairment and is therefore not recommended. No dosage adjustment is necessary in patients with mild or moderate hepatic impairment.

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

Util A	Util B	Util C
Canagliflozin	Cirrhosis	
	Chronic Liver Disease	
	Necrosis of the Liver	

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

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

65. Canagliflozin / Pregnancy / Miscarriage, Abortion, Delivery Negating ___√_____ _____ _____

Alert Message: Invokana (canagliflozin) should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. No adequate and well-controlled studies of canagliflozin use in pregnant women have been conducted. Canagliflozin is classified as pregnancy category C.

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

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

References:
Invokana Prescribing Information, March 2013, Janssen Pharmaceuticals, Inc.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

66. Ezogabine / FDA Safety Warning ___√_____ _____ _____

Alert Message: Potiga (ezogabine) can cause blue skin discoloration and eye abnormalities characterized by pigment changes in the retina. All patients taking ezogabine or about to start ezogabine should have an eye exam, followed by periodic eye exams thereafter. Discontinue ezogabine if ophthalmic changes are observed unless no other treatment options are available. If skin discoloration develops give serious consideration to changing to an alternative medication.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Ezogabine		

References:
FDA Drug Safety Communication: Antiseizure Drug Potiga (ezogabine) Linked to Retinal Abnormalities and Blue Skin Discoloration. [04/26/2013].
Available at: http://www.fda.gov/Drugs/DrugSafety/ucm349538.htm

Stephanie McGee Azar, Acting Commissioner (X) Approve ( ) Deny 9-16-13 Date

Robert Moon, M.D., Deputy Commissioner and Medical Director (X) Approve ( ) Deny 9-13-13 Date

Kathy Hall, Deputy Commissioner (X) Approve ( ) Deny 9/10/13 Date