

**Alabama Medicaid DUR Board Meeting Minutes  
April 22, 2015**

**Members Present:** Denyse Thornley-Brown, Kelli Littlejohn, Robert Moon, Paula Thompson, Bernie Olin, Frank Pettyjohn, Dan McConaghy, P.J. Hughes, Sandra Parker, Christopher Randolph

**Also Present:** Tiffany Minnifield, Clemice Hurst, Heather Vega, Lori Thomas, Kristin Marvin

**Present via Conference Call:** Kristian Testerman, Amy Donaldson, Lauren Ward

**Members Absent:** Marilyn Bulloch, Richard Glaze, Donald Kern, Chris Phung

**Call to Order:** The DUR meeting was called to order by D. Thornley-Brown at approximately 1:02p.m.

**Review and Adoption of Minutes:** The minutes of the January 28, 2015 meeting were presented and P. Thompson made a suggestion to update a sentence in the Cost Management Analysis. F. Pettyjohn made a motion to approve the update and S. Parker seconded the motion. The motion was approved unanimously. P. Thompson asked if concurrent use of buprenorphine and pure opiate agonist criteria were reviewed for each period indicated. L. Thomas reminded the Board that this criterion was reviewed during every RDUR cycle.

**Prior Authorization and Overrides Update:** L. Thomas began the Prior Authorization and Overrides Update with the Monthly Manual Prior Authorizations and Overrides Report for the month of October 2014. She reported 9,716 total manual requests. She then reported 21,390 electronic requests for the same time frame. From the Prior Authorization and Override Response Time Ratio report for October 2014, L. Thomas reported that approximately 39% of all manual PAs and 32% of all overrides were responded to in less than two hours. Seventy percent of all manual PAs and 64% of all overrides were responded to in less than four hours. Ninety-four percent of all manual PAs and 91 % of all overrides were responded to in less than eight hours. For the month of November 2014, L. Thomas reported 8,172 manual PA requests and 18,498 electronic PA requests. She reported that 30% of manual PAs and 29% of overrides were responded to in less than two hours and 66% of all manual PA requests and 60% of all override requests were completed in less than four hours. Ninety-one percent of all manual PAs and 90% of all overrides were responded to in less than eight hours. For the month of December 2014, L. Thomas reported 8,481 manual PA requests and 18,911 electronic PA requests. L. Thomas reported over 38% of requests was completed in less than two hours, 74-76% in less than four hours, and 99% completed in less than eight hours.

**Program Summary Review:** L. Thomas briefly reviewed the Alabama Medicaid Program Summary. She reported 3,693,252 total prescriptions, 226,195 average recipients per month using pharmacy benefits and an average paid per prescription of \$85.15 for the months of July 2014 through December 2014.

**Cost Management Analysis:** L. Thomas reported an average cost per claim of \$87.92 for December 2014. L. Thomas reminded the Board members that the Maintenance Supply was phased in on October 1<sup>st</sup> and became mandatory on January 1, 2014. This includes 84-, 90-, and 91-day supplies. L. Thomas reported that an average cost per claim for a maintenance supply prescription was approximately \$40.00. From the 4<sup>th</sup> Quarter 2014 Drug Analysis, L. Thomas reported 78.5% generic utilization, 1.1.6% brand single-source, 6.4% brand multi-source (those requests which required a DAW override), and 3.5% OTC and "other". L. Thomas reminded the Board that OTC coverage was discontinued on October 1, 2013, but that OTC insulin and nutritional are still covered. From the Top 25 Drugs Based on Number of Claims from 10/01/2014-12/31/2014, L. Thomas reported the top five drugs: amoxicillin, hydrocodone-acetaminophen, ProAir<sup>®</sup> HFA, azithromycin, and cetirizine. L. Thomas emphasized that the hydrocodone

claims had reduced by almost 11,000 claims. She then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 10/01/2014-12/31/2014: Abilify®, Vyvanse®, Tamiflu®, Invega® Sustenna®, and Adderall XR®. 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, Corticosteroids (Respiratory Tract), Hemostatics, and Respiratory and Miscellaneous Anticonvulsants.

## UPDATES

**Hydrocodone Utilization:** L. Thomas presented a summary of prescriber responses received from the top 100 prescribers of hydrocodone focused intervention letter distributed by the Academic Detailers. L. Thomas stated that 39 responses had been returned. P. Thompson asked where the majority of the prescribers who returned a summary were ranked. L. Thomas said most of the responses were from providers who were ranked between one and fifty. P.J. Hughes then asked if there was a specific provider specialty that most prescribers fell under. L. Thomas replied that most prescribers fell under the specialty of general practitioner or internal medicine.

**RDUR Intervention Report:** L. Thomas presented the RDUR Activity Report for October 2014. She reported 722 profiles reviewed and 651 letters sent with 140 responses received as of the date of the report. She reported 74 of 118 physicians indicated that they found the RDUR letters “useful” or “extremely useful”. The criteria for the cycle of intervention letters included drug-drug interaction (colchicine and statins or fibric acid derivatives; combination of trazodone and CYP3A4 inhibitors); drug-disease interaction (use of pregabalin in patients with heart failure); overutilization (pregabalin overutilization; pregabalin use in patients with renal impairment); and appropriate use (concurrent use of buprenorphine and pure opiate agonist). L. Thomas then presented the RDUR Activity Report for November 2014. She reported 617 profiles reviewed and 557 letters sent with 86 responses received as of the date of the report. She reported 45 of 66 physicians indicated that they found the RDUR letters “useful” or “extremely useful”. The criteria for the cycle of intervention letters were therapeutic appropriateness (ACC/AHA Blood Cholesterol Guidelines) and appropriate use (concurrent use of buprenorphine and pure opiate agonist). The December 2014 Activity Report indicated 674 profiles reviewed and 751 letters sent with 156 responses received as of the date of the report. L. Thomas reported 86 of 122 physicians indicated that they found the RDUR letters “useful” or “extremely useful”. The criteria for the cycle of intervention letters were drug-disease interaction (stimulant use in patients with hypertension; stimulant use in patients with a history of drug abuse; stimulant use in patients with non-FDA approved diagnosis of obesity) and appropriate use (concurrent use of buprenorphine and pure opiate agonist).

**Proposed Criteria:** L. Thomas presented the proposed set of 35 criteria to the Board. T. Minnifield instructed the Board members to mark their ballots. Of the 35 criteria, results from the criteria vote returned 35 approved.

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

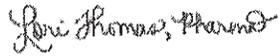
**P & T Committee Update:** C. Hurst began the P & T Update by informing the Board that the last meeting was held on February 11, 2014 and covered the First Generation Antihistamines, Estrogens, and Diabetic Agents. The next P and T meeting is scheduled for May 20, 2015, at 9am and will cover the Cardiac Agents and the Cholesterol-lowering Agents.

**New Business:** D. Thornley-Brown notified the Board that the next DUR meeting will be held on July 22, 2015. B. Olin asked if the Agency had noticed any changes due to hydrocodone rescheduling. K. Littlejohn mentioned that the decrease in claims was not as significant as expected. She also indicated that the Lock-in Program would be incorporated into the Health Homes. R. Moon told the Board that the Agency is looking into other state’s policies on opioid use. P. Thompson made a motion to adjourn the

meeting. The motion was seconded by P.J. Hughes. A voice vote to adjourn was unanimous. The meeting was adjourned at 2:20p.m.

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

Respectfully submitted,

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

Lori Thomas, PharmD

# ALABAMA MEDICAID RETROSPECTIVE DRUG UTILIZATION REVIEW CRITERIA RECOMMENDATIONS

## Criteria Recommendations

*Accepted Approved Rejected*  
*As*  
*Amended*

### 1. Triumeq / Non-adherence

Alert Message: Nonadherence to antiretroviral therapy may result in insufficient plasma levels and partial suppression of viral load leading to the development of resistance, HIV progression, and increased mortality.

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Conflict Code: LR – Non-adherence

Drugs/Diseases

Util A

Util B

Util C

Abacavir/dolutegravir/lamivudine

References:

Hoffman C, Mulcahy F, Goals and Principles of Therapy - Eradication, Cost, Prevention and Adherence. Hoffman C, Rockstroh J, Kamps BS, eds. HIV Medicine, Flying Publishers-Paris, Cagliari, Wuppertal, Sevilla, 2005:167-173.

Cheever LW, Chapter V: Adherence to HIV Therapies. In: A Guide to Clinical Care of Women with HIV/AIDS, 2005 Edition, HIV/AIDS Bureau, US Department of Health and Human Services.

<http://hab.hrsa.gov/publications/womencare05/WG05chap5.htm>

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents. Department of Health and Human Services. May 1, 2014.

Available at: <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>.

### 2. Triumeq / Overutilization

Alert Message: Triumeq (abacavir/dolutegravir/lamivudine) may be over-utilized. The manufacturer's maximum recommended dose of abacavir/dolutegravir/lamivudine in adults not receiving potent UGT1A/CYP3A inducers is one tablet daily.

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Conflict Code: ER - Overutilization

Drugs/Diseases

Util A

Util B

Util C

Abacavir/dolutegravir/lamivudine

Max Dose: 600mg/ 50mg/300mg per day

References:

Triumeq Prescribing Information, August 2014, ViiV Healthcare.

Clinical Pharmacology, 2014 Elsevier/Gold Standard.

### 3. Triumeq / UGT1A1 & CYP3A4 Inducers / Dolutegravir (Negating)

Alert Message: Concurrent use of Triumeq (abacavir/dolutegravir/lamivudine) with an efavirenz-containing agent, fosamprenavir/rtv, tipranavir/rtv, or rifampin may result in decreased dolutegravir plasma concentrations and loss of efficacy. If co-administration is necessary it is recommended that an additional dolutegravir 50 mg tablet separated by 12 hours from Triumeq should be taken.

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Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A

Util B

Util C (Negating)

Abacavir/dolutegravir/lamivudine

Efavirenz

Dolutegravir

Fosamprenavir/ritonavir

Tipranavir/ritonavir

Rifampin

References:

Triumeq Prescribing Information, August 2014, ViiV Healthcare.

Clinical Pharmacology, 2014 Elsevier/Gold Standard.



**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**7. Triumeq / Renal Impairment**

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Alert Message: Triumeq (abacavir/dolutegravir/lamivudine) use is not recommended for patients with impaired renal function (CrCl less than 50 mL/min). The fixed-dose combination agent contains lamivudine which requires dosage adjustment when CrCl is < 50 mL/min. If a dose reduction of lamivudine is required then the individual components should be used.

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C (Include)

Abacavir/dolutegravir/lamivudine

Renal Impairment

References:

Triumeq Prescribing Information, August 2014, ViiV Healthcare.

**8. Omalizumab / Therapeutic Appropriateness**

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Alert Message: A 5-year FDA safety review of Xolair (omalizumab) use found a potential for increased risk of serious cardiovascular and cerebrovascular events including heart attacks, TIA, pulmonary hypertension, and pulmonary embolism/venous thrombosis. Patients should be periodically reassessed for the need for continued therapy with omalizumab.

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C

Omalizumab

References:

Xolair Prescribing Information, September 2014, Genentech.

MedWatch: The FDA Safety Information and Adverse Event Reporting Program. Xolair (omalizumab): Drug Safety Communication – Slightly Elevated Risk of Cardiovascular and Cerebrovascular Serious Adverse Events. [09/26/2014].

**9. Atazanavir / Nevirapine**

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Alert Message: Concurrent use of Reyataz (atazanavir) with nevirapine is contraindicated. Both agents are CYP3A4 substrates. Nevirapine is a strong CYP3A4 inducer and use with atazanavir can result in substantially decreased atazanavir exposure which may lead to loss of therapeutic effect and development of resistance. Atazanavir is a CYP3A4 inhibitor and concurrent use may cause increased nevirapine exposure and risk of nevirapine adverse reactions.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A

Util B

Util C

Atazanavir

Nevirapine

References:

Clinical Pharmacology, 2014 Elsevier/Gold Standard

Facts & Comparisons, 2014 Updates, Wolters Kluwer Health.

Reyataz Prescribing Information, June 2014, Bristol-Myers Squibb.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**10. Alosetron / Fluvoxamine**

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Alert Message: Concurrent use of Lotronex (alosectron) with fluvoxamine is contraindicated due to the risk of significantly elevated alosetron plasma levels which may result in severe constipation. Fluvoxamine, a CYP3A4 & CYP1A2 inhibitor, has been shown to increase the AUC of alosetron, a CYP3A4 & CYP1A2 substrate, approximately 6-fold and prolong the half-life by 3-fold.

Conflict Code: DD – Drug/Drug Interaction  
Drugs/Diseases  
Util A                      Util B                      Util C  
AlosetronFluvoxamine

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

**11. Dulaglutide / Medullary Thyroid Cancer & MENS II**

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Alert Message: The use of Trulicity (dulaglutide), a glucagon-like peptide-1 (GLP-1) receptor agonist, is contraindicated in patients with a personal or family history of medullary thyroid carcinoma (MTC) or with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). GLP-1 receptor agonists have been shown to increase the incidence of thyroid C-cell tumors in rodents. Counsel patients regarding the risk of MTC and the symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, or persistent hoarseness).

Conflict Code: MC – Drug Disease Warning/Contraindication  
Drugs/Diseases:  
Util A                      Util B                      Util C (Include)  
Dulaglutide    Medullary Thyroid Cancer & MENS II

References:  
Trulicity Prescribing Information, Sept. 2014, Eli Lilly and Company.

**12. Dulaglutide / Black Box Warning**

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Alert Message: Trulicity (dulaglutide) is a glucagon-like peptide-1 (GLP-1) receptor agonist and GLP-1 agonists have been shown to cause thyroid C-cell tumors at clinically relevant exposure in rodents. It is unknown whether dulaglutide causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans. Counsel patients regarding the risk of medullary thyroid carcinoma and the symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, or persistent hoarseness).

Conflict Code: TA – Therapeutic Appropriateness  
Drugs/Diseases:  
Util A                      Util B                      Util C  
Dulaglutide

References:  
Trulicity Prescribing Information, Sept. 2014, Eli Lilly and Company.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**13. Dulaglutide / Pancreatitis**

Alert Message: In clinical trials, there were more cases of pancreatitis related adverse reactions among patients treated with Trulicity (dulaglutide) than placebo-treated. If pancreatitis is suspected, promptly discontinue dulaglutide and if confirmed dulaglutide should not be restarted. Consider other antidiabetic therapies in patients with a history of pancreatitis.

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Conflict Code: MC – Drug Disease Warning/Contraindication

Drugs/Diseases:

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Dulaglutide	Pancreatitis	

References:

Trulicity Prescribing Information, Sept. 2014, Eli Lilly and Company.

**14. Dulaglutide / Insulin & Insulin Secretagogues**

Alert Message: The risk of hypoglycemia is increased when Trulicity (dulaglutide) is used in combination with insulin secretagogues (e.g. sulfonylureas) or insulin. Therefore, patients may require a lower dose of sulfonylurea or insulin to reduce the risk of hypoglycemia in this setting.

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Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases:

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Dulaglutide	Insulins Chlorpropamide Glimepiride Glipizide Glyburide Tolazamide Tolbutamide	

References:

Trulicity Prescribing Information, Sept. 2014, Eli Lilly and Company.

**15. Dulaglutide / Renal Impairment**

Alert Message: Use caution when initiating or escalating doses of Trulicity (dulaglutide) in patients with renal impairment. Dulaglutide is a glucagon-like peptide-1 receptor (GLP-1) agonist and there have been postmarketing reports of acute renal failure and worsening of chronic renal failure in patients treated with these agents. No dosage adjustment is recommended in renal impairment but monitoring renal function is recommended in patients reporting severe adverse gastrointestinal reactions.

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Conflict Code: MC – Drug Disease Warning/Contraindication

Drugs/Diseases:

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Dulaglutide		Renal Impairment

References:

Trulicity Prescribing Information, Sept. 2014, Eli Lilly and Company.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**16. Dulaglutide / Severe Gastrointestinal Disorders**

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Alert Message: Trulicity (dulaglutide), a glucagon-like peptide-1 (GLP-1) receptor agonist, has not been studied and its use is not recommended in patients with pre-existing severe gastrointestinal disease, including severe gastroparesis. GLP-1 receptor agonists slow gastric emptying and can exacerbate gastrointestinal disorders.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Dulaglutide		Gastroparesis Irritable Bowel Syndrome Diverticular Disease Crohn’s Disease Ulcerative Colitis

References:

Trulicity Prescribing Information, Sept. 2014, Eli Lilly and Company.

**17. Dulaglutide / Therapeutic Appropriateness < 18 years of age**

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Alert Message: Safety and effectiveness of Trulicity (dulaglutide) have not been established in pediatric patients and dulaglutide use is not recommended in pediatric patients younger than 18 years of age.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

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

Age Range: 0-17 yoa

References:

Trulicity Prescribing Information, Sept. 2014, Eli Lilly and Company.

**18. Dulaglutide / Pregnancy / Delivery, Miscarriage & Abortion**

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Alert Message: There are no adequate and well-controlled studies of Trulicity (dulaglutide) in pregnant women. Dulaglutide is Pregnancy Category C and should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus.

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

Drugs/Diseases

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

Age Range: 11-55 yoa

Gender: Female

References:

Trulicity Prescribing Information, Sept. 2014, Eli Lilly and Company.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**19. Dulaglutide / Non-adherence**

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Alert Message: Non-adherence to Trulicity (dulaglutide) therapy may result in loss of glycemic control and an increased risk of developing adverse diabetic-related complications.

Conflict Code: LR – Non-adherence

Drugs/Diseases

Util A                      Util B                      Util C  
Dulaglutide

References:

Ho PM, Rumsfeld JS, Masoudi FA, et al., Effect of Medication Nonadherence on Hospitalization and Mortality Among Patients with Diabetes Mellitus. Arch Intern Med. 2006;166:1836-1841.  
Currie CJ, Peyrot M, Morgan CL, et al. The Impact of Treatment Noncompliance on Mortality in People With Type 2 Diabetes. Diabetes Care 35:1279-1284, June 2012.  
Butler RJ, Davis TK, Johnson WL, et al. Effects of Non adherence with Prescription Drugs Among Older Adults. Am J Manag Care. 2011 Feb; 17(2):153-60.

**20. Emsam / Therapeutic Appropriateness Age: 0-11 yoa**

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Alert Message: The use of EMSAM (selegiline transdermal) in patients under 12 years of age is contraindicated due to the potential for hypertensive crisis. Limited pharmacokinetic data with doses lower than commercially available formulations suggest that children under the age of 12 may be exposed to increased levels of selegiline compared to adolescents and adults.

Conflict Code: TA - Therapeutic Appropriateness (Black Box Warning)

Drugs/Diseases

Util A                      Util B                      Util C  
Selegiline Transdermal

Age Range: 0-11 yoa

References:

EMSAM Prescribing Information, September 2014, Mylan Specialty L.P.

**21. Emsam / Therapeutic Appropriateness Age 12 to17 yoa**

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Alert Message: Efficacy of EMSAM (selegiline transdermal) has not been established in pediatric patients ages 12 to 17 years with major depressive disorder (MDD) and therefore the agent is not recommended for use in this age range.

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

Util A                      Util B                      Util C  
Selegiline Transdermal

Age Range: 12 - 17 yoa

References:

EMSAM Prescribing Information, September 2014, Mylan Specialty L.P.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**22. Diclofenac/Misoprostol / Active GI Bleed**

Alert Message: Diclofenac/misoprostol is contraindicated in patients with active gastrointestinal bleeding.

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

Util A                      Util B                      Util C  
Diclofenac/Misoprostol      GI Bleed

References:

Arthrotec Prescribing Information, Sept. 2014, Pfizer.

**23. Varenicline / Therapeutic Appropriateness**

Alert Message: New and worsening seizures have been observed in patients taking Chantix (varenicline). Varenicline should be used with caution in patients with a history of seizures or other factors that can lower the seizure threshold. Advise patients to discontinue varenicline and contact the prescriber immediately if they experience a seizure while on varenicline.

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Conflict Code: TA -- Therapeutic Appropriateness  
Drugs/Diseases

Util A                      Util B                      Util C  
Varenicline

References:

Chantix Prescribing Information, Sept. 2014, Pfizer, Inc.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**24. Sofosbuvir / Overutilization**

Alert Message: The recommended dose of Sovaldi (sofosbuvir) is 400 mg taken once daily with or without food.

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Conflict Code: ER - Overutilization  
Drugs/Diseases

Util A                      Util B                      Util C  
Sofosbuvir

Max Dose: 400mg/day

References:

Sovaldi Prescribing Information, Dec. 2013, Gilead Science.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**25. Sofosbuvir / Ribavirin & Peginterferon Alfa (Negating)**

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Alert Message: Sovaldi (sofosbuvir) is not recommended as monotherapy. Sofosbuvir should be used in combination with ribavirin or in combination with peginterferon alfa and ribavirin for the treatment of chronic hepatitis C (CHC) in adults.

Conflict Code: TA – Therapeutic Appropriateness  
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>
Sofosbuvir		Ribavirin Peginterferon alfa

References:

Sovaldi Prescribing Information, Dec. 2013, Gilead Science.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**26. Sofosbuvir / Other P-gp Inducers**

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Alert Message: The concurrent use of Sovaldi (sofosbuvir) with a P-gp inducer is not recommended. Sofosbuvir is a P-gp substrate and co-administration of a P-gp inducer may result in decreased sofosbuvir plasma concentrations and reduced therapeutic effect of sofosbuvir.

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

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

References:

Sovaldi Prescribing Information, Dec. 2013, Gilead Science.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**27. Sofosbuvir / Tipranavir / Ritonavir**

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Alert Message: The concurrent use of Sovaldi (sofosbuvir) with ritonavir-boosted tipranavir is not recommended. Tipranavir is a P-gp inducer and co-administration with the P-gp substrate sofosbuvir may result in decreased sofosbuvir plasma concentrations and reduced therapeutic effect of sofosbuvir.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Sofosbuvir	Tipranavir	Ritonavir

References:

Sovaldi Prescribing Information, Dec. 2013, Gilead Science.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**28. Sofosbuvir / Therapeutic Appropriateness**

Alert Message: Safety and effectiveness of Sovaldi (sofosbuvir) in children less than 18 years of age have not been established.

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Conflict Code: TA – Therapeutic Appropriateness  
Drugs/Diseases

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

Age Range: 0-17 yoa

References:

Sovaldi Prescribing Information, Dec. 2013, Gilead Science.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**29. Fluconazole / CCBs**

Alert Message: Fluconazole is a moderate CYP3A4 inhibitor and concurrent use with a calcium channel blocker (CCB) may result in increased CCB plasma concentrations due to inhibition of the CYP3A4-mediated CCB metabolism by fluconazole. Frequent monitoring for CCB adverse effects is recommended.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Fluconazole	Verapamil Diltiazem Amlodipine Felodipine Isradipine Nicardipine Nifedipine Nimodipine Nisoldipine	

References:

Diflucan Prescribing Information, Oct. 2014, Pfizer.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**30. Itraconazole / Felodipine & Nisoldipine**

Alert Message: Concurrent use of itraconazole with felodipine or nisoldipine is contraindicated. Calcium channel blockers (CCBs) can have a negative inotropic effect and this may be additive to those of itraconazole. Felodipine and nisoldipine are CYP3A4 substrates and use with the potent CYP3A4 inhibitor itraconazole may result in increased CCB plasma concentrations.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Itraconazole	Felodipine Nisoldipine	

References:

Sporanox Prescribing Information, June 2014, Janssen Pharmaceuticals, Inc.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**31. Rosuvastatin 20 & 40mg / Teriflunomide**

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Alert Message: The dose of Crestor (rosuvastatin) should not exceed 10 mg once daily in patients concurrently taking Aubagio (teriflunomide) due to potential for additive hepatotoxicity. Co-administration of these two agents may result in increased rosuvastatin exposure due to inhibition of BCRP- and OATP1B1/B3- mediated transport by teriflunomide.

Conflict Code: DD-Drug Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Rosuvastatin 20	Teriflunomide	
Rosuvastatin 40		

References:

Aubagio Prescribing Information, Oct. 2014, Genzyme Corporation.

**32. Teriflunomide / BCRP & OATP1B1/B3 Substrates**

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Alert Message: Aubagio (teriflunomide) is a BCRP- and OATP1B1/B3 inhibitor and concomitant use with a BCRP and/or OATP1B1/B3 substrate may increase the substrate plasma concentrations. Consider reducing the dose of the substrate drug and monitor the patient closely for signs and symptoms of increased exposure to the substrate while taking teriflunomide.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>		<u>Util C</u>
Teriflunomide	Methotrexate	Simvastatin	Pitavastatin
	Rifampin	Pravastatin	Valsartan
	Repaglinide	Atorvastatin	
	Nateglinide	Fluvastatin	

References:

Aubagio Prescribing Information, Oct. 2014, Genzyme Corporation.

FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors and Inducers. Available at: <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionsLabeling/ucm093664.htm>  
Micromedex 2.0 DRUGDEX Drug Evaluations, 2014, Truven Health Analytics, Inc.

**33. Teriflunomide / OAT3 Substrates**

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Alert Message: Aubagio (teriflunomide) is an OAT3 transport inhibitor and use with an OAT3 substrate may increase the substrate plasma concentrations. Monitor the patient and adjust the dose of the concomitant OAT3 substrate as required.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Teriflunomide	Cefaclor	
	Cimetidine	
	Ciprofloxacin	
	Penicillin G	
	Ketoprofen	
	Furosemide	
	Zidovudine	

References:

Aubagio Prescribing Information, Oct. 2014, Genzyme Corporation.

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

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**34. Naftifine 2% Cream & Gel / Therapeutic Appropriateness Age**

Alert Message: The safety and effectiveness of Naftin 2% cream and gel (naftifine) have not been established in pediatric patients less than 12 year of age.

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Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C

Naftifine 2%

Age Range: 0-11 yoa

References:

Naftin Cream & Gel Prescribing Information, Oct. 2014, Merz Pharmaceuticals, LLC.  
Clinical Pharmacology, 2014 Elsevier/Gold Standard.

**35. Anagrelide / Hepatic Impairment**

Alert Message: Hepatic impairment increases anagrelide exposure and could increase the risk of QTc prolongation. In patients with moderate hepatic impairment anagrelide should be initiated at a dose of 0.5 mg/day and monitored frequently for cardiovascular events. If tolerated in these patients their dose can be increased but the increase increment should not exceed 0.5 mg/day in any one week. Avoid use of anagrelide in patients with severe hepatic impairment.

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Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C (Include)

Anagrelide

Hepatic Impairment

References:

Agrilyn Prescribing Information, Oct. 2014, Shire US, Inc.

Stephanie Azar  Approve ( ) Deny  
Stephanie McGee Azar, Acting Commissioner

5-28-15  
Date

Robert Moon  Approve ( ) Deny  
Robert Moon, M.D., Deputy Commissioner  
and Medical Director

5/26/15  
Date

Kathy Hall  Approve ( ) Deny  
Kathy Hall, Deputy Commissioner

5/22/15  
Date