

**Alabama Medicaid DUR Board Meeting Minutes  
July 27, 2016**

**Members Present:** Kelli Littlejohn Newman, Melinda Rowe, Paula Thompson, P.J. Hughes, Marilyn Bulloch, Dan McConaghy, Donald Kern, Christopher Randolph, Frank Pettyjohn, Denyse Thornley-Brown

**Also Present:** Tiffany Minnifield, Lori Thomas, Clemice Hurst, Kristin Marvin, Jessica Dickson

**Present via Conference Call:** Kristian Testerman, Lauren Ward, Samir Hadid, Amy Donaldson, Michelle Stiles, Tammy Dubac, Holley Rice, Elaine Alexander, Lisa Channell

**Members Absent:** Sandra Parker, Bernie Olin, Chris Phung, Robert Moon

**Call to Order:** The DUR meeting was called to order by P. Thompson at approximately 1:02p.m.

**Review and Adoption of Minutes:** The minutes of the July 27, 2016 meeting were presented and P. Thompson made a motion to approve the minutes. F. Pettyjohn seconded the motion and the motion was approved unanimously.

**Prior Authorization and Overrides Update:** L. Thomas began the Prior Authorization and Overrides Update with the Monthly Manual Prior Authorizations and Overrides Report for the month of January 2016. She reported 9,361 total manual requests and 23,589 total electronic requests. From the Prior Authorization and Override Response Time Ratio report for January 2016, L. Thomas reported that approximately 42% of all manual PAs and 36% of all overrides were completed in less than two hours. Seventy-four percent of all manual PAs and 76% of all overrides were completed in less than four hours. Ninety-two percent of all manual PAs and 91% of all overrides were completed in less than eight hours. For the month of February 2016, L. Thomas reported 9,798 manual PA requests and 21,439 electronic PA requests were received. She reported that 61% of all manual PAs and all overrides were completed in less than two hours. Eighty-six percent of all manual PAs and 88% of all overrides were completed in less than four hours. Ninety-three percent of all manual PAs and 94% of all overrides were completed in less than eight hours. For the month of March 2016, L. Thomas reported 10,227 manual PA requests and 20,974 electronic PA requests. L. Thomas reported that approximately 59% of all manual PAs and 54% of all overrides were completed in less than two hours. Eighty-five percent of all manual PA requests and 84% of all overrides were completed in less than four hours. Ninety-three percent of all manual PA requests and all overrides were completed in less than eight hours.

**Program Summary Review:** L. Thomas briefly reviewed the Alabama Medicaid Program Summary for the months of October 2015 through March 2016. She reported 4,081,230 total prescriptions, 229,533 average recipients per month using pharmacy benefits, and an average paid per prescription of \$96.90.

**Cost Management Analysis:** L. Thomas reported an average cost per claim of \$100.12 for March 2016 and emphasized that the table contained the average cost per claim over the past two years. M. Bulloch asked about the increased costs of medications over the past two years. K. Newman replied that the cost of medications has continued to increase over the past few years. She also reminded the Board of the prescription limit and how that shifted costs to the more expensive medications, and she mentioned that the newer Hepatitis C antiviral medications have increased costs, as well. K. Newman informed the Board of an informative presentation from the Medicaid Commissioner that reviewed historical trends of the pharmacy program. From the 1<sup>st</sup> Quarter 2016 Drug Analysis, L. Thomas reported 78.9% generic utilization, 10.1% brand single-source, 7.2% brand multi-source (those requests which required a DAW override), and 3.8% OTC and "other". From the Top 25 Drugs Based on Number of Claims from 01/01/2016-03/31/2016, L. Thomas reported the top five drugs: amoxicillin, hydrocodone-acetaminophen, cetirizine, ProAir<sup>®</sup> HFA, and azithromycin. L. Thomas then reported the top five drugs

from the Top 25 Drugs Based on Claims Cost from 01/01/2016-03/31/2016: Vyvanse<sup>®</sup>, Focalin XR<sup>®</sup>, Harvoni<sup>®</sup>, Invega<sup>®</sup> Sustenna<sup>®</sup>, and aripiprazole. 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, Respiratory and CNS Stimulants, Miscellaneous Anticonvulsants, and Respiratory Tract Corticosteroids.

**Review of Palivizumab Utilization for the 2015-2016 Season:** The 2015-2016 RSV season ended March 31, 2016. L. Thomas provided an update which compared the results of the 2015-16 season to previous seasons. L. Thomas referred to Alabama RSV data from the CDC which supported Alabama Medicaid's policy of limiting the Synagis<sup>®</sup> timeframe to October 2015 – March 2016. L. Thomas reminded the Board that each recipient could receive a maximum of 5 doses per season and that all policies relating to Synagis<sup>®</sup> were based on clinical literature and recommendations. L. Thomas informed the Board that effective January 1, 2016, palivizumab could only be dispensed by pharmacies and physicians' offices could no longer buy and bill. For the 2015-16 season, there were 2,413 claims for 489 recipients. The average cost per claim was \$2,318 while the average cost per recipient was \$11,436. L. Thomas pointed out that there were 1,348 prior authorizations requested over the course of the season, with an approval rate of 72%. L. Thomas briefly reviewed the top dispensing pharmacies and the top PA denial reasons. L. Thomas reviewed the graphs comparing the total spend of all drugs compared to the total spend of Synagis<sup>®</sup> per RSV season.

**RDUR Intervention Report:** L. Thomas presented the RDUR Activity Report for January 2016. She reported 649 profiles reviewed and 815 letters sent with 125 responses received as of the date of the report. She reported 59 of 99 physicians indicated that they found the RDUR letters "useful" or "extremely useful". The criteria for the cycle of intervention letters included Drug-Drug Interaction (increased risk of serotonin syndrome) and Appropriate Use (concurrent use of buprenorphine and pure opiate agonists). L. Thomas then presented the RDUR Activity Report for February 2016. She reported 650 profiles reviewed and 637 letters sent with 51 responses received as of the date of the report. She reported 18 of 30 physicians indicated that they found the RDUR letters "useful" or "extremely useful". The criteria for the cycle of intervention letters included Appropriate Use (adverse metabolic effects of atypical antidepressants); Hepatitis C SVR Response Rates; Appropriate Use (concurrent use of buprenorphine and pure opiate agonists). The March 2016 Activity Report indicated 674 profiles reviewed and 594 letters sent with 77 responses received as of the date of the report. L. Thomas reported 35 of 57 physicians indicated that they found the RDUR letters "useful" or "extremely useful". The criteria for the cycle of intervention letters were Underuse Precaution (statin adherence); Hepatitis C SVR Response Rates; Appropriate Use (concurrent use of buprenorphine and pure opiate agonists).

**Proposed Criteria:** L.Thomas presented the proposed set of 48 criteria to the Board. T.Minnifield instructed the Board members to mark their ballots. Of the 48 criteria, results from the criteria vote returned 47 approved and 1 approved as amended.

**Medicaid Update:** T. Minnifield reminded the Board members that all Medicaid information discussed is available online. T. Minnifield reminded the Board that every July the Board would vote on a Vice Chair and asked the members to mark their ballots and pass them to the front. Results of the vote elected Dr. Marilyn Bulloch as Vice Chair. The current Vice Chair, Dr. Frank Pettyjohn will begin his term as Chairman of the board beginning with the October 2016 meeting.

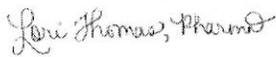
**New Business:** K. Newman briefly reviewed the budget shortfall and the potential impact to Alabama Medicaid. She informed the Board that Governor Bentley had called a special session to address state funding issues. D. Kern asked if there had been any new discussion regarding opioid utilization. K. Newman responded that there is still discussion between the Alabama Department of Public Health and Alabama Medicaid to allow Medicaid access to PDMP data. L. Thomas mentioned that methadone began requiring a prior authorization on July 1, 2016. K. Newman added that this was due to guidance released from CMS.

**P & T Committee Update:** C. Hurst began the P & T Update by informing the Board that the last meeting was held on May , 2016 and covered the Alzheimer's Agents; Antidepressants; Cerebral Stimulants for ADHD; Wakefulness Promoting Agents; Anxiolytics, Sedatives, and Hypnotics; Genitourinary Smooth Muscle Relaxants; and Disease-Modifying Antirheumatic Agents. C. Hurst also discussed the PDL changes that were effective July 1, 2016 and explained the Preferred with Clinical Criteria classes (Hepatitis C medications and DMARDs). She also provided background related to CMS guidance on methadone and the PA requirement. The next P & T meeting is scheduled for August 10, 2016, at 9am and will cover the Skin and Mucous Membrane Agents and drug reviews of Daklinza™ and Zepatier™.

**Next Meeting Date:** P. Thompson notified the Board that the next DUR meeting will be held on October 26, 2016.

The meeting was adjourned at 2:02 p.m.

Respectfully submitted,

A handwritten signature in cursive script that reads "Lori Thomas, PharmD".

Lori Thomas, Pharm

**ALABAMA MEDICAID  
RETROSPECTIVE DRUG UTILIZATION REVIEW  
CRITERIA RECOMMENDATIONS**

**Criteria Recommendations**

*Accepted Approved Rejected  
As  
Amended*

**1. Synjardy / Overutilization**

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Alert Message: Synjardy (empagliflozin/metformin) may be over-utilized. The manufacturer's maximum recommended dose of empagliflozin/metformin is 12.5/1000 mg twice daily.

Conflict Code: ER - Overutilization  
Drugs/Diseases

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

Max Dose: 25/2000 mg/day

References:  
Synjardy Prescribing Information, August 2015, Boehringer Ingelheim Pharmaceuticals.

**2. Synjardy / Mild Renal Impairment**

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Alert Message: Assessment of renal function is recommended prior to initiation of Synjardy (empagliflozin/metformin) and periodically thereafter. Do not initiate or continue empagliflozin/metformin in patients with serum creatinine levels greater than or equal to 1.5 mg/dL for males and 1.4 mg/dL for females. In patients eligible for empagliflozin/metformin based on creatinine cutoff criteria, do not initiate or continue empagliflozin/metformin 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/metformin		CKD Stage 1 & 2

References:  
Synjardy Prescribing Information, August 2015, Boehringer Ingelheim Pharmaceuticals.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**3. Synjardy / Mod to Sev. Renal Impairment, ESRD & Dialysis**

Alert Message: Synjardy (empagliflozin/metformin) use is contraindicated in patients with renal impairment (e.g., serum creatinine levels greater than or equal to 1.5 mg/dL for males or 1.4 mg/dL for females, or eGFR less than 45 mL/min/1.73m<sup>2</sup>), end-stage renal disease, or patients 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

Util A

Util B

Util C (Include)

Empagliflozin/metformin

CKD Stage 3, 4 & 5

ESRD

Dialysis

References:

Synjardy Prescribing Information, August 2015, Boehringer Ingelheim Pharmaceuticals.

**4. Synjardy / Therapeutic Appropriateness (Age 0-17 yoa)**

Alert Message: The safety and effectiveness of Synjardy (empagliflozin/metformin) 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/metformin

Age Range 0 - 17 yoa

References:

Synjardy Prescribing Information, August 2015, Boehringer Ingelheim Pharmaceuticals.



**7. Alirocumab / Overutilization**

\_\_\_\_✓\_\_\_\_

Alert Message: Praluent (alirocumab) may be over-utilized. The recommended starting dose of alirocumab is 75 mg administered subcutaneously once every 2 weeks. If the LDL-C response is inadequate, the dosage may be increased to the maximum dosage of 150 mg administered every 2 weeks.

Conflict Code: ER - Overutilization

Drugs/Diseases

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

Max Dose: 150 mg every 2 weeks

References:

Praluent Prescribing Information, July 2015, Sanofi.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**8. Alirocumab / Statin Therapy (Negating)**

\_\_\_\_✓\_\_\_\_

Alert Message: A review of the patient’s drug history does not reveal the concurrent use of a statin with Praluent (alirocumab). Alirocumab is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease who require additional lowering of LDL-cholesterol.

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>
Alirocumab		Lovastatin Fluvastatin Pravastatin Simvastatin Atorvastatin Rosuvastatin Pitavastatin

References:

Praluent Prescribing Information, July 2015, Sanofi.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**9. Alirocumab / Pediatric Use**

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Alert Message: The safety and efficacy of Praluent (alirocumab) in pediatric patients have not been established.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C

Alirocumab

Age Range: 0-18 yoa

References:

Praluent Prescribing Information, July 2015, Sanofi.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**10. Alirocumab / Nonadherence**

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Alert Message: Based on refill history, your patient may be under-utilizing Praluent (alirocumab). 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 - Nonadherence

Drugs/Diseases

Util A

Util B

Util C

Alirocumab

References:

Praluent Prescribing Information, July 2015, Sanofi.  
Osterberg L, Blaschke T. Adherence to Medication. N Eng Jrnl Med. 2005;353:487-97.  
Iuga AO, McGuire MJ. Adherence and Health Care Costs. Risk Manag Healthc Policy. 2014 Feb 20;7:35-44.

**11. Evolocumab / Overutilization**

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Alert Message: Repatha (evolocumab) may be over-utilized. The recommended dosage of evolocumab in patients with primary hyperlipidemia with established clinical atherosclerotic cardiovascular disease(CVD) is either 140 mg administered subcutaneously every 2 weeks OR 420 mg once monthly. The recommended dosage of evolocumab in patients with homozygous familial hypercholesterolemia (HoFH) is 420 mg once monthly.

Conflict Code: ER - Overutilization

Drugs/Diseases

Util A

Util B

Util C

Evolocumab

Max Dose: 420 mg per month

References:

Repatha Prescribing Information, August 2015, Amgen Medical Information.

**12. Evolocumab / Statin and Ezetimibe Therapy (Negating)**

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Alert Message: A review of the patient's drug history does not reveal the concurrent use of adjunct lipid lowering therapy with Repatha (evolocumab). Evolocumab is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (CVD), who require additional lowering of low density lipoprotein cholesterol (LDL-C). For the treatment of patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C evolocumab is indicated as an adjunct to diet and other LDL-lowering therapies.

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>	
Evolocumab		Lovastatin	Atorvastatin
		Fluvastatin	Rosuvastatin
		Pravastatin	Pitavastatin
		Simvastatin	Ezetimibe

References:

Repatha Prescribing Information, August 2015, Amgen Medical Information.

**13. Evolocumab / Pediatric Use**

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Alert Message: Repatha (evolocumab) should be used with caution in pediatric patients. The safety and effectiveness of evolocumab have not been established in pediatric patients with homozygous familial hypercholesterolemia (HoFH) who are younger than 13 years old nor in pediatric patients with primary hyperlipidemia or heterozygous familial hypercholesterolemia (HeFH).

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

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

Age Range: 0 - 12 yoa

References:

Repatha Prescribing Information, August 2015, Amgen Medical Information.

**14. Evolocumab / Nonadherence**

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Alert Message: Based on refill history, your patient may be under-utilizing Repatha (evolocumab). 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 - Nonadherence

Drugs/Diseases

Util A

Util B

Util C

Evolocumab

References:

Repatha Prescribing Information, August 2015, Amgen Medical Information.

Osterberg L, Blaschke T. Adherence to Medication. N Eng Jnl Med. 2005;353:487-97.

Iuga AO, McGuire MJ. Adherence and Health Care Costs. Risk Manag Healthc Policy. 2014 Feb 20;7:35-44.

**15. Metformin / Dolutegravir**

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Alert Message: With concomitant use of a metformin-containing agent and a dolutegravir-containing agent, limit the total daily dose to 1000 mg of metformin either when starting metformin or dolutegravir. When stopping dolutegravir, the metformin dose may require an adjustment. Dolutegravir inhibits elimination of metformin via the renal cation transporter OCT2 resulting in increased metformin exposure.

Conflict Code: ER – Overutilization

Drugs/Diseases

Util A

Util B

Util C (Include)

Metformin

Dolutegravir

Max dose metformin: 1000 mg/day

References:

Tivicay Prescribing Information, August 2015, ViiV healthcare.

Clinical Pharmacology, 2015 Elsevier/Gold Standard.

Triumeq Prescribing Information, August 2015, ViiV healthcare.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**16. Flibanserin / Overutilization**

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Alert Message: Addyi (flibanserin) may be over-utilized. The manufacturer’s recommended maximum daily dose of flibanserin is 100 mg once daily at bedtime. Flibanserin is dosed at bedtime because administration during waking hours increases the risk of hypotension, syncope, accidental injury, and central nervous system depression.

Conflict Code: ER - Overutilization

Drugs/Diseases

Util A

Util B

Util C

Flibanserin

Max dose: 100 mg/day

References:

Addyi Prescribing Information, August 2015, Sprout Pharmaceuticals, Inc.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**17. Flibanserin / Alcohol Use, Abuse & Dependence**

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Alert Message: The use of Addyi (flibanserin) and alcohol is contraindicated due to the increased risk of severe hypotension and syncope.

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

Drugs/Diseases

Util A

Util B

Util C

Flibanserin

Alcohol Use

Alcohol Dependence

Alcohol Abuse

References:

Addyi Prescribing Information, August 2015, Sprout Pharmaceuticals, Inc.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**18. Flibanserin / Moderate to Strong CYP3A4 Inhibitors** \_\_\_√\_\_\_

Alert Message: The concurrent use of Addyi (flibanserin) with a moderate to strong CYP3A4 inhibitor is contraindicated due to the risk of severe hypotension and syncope. If initiating flibanserin following moderate or strong CYP3A4 inhibitor use, start flibanserin 2 weeks after the last dose of the inhibitor. If initiating a moderate or strong CYP3A4 inhibitor following flibanserin use, start the inhibitor 2 days after the last dose of flibanserin.

Conflict Code: DD – Drug/Drug Interaction (Black Box Warning)

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>			<u>Util C</u>
Flibanserin	Nefazodone	Voriconazole	Nelfinavir	Diltiazem
	Clarithromycin	Fluconazole	Atazanavir	Erythromycin
	Telithromycin	Boceprevir	Fosamprenavir	Imatinib
	Ketoconazole	Saquinavir	Verapamil	Cobicistat
	Itraconazole	Ritonavir	Aprepitant	Crizotinib
	Posaconazole	Indinavir	Ciprofloxacin	

References:

Addyi Prescribing Information, August 2015, Sprout Pharmaceuticals, Inc.

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

**19. Flibanserin / Hepatic Impairment** \_\_\_√\_\_\_

Alert Message: The use of Addyi (flibanserin) in patients with any degree of hepatic impairment is contraindicated. Flibanserin primarily undergoes hepatic metabolism and hepatic impairment significantly increases flibanserin concentrations which can lead to severe hypotension and syncope.

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

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Flibanserin	Hepatic Impairment	

References:

Addyi Prescribing Information, August 2015, Sprout Pharmaceuticals, Inc.

Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**20. Flibanserin / CNS Depressants**

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Alert Message: The concurrent use of Addyi (flibanserin) with CNS depressants may increase the risk of CNS depression (e.g., somnolence and sedation) compared to the use of flibanserin alone.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Flibanserin	Sedatives Anxiolytics Narcotics Muscle Relaxants Sedating Antihistamines Antidepressants Antipsychotics	

References:

Addyi Prescribing Information, August 2015, Sprout Pharmaceuticals, Inc.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**21. Flibanserin / Weak CYP3A4 Inhibitors**

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Alert Message: Caution should be exercised when prescribing Addyi (flibanserin), a CYP3A4 substrate, with multiple weak CYP3A4 inhibitors due to the increased risk for flibanserin-related adverse effects. Patients who are receiving flibanserin with multiple CYP3A4 inhibitors should be counseled about and monitored for adverse reactions (e.g., hypotension, syncope, and somnolence).

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Flibanserin	Alprazolam Amiodarone Amlodipine Atorvastatin Cilostazol Cimetidine Fluoxetine	Nilotinib Zileuton Bicalutamide Oral Contraceptives Ranitidine Cyclosporine Ranolazine Cyclosporine Isoniazid Ticagrelor

References:

Addyi Prescribing Information, August 2015, Sprout Pharmaceuticals, Inc.  
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at:  
<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionalabeling/ucm093664.htm>  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**22. Flibanserin / Strong CYP2C19 Inhibitors**

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Alert Message: Caution should be exercised when prescribing Addyi (flibanserin), a CYP2C19 substrate, with strong CYP2C19 inhibitors due to the increased risk for flibanserin-related adverse effects. Patients who are receiving flibanserin with a strong CYP2C19 inhibitor should be counseled about and monitored for adverse reactions (e.g., hypotension, syncope, and somnolence).

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Flibanserin	Fluvoxamine	
	Ticlopidine	
	Omeprazole	
	Esomeprazole	

References:

Addyi Prescribing Information, August 2015, Sprout Pharmaceuticals, Inc.  
 Li XQ, Andersson TB, Ahlstrom M, Weidolf L. Comparison of Inhibitory Effects of the Proton Pump-Inhibiting Drugs Omeprazole, Esomeprazole, Lansoprazole, Pantoprazole, and Rabeprazole on Human Cytochrome Activities. *Drug Metab Dispos.* 2001 Aug;32(8):821-7.  
 FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at: <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Drug\InteractionalLabeling/ucm093664.htm>  
 Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**23. Flibanserin / CYP3A4 Inducers**

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Alert Message: Concurrent use of Addyi (flibanserin) with CYP3A4 inducers is not recommended. Flibanserin is a CYP3A4 substrate and concomitant use with a CYP3A4 inducer may result in substantially decreased flibanserin exposure and decreased efficacy.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Flibanserin	Carbamazepine	Bosentan
	Phenytoin	Efavirenz
	Phenobarbital	Etravirine
	Primidone	Modafinil
	Rifampin	Nevirapine
	Rifapentine	Oxcarbazepine
	Rifabutin	

References:

Addyi Prescribing Information, August 2015, Sprout Pharmaceuticals, Inc.  
 Clinical Pharmacology, 2015 Elsevier/Gold Standard.  
 FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at: <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Drug\InteractionalLabeling/ucm093664.htm>

**24. Flibanserin / P-gp Substrates** \_\_\_✓\_\_\_

Alert Message: The concurrent use of Addyi (flibanserin) with a P-gp substrate may result in increased P-gp substrate concentrations due to flibanserin inhibition of P-gp transport. Increased monitoring of concentrations of drugs transported by P-gp that have a narrow therapeutic index is recommended.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Flibanserin	Digoxin	
	Sirolimus	
	Tacrolimus	
	Dabigatran	

References:

Addyi Prescribing Information, August 2015, Sprout Pharmaceuticals, Inc.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**25. Sonidegib / Overutilization** \_\_\_✓\_\_\_

Alert Message: Odomzo (sonidegib) may be over-utilized. The manufacturer’s recommended maximum daily dose is 200 mg.

Conflict Code: ER - Overutilization

Drugs/Diseases

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

Max Dose: 200 mg/day

References:

Odomzo Prescribing Information, July 2015, Novartis Pharmaceuticals Corporation.

**26. Sonidegib / Strong CYP3A4 Inhibitors** \_\_\_✓\_\_\_

Alert Message: Avoid concomitant administration of Odomzo (sonidegib) with a strong CYP3A4 Inhibitor. Sonidegib is a CYP3A4 substrate and concurrent use with a strong CYP3A4 inhibitor may significantly increase sonidegib exposure and risk of sonidegib-related adverse effects, particularly musculoskeletal toxicity.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

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

References:

Odomzo Prescribing Information, July 2015, Novartis Pharmaceuticals Corporation.

**27. Sonidegib / Moderate CYP3A4 Inhibitors**

\_\_\_✓\_\_\_ \_\_\_ \_\_\_

Alert Message: The concomitant administration of Odomzo (sonidegib) with a moderate CYP3A4 inhibitor should be avoided. Sonidegib is a CYP3A4 substrate and concurrent use with a moderate CYP3A4 inhibitor may significantly increase sonidegib exposure. If a moderate CYP3A4 inhibitor must be used, administer the moderate inhibitor for less than 14 days and monitor closely for adverse reactions, particularly musculoskeletal adverse reactions.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Sonidegib	Atazanavir	Fluconazole
	Aprepitant	Fosamprenavir
	Ciprofloxacin	Imatinib
	Diltiazem	Verapamil
	Erythromycin	

References:

Odomzo Prescribing Information, July 2015, Novartis Pharmaceuticals Corporation.

**28. Sonidegib / Strong & Moderate CYP3A4 Inducers**

\_\_\_✓\_\_\_ \_\_\_ \_\_\_

Alert Message: The concomitant administration of Odomzo (sonidegib) with a strong or moderate CYP3A4 inducer should be avoided. Sonidegib is a CYP3A4 substrate and concurrent use with one of these CYP3A4 inducers may result in significantly reduced sonidegib exposure and decreased therapeutic effect.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Sonidegib	Phenobarbital	Bosentan
	Primidone	Efavirenz
	Phenytoin	Etravirine
	Carbamazepine	Modafinil
	Rifabutin	Oxcarbazepine
	Rifapentine	
	Rifampin	

References:

Odomzo Prescribing Information, July 2015, Novartis Pharmaceuticals Corporation.



**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**32. Tiotropium/Olodaterol / Overutilization**

  ✓                      

Alert Message: The manufacturer's recommended dose of Stiolto Respimat (tiotropium/olodaterol) is 2 inhalations once-daily. Do not use tiotropium/olodaterol inhalation more than two inhalations every 24 hours. Clinically significant cardiovascular effects and fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs.

Conflict Code: ER – Overutilization

Drugs/Diseases

Util A

Util B

Util C

Tiotropium/Olodaterol

Max Dose: 2 inhalations/day (5mcg tiotropium/ 5mcg olodaterol)

References:

Stiolto Respimat Prescribing Information, June 2015, Boehringer Ingelheim Pharmaceuticals, Inc.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**33. Tiotropium/Olodaterol / Black Box Warning**

  ✓                      

Alert Message: Stiolto Respimat (tiotropium/olodaterol) is a combination agent which contains a long-acting beta-2 adrenergic agonist (LABA) and all LABAs increase the risk of asthma-related death. The safety and efficacy of olodaterol in patients with asthma have not been established. Olodaterol is not indicated for the treatment of asthma.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C

Tiotropium/Olodaterol

References:

Stiolto Respimat Prescribing Information, June 2015, Boehringer Ingelheim Pharmaceuticals, Inc.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**34. Tiotropium/Olodaterol / Cardiovascular, Convulsive Disorders,  
Diabetes & Thyrotoxicosis**

     ✓               

Alert Message: Stiolto Respimat (tiotropium/olodaterol) should be used with caution in patients with cardiovascular or convulsive disorders, thyrotoxicosis, or sensitivity to sympathomimetic drugs. The olodaterol component of the combination product is a sympathomimetic amine and can exacerbate these conditions.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Tiotropium/Olodaterol	Hypertension Arrhythmias Heart Failure Diabetes Seizures Epilepsy	

References:  
Stiolto Respimat Prescribing Information, June 2015, Boehringer Ingelheim Pharmaceuticals, Inc.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

35. Tiotropium/Olodaterol / MAOIs, TCAs & Other QTc Prolonging Meds   

Alert Message: Stiolto Respimat (tiotropium/olodaterol) should be administered with extreme caution to patients being treated with MAOIs, TCAs, or drugs known to prolong the QTc interval because the action of the adrenergic agonist, olodaterol, on the cardiovascular system may be potentiated by these agents.

Conflict Code: DD –Drug/Drug Interactions

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>				<u>Util C</u>
Tiotropium/Olodaterol	Albuterol	Disopyramide	Imipramine	Pazopanib	Thioridazine
	Alfuzosin	Dofetilide	Indapamide	Pentamidine	Tizanidine
	Amantadine	Dolasetron	Isradipine	Pimozide	Tolterodine
	Amiodarone	Doxepin	Itraconazole	Posaconazole	Trazodone
	Amitriptyline	Dronedarone	Ketoconazole	Procainamide	TMP/SMZ
	Amphetamine	Droperidol	Lapatinib	Propafenone	Trimipramine
	Arsenic Trioxide	Ephedrine	Levalbuterol	Protriptyline	Vandetanib
	Asenapine	Epinephrine	Levofloxacin	Quetiapine	Vardenafil
	Atazanavir	Erythromycin	Lithium	Quinidine	Venlafaxine
	Atomoxetine	Escitalopram	Metaproterenol	Ranolazine	Ziprasidone
	Azithromycin	Felbamate	Methadone	Risperidone	Zolmitriptan
	Chloral Hydrate	Flecainide	Moexipril/HCTZ	Ritonavir	Ezogabine
	Chloroquine	Fluconazole	Moxifloxacin	Salmeterol	Isocarboxazid
	Chlorpromazine	Fluoxetine	Nicardipine	Saquinavir	Phenelzine
	Ciprofloxacin	Foscarnet	Nilotinib	Sertraline	Iloperidone
	Citalopram	Fosphenytoin	Norfloxacin	Solifenacin	Linezolid
	Clarithromycin	Galantamine	Nortriptyline	Sotalol	Rasagiline
	Clomipramine	Gemifloxacin	Octreotide	Sunitinib	
	Clozapine	Granisetron	Ofloxacin	Tacrolimus	
	Dasatinib	Haloperidol	Ondansetron	Tamoxifen	
	Desipramine	Ibutilide	Paliperidone	Telithromycin	
	Diphenhydramine		Paroxetine	Terbutaline	

## References:

Clinical Pharmacology, 2015 Elsevier/Gold Standard.

Stiolto Respimat Prescribing Information, June 2015, Boehringer Ingelheim Pharmaceuticals, Inc.

**36. Tiotropium/Olodaterol / Adrenergic Drugs** \_\_\_√\_\_\_

Alert Message: Caution should be exercised when Stiolto Respimat (tiotropium/olodaterol) is prescribed concurrently with other adrenergic sympathomimetic agents, administered by any route, because the sympathetic effects of the olodaterol component of the combination agent may be potentiated.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Tiotropium/Olodaterol	Ephedrine	Methamphetamine
	Epinephrine	Phendimetrazine
	Pseudoephedrine	Methylphenidate
	Phenylephrine	Amphetamine
	Albuterol	Dextroamphetamine
	Pirbuterol	Lisdexamfetamine
	Metaproterenol	Diethylpropion
	Terbutaline	Benzphetamine
		Phentermine

References:

Stiolto Respimat Prescribing Information, June 2015, Boehringer Ingelheim Pharmaceuticals, Inc.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**37. Tiotropium/Olodaterol / Nonselective  $\beta$ -Blockers / Selective  $\beta$ -Blockers** \_\_\_√\_\_\_

Alert Message: Concurrent use of a beta-adrenergic blocker with Stiolto Respimat (tiotropium/olodaterol) may diminish the pulmonary effect of olodaterol, the beta-agonist component in the combination product. Beta-blockers not only block the therapeutic effects of beta-agonists, but may produce severe bronchospasm in patients with asthma and COPD. If concomitant therapy cannot be avoided, consider a cardioselective beta-blocker, but administer with caution.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>
Tiotropium/Olodaterol	Carvedilol	Acebutolol
	Nadolol	Atenolol
	Labetalol	Betaxolol
	Penbutolol	Bisoprolol
	Pindolol	Metoprolol
	Propranolol	Nebivolol
	Sotalol	
	Timolol	

References:

Stiolto Respimat Prescribing Information, June 2015, Boehringer Ingelheim Pharmaceuticals, Inc.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

38. Tiotropium/Olodaterol / Xanthine Deriv., Steroids, & K+ Depl. Diuretics   ✓   \_\_\_\_\_

Alert Message: Caution should be exercised when Stiolto Respimat (tiotropium/olodaterol) is prescribed concurrently with xanthine derivatives, steroids, or non-potassium sparing diuretics because concomitant administration may potentiate the hypokalemic effect of olodaterol, the beta-agonist component of the combination agent. The ECG changes or hypokalemia that may result from the administration of non-potassium sparing diuretics can be acutely worsened by beta-agonists.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>		<u>Util C</u>
Tiotropium/Olodaterol	Theophylline	Prednisolone	Chlorothiazide
	Aminophylline	Prednisone	Chlorthalidone
	Dyphylline	HCTZ	
	Betamethasone	Indapamide	
	Budesonide	Methyclothiazide	
	Cortisone	Metolazone	
	Dexamethasone	Furosemide	
	Hydrocortisone	Bumetanide	
	Methylprednisolone	Torsemide	

References:

Stiolto Respimat Prescribing Information, June 2015, Boehringer Ingelheim Pharmaceuticals, Inc.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**39. Tiotropium/Olodaterol / Anticholinergic Agents**

\_\_\_\_√\_\_\_\_

Alert Message: The concurrent use of Stiolto Respimat (tiotropium/olodaterol) with other anticholinergic agents should be avoided. The tiotropium component of the combination product is an anticholinergic and concomitant use with other anticholinergics may lead to an increase in anticholinergic adverse effects.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Tiotropium/Olodaterol	Trihexyphenidyl Benztropine Orphenadrine Darifenacin Fesoterodine Flavoxate Oxybutynin Solifenacin Tolterodine Tropium Hyoscyamine Scopolamine Propantheline Glycopyrrolate Mepenzolate Methscopolamine Dicyclomine	

References:  
Stiolto Respimat Prescribing Information, June 2015, Boehringer Ingelheim Pharmaceuticals, Inc.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**40. Tiotropium/Olodaterol / Non-adherence**

\_\_\_\_√\_\_\_\_

Alert Message: Based on refill history, your patient may be under-utilizing Stiolto Respimat (tiotropium/olodaterol). 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 - Nonadherence  
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Tiotropium/Olodaterol		

References:  
Stiolto Respimat Prescribing Information, June 2015, Boehringer Ingelheim Pharmaceuticals, Inc.  
van Boven JF, Chavannes NH, van der Molen T, et al. Clinical and Economic Impact of Non-adherence in COPD: A Systematic Review. Respir Med. 2014 Jan;108(1):103-113.  
Restrepo RD, Alvarez MT, Wittnebel LD, et al., Medication Adherence Issues in Patients Treated for COPD. International Journal of COPD. 2008;3(3):371-384.  
Simoni-Wastila L, Wei Y, Qian J, et al., Association of Chronic Obstructive Pulmonary Disease Maintenance Medication Adherence With All-Cause Hospitalization and Spending in a Medicare Population. Am Jnl Geriatr Pharmacother. 2012 Jun;10(3):201-210.  
Lareau SC, Yawn BP. Improving Adherence with Inhaler Therapy in COPD. International Journal COPD. 2010 Nov 24;5:401-406.

**41. Disulfiram / Benzodiazepines Metabolized by Hepatic Oxidation**

  ✓        

Alert Message: Concurrent use of disulfiram with a benzodiazepine that undergoes hepatic oxidation may potentiate the pharmacologic and adverse effects of the benzodiazepine due to disulfiram inhibition of benzodiazepine metabolism. Dosage reduction of the benzodiazepine or changing to a benzodiazepine that is not cleared by hepatic oxidation (i.e., lorazepam or oxazepam) may be necessary.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Disulfiram	Alprazolam	
	Chlordiazepoxide	
	Clonazepam	
	Clorazepate	
	Diazepam	
	Estazolam	
	Flurazepam	
	Midazolam	
	Quazepam	
	Temazepam	
	Triazolam	

References:

Clinical Pharmacology, 2015 Elsevier/Gold Standard.  
 Facts & Comparisons, 2015 Updates, Wolters Kluwer Health, Inc.  
 Micromedex Healthcare Series, DrugDex Drug Evaluations, Truven Health Analytics.  
 Antabuse Prescribing Information, April 2012, Physicians Total Care, Inc.

**42. Tuzistra XR / Therapeutic Appropriateness**

  ✓        

Alert Message: Safety and effectiveness of Tuzistra XR (codeine/chlorpheniramine extended-release oral suspension) in pediatric patients under 18 years of age have not been established. The use of codeine in children has been associated with fatal respiratory depression.

Conflict Code: TA – Therapeutic Appropriateness

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Codeine/chlorpheniramine extended-release		

Age Range: 0-17 yoa

References:

Tuzistra XR Prescribing Information, April 2015, Vernalis Therapeutics, Inc.  
 Facts & Comparisons, 2015 Updates, Wolters Kluwer Health.



**45. Dextroamphetamine-Amphetamine / PPIs**

\_\_\_\_✓\_\_\_\_

Alert Message: Patients receiving dextroamphetamine/amphetamine IR or XR formulations with a proton pump inhibitor (PPI) should be monitored for changes in clinical efficacy. Concurrent use of these agents has been shown to decrease the Tmax of dextroamphetamine/amphetamine but have no effect on AUC or Cmax.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A

Dextroamphetamine/Amphetamine

Util B

Omeprazole  
Esomeprazole  
Lansoprazole  
Rabeprazole  
Pantoprazole

Util C

References:

Adderall Prescribing Information, Oct. 2015, Teva Pharmaceuticals USA.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**46. Vivlodex / Overutilization**

\_\_\_\_✓\_\_\_\_

Alert Message: Vivlodex (meloxicam) may be over-utilized. The manufacturer’s maximum recommended daily dose of this formulation of meloxicam is 10 mg per day. Exceeding the maximum dose may increase the risk of adverse events (e.g., heart attack, stroke, and gastrointestinal ulceration).

Conflict Code: ER - Overutilization

Drugs/Diseases

Util A

Meloxicam 5 mg & 10 mg

Util B

Util C

Max Dose: 10 mg/day

References:

Clinical Pharmacology, 2015 Elsevier/Gold Standard.  
Vivlodex Prescribing Information, Oct. 2015, Iroko Pharmaceuticals.

**47. Orlistat / Amiodarone**

\_\_\_\_\_✓\_\_\_\_\_

Alert Message: The concurrent use of orlistat (Alli and Xenical) and amiodarone may result in a reduction in exposure to amiodarone and its active metabolite, desethylamiodarone. Monitor patients for altered efficacy of amiodarone when orlistat is added or discontinued from their regimen.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Orlistat	Amiodarone	

References:

Xenical Prescribing Information, August 2015, Genentech.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**48. Orlistat / Antiepileptic Agents**

\_\_\_\_\_✓\_\_\_\_\_

Alert Message: Convulsions have been reported in patients treated concomitantly with orlistat (Alli and Xenical) and antiepileptic agents. Patients should be monitored for possible changes in frequency and/or severity of convulsions. A mechanism for the potential interaction has not been stated.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>			<u>Util C</u>
Orlistat	Clobazam	Lacosamide	Tiagabine	Clonazepam
	Lamotrigine	Topiramate	Clorazepate	Levetiracetam
	Valproic Acid	Diazepam	Oxcarbazepine	Vigabatrin
	Carbamazepine	Perampanel	Eslicarbazepine	Ezogabine
	Felbamate	Primidone	Gabapentin	Rufinamide
	Pregabalin	Ethosuximide	Ethotoin	Methsuximide
	Phenytoin	Zonisamide		

References:

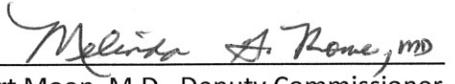
Xenical Prescribing Information, August 2015, Genentech.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.



Stephanie McGee Azar, Commissioner

Approve     Deny

9-22-16  
Date

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

*Assistant Medical Director*

Approve     Deny

9/14/16  
Date

  
Kathy Hall, Deputy Commissioner

Approve     Deny

9/15/16  
Date