

**Alabama Medicaid DUR Board Meeting Minutes**  
**October 26, 2016**

**Members Present:** Kelli Littlejohn Newman, Melinda Rowe, Dan McConaghy, Donald Kern, Christopher Randolph, Frank Pettyjohn, Denyse Thornley-Brown, Bernie Olin, Chris Phung

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

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

**Members Absent:** Robert Moon

**Call to Order:** The DUR meeting was called to order by F. Pettyjohn at approximately 1:04p.m.

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

**Prior Authorization and Overrides Update:** L. Thomas began the Prior Authorization and Overrides Update with the Monthly Manual Prior Authorizations and Overrides Report for the month of April 2016. She reported 9,516 total manual requests and 19,252 total electronic requests. From the Prior Authorization and Override Response Time Ratio report for April 2016, L. Thomas reported that approximately 56% of all manual PAs and 50% of all overrides were completed in less than two hours. Eighty percent of all manual PAs and 77% of all overrides were completed in less than four hours. Ninety percent of all manual PAs and 88% of all overrides were completed in less than eight hours. For the month of May 2016, L. Thomas reported 9,388 manual PA requests and 18,190 electronic PA requests were received. She reported that 59% of all manual PAs and 57% of all overrides were completed in less than two hours. Eighty-two percent of all manual PAs and 82% of all overrides were completed in less than four hours. Eighty-nine percent of all manual PAs and 90% of all overrides were completed in less than eight hours. For the month of June 2016, L. Thomas reported 9,941 manual PA requests and 18,627 electronic PA requests. L. Thomas reported that approximately 82% of all manual PAs and 83% of all overrides were completed in less than two hours. Ninety-two percent of all manual PA requests and 93% of all overrides were completed in less than four hours. Ninety-four percent of all manual PA requests and 95% of all overrides were completed in less than eight hours.

**Program Summary Review:** L. Thomas briefly reviewed the Alabama Medicaid Program Summary for the months of January 2016 through June 2016. She reported 3,830,376 total prescriptions, 230,202 average recipients per month using pharmacy benefits, and an average paid per prescription of \$100.53.

**Cost Management Analysis:** L. Thomas reported an average cost per claim of \$106.04 for June 2016 and emphasized that the table contained the average cost per claim over the past two 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. From the 1<sup>st</sup> Quarter 2016 Drug Analysis, L. Thomas reported 79.3% generic utilization, 9.6% brand single-source, 7.1% brand multi-source (those requests which required a DAW override), and 4% OTC and "other". From the Top 25 Drugs Based on Number of Claims from 04/01/16 – 06/30/2016, L. Thomas reported the top five drugs: amoxicillin, hydrocodone-acetaminophen, cetirizine, montelukast, and ProAir<sup>®</sup> HFA. L. Thomas then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 04/01/16 – 06/30/2016: Vyvanse<sup>®</sup>, Focalin XR<sup>®</sup>, Invega<sup>®</sup> Sustenna<sup>®</sup>, Harvoni<sup>®</sup>, and Adderall XR<sup>®</sup>. L. Thomas reminded the Board that Vyvanse<sup>®</sup>, Focalin XR<sup>®</sup>, and Adderall XR<sup>®</sup> are all preferred agents. From the Top 15 Therapeutic Classes by Total Cost of Claims for the same time frame,

L.Thomas reported the top five classes: Antipsychotic Agents, Amphetamines, Miscellaneous Anticonvulsants, Respiratory and CNS Stimulants, and Insulins.

**Review of Hepatitis C Utilization Data:** L. Thomas provided utilization data for each of the newer Hepatitis C antiviral medications. This information included the amount paid, number of claims, and number of recipients for the following medications: Daklinza®, Epclusa®, Harvoni®, Sovaldi®, Viekira PAK™, and Zepatier™. For each medication, L. Thomas also provided the number of approved prior authorizations, the number of denied prior authorizations, and the number of unique recipients.

**Review of Hepatitis C Informed Consent Form:** K. Newman began the Informed Consent form discussion by letting the Board know that the Agency strives to keep patient documents on a 7<sup>th</sup> grade level or below. The document included in the DUR Pack was a draft form covering the main topics and was open for Board review and input. L. Thomas added that the Academic Detailers could go over the form with prescribers and let the prescribers know the form must be attached to the PA form when submitted for review. After Board review and input, K. Newman asked the Board for a recommendation and vote. D. Thornley-Brown recommended the Board approve the form as amended. F. Pettyjohn seconded the motion and the motion was approved unanimously.

**RDUR Intervention Report:** L. Thomas presented the RDUR Activity Report for April 2016. She reported 700 profiles reviewed and 741 letters sent with 183 responses received as of the date of the report. She reported 108 of 160 physicians indicated that they found the RDUR letters “useful” or “extremely useful”. The criteria for the cycle of intervention letters included Drug-Disease Precaution (use of narcotics/opioids and osteoporosis); Therapeutic Appropriateness (use of narcotics/opioids and sickle cell disease); Drug-Drug Interactions (narcotics/opioids and benzodiazepines); Hepatitis C SVR Response Rates; and Appropriate Use (concurrent use of buprenorphine and pure opiate agonists). L. Thomas then presented the RDUR Activity Report for May 2016. She reported 693 profiles reviewed and 829 letters sent with 169 responses received as of the date of the report. She reported 86 of 128 physicians indicated that they found the RDUR letters “useful” or “extremely useful”. The criteria for the cycle of intervention letters included Therapeutic Duplication (anxiolytic and hypnotic agents); Therapeutic Duplication of NSAIDs; Hepatitis C SVR Response Rates; Appropriate Use (concurrent use of buprenorphine and pure opiate agonists). The June 2016 Activity Report indicated 779 profiles reviewed and 529 letters sent with 128 responses received as of the date of the report. L. Thomas reported 73 of 116 physicians indicated that they found the RDUR letters “useful” or “extremely useful”. The criteria for the cycle of intervention letters were Drug-Disease Precaution (stimulants and hypertension; stimulants and glaucoma; stimulants and anxiety; stimulants and obesity); Hepatitis C SVR Response Rates; Appropriate Use (concurrent use of buprenorphine and pure opiate agonists).

**Proposed Criteria:** L.Thomas presented the proposed set of 42 criteria to the Board. T.Minnifield instructed the Board members to mark their ballots. Of the 42 criteria, results from the criteria vote returned 42 approved.

**Medicaid Update:** T. Minnifield reminded the Board members that all Medicaid information discussed is available online. T. Minnifield informed the Board that F. Pettyjohn will be stepping down from Board duties after the January 2017 meeting.

**New Business:** K. Newman told the Board that two Regional Care Organizations (RCOs) notified the Agency that they will not move forward seeking certification. This will not affect services being performed under the current Health Home program.

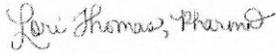
**P & T Committee Update:** C. Hurst began the P & T Update by informing the Board that the last meeting was held on August 10, 2016 and covered the Skin and Mucous Membrane Agents and new drug reviews for Daklinza® and Zepatier®. The next P & T meeting is scheduled for November 9, 2016, at

9 a.m. and will cover the Anti-infectives and new drug reviews for Praluent®, Eplusa®, and Viekira XR™. C. Hurst also told the Board that folic acid was added to the maintenance supply medications.

**Next Meeting Date:** F. Pettyjohn notified the Board that the next DUR meeting will be held on January 25<sup>th</sup>, 2017. A motion to accept the resignation of F. Pettyjohn was made by D. McConaghy. D. Thornley-Brown seconded the motion and the motion was approved unanimously.

The meeting was adjourned at 2:36 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. Eluxadoline / Overutilization**

Alert Message: The manufacturer's recommended maximum daily dose of Viberzi (eluxadoline) is 100 mg twice daily.

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Conflict Code: ER - Overutilization

Drugs/Diseases

Util A

Util B

Util C (Negating)

Eluxadoline

Hepatic Impairment	Telithromycin
Cyclosporine	Clarithromycin
Gemfibrozil	Cobicistat
Saquinavir	Rifampin
Ritonavir	
Lopinavir	
Atazanavir	
Tipranavir	

Max Dose: 200 mg/day

References:

Viberzi Prescribing Information, May 2015, Forest Pharmaceuticals, Inc.

**2. Eluxadoline / Hepatic Impairment**

Alert Message: The recommended maximum daily dose of Viberzi (eluxadoline) in patients with mild (Child Pugh Class A) to moderate (Child Pugh Class B) hepatic impairment is 75 mg twice daily. Eluxadoline plasma concentrations can increase by 4- and 6-fold, respectively, in these patients. Patients with mild to moderate hepatic impairment receiving eluxadoline should be monitored for impaired mental and physical abilities needed to perform potentially hazardous activities.

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Conflict Code: ER - Overutilization

Drugs/Diseases

Util A

Util B

Util C (Include)

Eluxadoline 100 mg

Hepatic Impairment

Max Dose: 150 mg/day

References:

Viberzi Prescribing Information, May 2015, Forest Pharmaceuticals, Inc.

**3. Eluxadoline / Severe Hepatic Impairment**

Alert Message: Viberzi (eluxadoline) is contraindicated in patients with severe hepatic impairment (Child-Pugh Class C) as plasma concentrations of eluxadoline increases significantly (16-fold) and there is no information to support the safety of eluxadoline in these patients.

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Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C (Include)

Eluxadoline

Severe Hepatic Impairment

References:

Viberzi Prescribing Information, May 2015, Forest Pharmaceuticals

**4. Eluxadoline / OATP1B1 Inhibitors**

Alert Message: The manufacturer’s recommended maximum daily dose of Viberzi (eluxadoline) is 75 mg twice daily in patients who are receiving concomitant OATP1B1 inhibitors. Eluxadoline is an OATP1B1 substrate and use with an OATP1B1 inhibitor may increase eluxadoline exposure. Patients receiving eluxadoline and an OATP1B1 inhibitor should be monitored for impaired mental and physical abilities needed to perform potentially hazardous activities.

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Conflict Code: ER - Overutilization

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Eluxadoline 100mg	Cyclosporine Gemfibrozil Saquinavir Ritonavir Lopinavir Atazanavir Tipranavir Rifampin	Telithromycin Clarithromycin Cobicistat

Max Dose: 150 mg/day

References:

Viberzi Prescribing Information, May 2015, Forest Pharmaceuticals, Inc.  
Karlgrén M, Vildhede A, Norinder U, et al. Classification of Inhibitors of Hepatic Organic Anion Transporting Polypeptides (OATPs): Influence on Protein Expression on Drug-Drug Interactions. Jnl Med Chem. 2012 May 24;55(10):4740-63.

**5. Eluxadoline / Obstruction of Biliary Duct & Sphincter of Oddi Dysfunction**

Alert Message: Viberzi (eluxadoline) is contraindicated in patients with known or suspected biliary duct obstruction or sphincter of Oddi disease or dysfunction. Eluxadoline is a mu opioid receptor agonist and these patients are at increased risk for sphincter of Oddi spasm, resulting in pancreatitis or hepatic enzyme elevation associated with acute abdominal pain.

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Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Eluxadoline		Obstruction of Bile Duct Sphincter of Oddi Dysfunction (576.5)

References:

Viberzi Prescribing Information, May 2015, Forest Pharmaceuticals, Inc.

**6. Eluxadoline / Alcoholism & Alcohol Abuse**

Alert Message: Viberzi (eluxadoline) is contraindicated in patients with alcoholism, alcohol abuse or alcohol addiction, or in patients who drink more than 3 alcoholic beverages per day due to the potential for increased risk of pancreatitis. Instruct all patients to avoid chronic or acute excessive alcohol use while taking eluxadoline.

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Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Eluxadoline		Alcohol Dependence Alcohol Abuse

References:

Viberzi Prescribing Information, May 2015, Forest Pharmaceuticals, Inc.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**7. Eluxadoline / Pancreatitis**

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Alert Message: Viberzi (eluxadoline) is contraindicated in patients with a history of pancreatitis, structural diseases of the pancreas, including known or suspected pancreatic duct obstruction. These patients are at increased risk for acute pancreatitis.

Conflict Code: TA – Therapeutic Appropriateness  
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Eluxadoline		Pancreatitis Pancreatic Duct Obstruction

References:

Viberzi Prescribing Information, May 2015, Forest Pharmaceuticals, Inc.

**8. Eluxadoline / Gastrointestinal Obstruction & Constipation**

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Alert Message: Viberzi (eluxadoline) is contraindicated in patients with chronic or severe constipation or sequelae from constipation or known or suspected mechanical gastrointestinal obstruction. These patients may be at risk for severe complications of bowel obstruction. Eluxadoline therapy should be discontinued in patients who develop constipation lasting for more than 4 days.

Conflict Code: TA – Therapeutic Appropriateness  
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Eluxadoline		Gastrointestinal Obstruction Constipation

References:

Viberzi Prescribing Information, May 2015, Forest Pharmaceuticals, Inc.

**9. Eluxadoline / Strong CYP Inhibitors**

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Alert Message: The concurrent use of Viberzi (eluxadoline) with strong CYP inhibitors may result in increased eluxadoline exposure and risk of eluxadoline-related adverse effects (e.g., impaired mental and physical abilities). Although the effect of CYP enzymes on the metabolism of eluxadoline has not been definitely established, the manufacturer recommends caution when administering eluxadoline with these agents.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Eluxadoline	Ciprofloxacin Nefazodone Fluconazole Paroxetine Bupropion Fluoxetine Ketoconazole	Posaconazole Voriconazole Nelfinavir Boceprevir Fluvoxamine Ticlopidine Itraconazole

References:

Viberzi Prescribing Information, May 2015, Forest 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 Rejected  
As  
Amended**

**10. Eluxadoline / CYP3A Substrates w/ Narrow Therapeutic Index**

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Alert Message: The concurrent use of Viberzi (eluxadoline) with an agent that is a CYP3A substrate with a narrow therapeutic index may result in increased CYP3A substrate plasma concentrations and risk adverse effects. Although the CYP3A inhibitory effects of eluxadoline have not been definitely established, the manufacturer recommends caution when administering eluxadoline with these agents.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Eluxadoline	Quinidine	Tacrolimus
	Everolimus	Sirolimus
	Fentanyl	Ergotamine
	Pimozide	Dihydroergotamine

References:

Viberzi Prescribing Information, May 2015, Forest Pharmaceuticals, Inc.

**11. Eluxadoline / Drugs That Cause Constipation**

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Alert Message: The concurrent use of Viberzi (eluxadoline) with other agents that cause constipation should be avoided. The most common adverse reaction associated with eluxadoline therapy is constipation and co-administration of eluxadoline with these agents may increase the risk of developing constipation. If the patient develops severe constipation that lasts more than 4 days eluxadoline therapy should be discontinued.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Eluxadoline	Opioids	Fesoterodine
	Anticholinergics	Verapamil
	Alosetron	Clozapine
	Loperamide	Iron
	Cholestyramine	Sevelamer
	Colesevelam	Darifenacin
	Colestipol	Glycopyrrolate
		Tricyclic Antidepressants

References:

Viberzi Prescribing Information, May 2015, Forest Pharmaceuticals, Inc.

**12. Eluxadoline / OATP1B1 & BCRP Substrates**

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Alert Message: The concurrent use of Viberzi (eluxadoline) with an agent that is an OATP1B1 and BCRP (breast cancer resistance protein) substrate may result in increased substrate plasma concentrations and risk for adverse effects. A drug interaction study with eluxadoline and rosuvastatin (an OATP1B1/BCRP substrate) resulted in an increase in the AUC (40%) and Cmax (18%) of rosuvastatin as compared to rosuvastatin alone. Dosing adjustment of the OATP1B1/BCRP substrate may be required.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Eluxadoline	Rosuvastatin	
	Pitavastatin	
	Atorvastatin	
	Methotrexate	

References:

Viberzi Prescribing Information, May 2015, Forest Pharmaceuticals, Inc.

Pharmacology Weekly Comprehensive Drug Reference Table. Available at:

<http://www.pharmacologyweekly.com/content/pages/drug-reference-table-cyp-p450-ugt-enzymes-transporters-ab>

13. Rolapitant / Thioridazine

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Alert Message: Concurrent use of Varubi (rolapitant) with thioridazine is contraindicated. Thioridazine is a CYP2D6 substrate and use the moderate CYP2D6 inhibitor rolapitant may result in a significant increase in thioridazine plasma concentrations and increased risk of QT prolongation and torsade de pointes. The inhibitory effect of rolapitant on CYP2D6 isoenzyme lasts at least 7 days after a single dose.

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

Util A                      Util B                      Util C  
Rolapitant                      Thioridazine

References:

Varubi Prescribing Information, September 2015, Tesaro.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

14. Rolapitant / Pimozide

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Alert Message: Concurrent use of Varubi (rolapitant) with pimozide, a CYP2D6 substrate, should be avoided due to the increased risk for QT prolongation and torsade de pointes. Rolapitant is a moderate CYP2D6 inhibitor and concomitant use with pimozide may significantly increase pimozide concentrations. The inhibitory effect of rolapitant on CYP2D6 isoenzyme lasts at least 7 days after a single dose. Monitor patient for QT prolongation if co-administration cannot be avoided.

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

Util A                      Util B                      Util C  
Rolapitant                      Pimozide

References:

Varubi Prescribing Information, September 2015, Tesaro.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

15. Rolapitant / CYP2D6 Substrates with Narrow Therapeutic Indices

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Alert Message: Caution should be exercised when Varubi (rolapitant) is used concurrently with a drug that is a CYP2D6 substrate and has a narrow therapeutic index. Rolapitant is a moderate CYP2D6 inhibitor and its inhibitory effect on CYP2D6 isoenzyme lasts at least 7 days after a single dose. Monitor patient for adverse reactions if concomitant use with a CYP2D6 substrate with a narrow therapeutic index cannot be avoided.

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

Util A                      Util B                      Util C  
Rolapitant                      Flecainide  
   Propafenone  
   Mexiletine  
   Warfarin

References:

Varubi Prescribing Information, September 2015, Tesaro.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**16. Cariprazine / Overutilization**

Alert Message: Vraylar (cariprazine) may be over-utilized. The manufacturer’s recommended maximum daily dose of cariprazine for patients with schizophrenia or bipolar I with mania or mixed episodes is 6 mg once daily. Dosages above 6 mg daily have not been shown to confer increased effectiveness sufficient to outweigh dose-related adverse reactions (e.g., extrapyramidal symptoms and akathisia).

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Conflict Code: ER – Overutilization

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Cariprazine		Schizophrenia Bipolar I

Max Dose: 6 mg/day

References:

Vraylar Prescribing Information, September 2015, Actavis.

**17. Cariprazine / Therapeutic Appropriateness**

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

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Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

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

Age Range: 0-17 yoa

References:

Vraylar Prescribing Information, September 2015, Actavis.

**18. Cariprazine / Cardio & Cerebrovascular Disease**

Alert Message: Vraylar (cariprazine) should be used with caution in patients with known cardiovascular disease, cerebrovascular disease, or conditions which would predispose patients to hypotension (e.g., dehydration, hypovolemia, and treatment with antihypertensives). Cariprazine has been shown to cause orthostatic hypotension and these patients may be at increased risk.

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

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Cariprazine	Heart Failure Myocardial Infarction Coronary Artery Disease Ischemia Conduction Abnormalities Dehydration Hypovolemia	

References:

Vraylar Prescribing Information, September 2015, Actavis.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**19. Cariprazine / Antihypertensive Medications**

Alert Message: Vraylar (cariprazine) should be used with caution in patients with known cardiovascular disease, cerebrovascular disease, or conditions which would predispose patients to hypotension (e.g., dehydration, hypovolemia, treatment with antihypertensives). Cariprazine has been shown to cause orthostatic hypotension and these patients may be at increased risk.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Cariprazine	ACEIs ARBs CCBs B-Blockers α-B Blockers Direct Renin Inhibitors Selective Aldosterone Antagonist Diuretics Centrally-Acting Adrenergic Agents Peripherally-Acting Adrenergic Agents	

References:  
Vraylar Prescribing Information, September 2015, Actavis.

**20. Cariprazine / Strong CYP3A4 Inhibitors**

Alert Message: Concurrent use of Vraylar (cariprazine) with a strong CYP3A4 inhibitor may result in increased cariprazine exposure due to inhibition of cariprazine CYP3A4-mediated metabolism. If a strong CYP3A4 inhibitor is initiated, reduce the current cariprazine dosage by half. If cariprazine is added onto a regimen already containing a strong CYP3A4 inhibitor the maximum dose should not exceed 3 mg daily. If the strong CYP3A4 inhibitor is discontinued, the cariprazine dosage may need to be increased.

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

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

References:  
Vraylar Prescribing Information, September 2015, Actavis.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**21. Cariprazine / Strong CYP3A4 Inducers**

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Alert Message: Concurrent use of Vraylar (cariprazine) with a strong CYP3A4 inducer has not been evaluated and is not recommended because the net effect on the active drug and metabolites is unclear.

Conflict Code: DD – Drug Interaction

Drugs/Diseases

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

References:

Vraylar Prescribing Information, September 2015, Actavis.

**22. Cariprazine / Non-Adherence**

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

Conflict Code: LR – Non-adherence

Drugs/Diseases

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

References:

Vraylar Prescribing Information, September 2015, Actavis.

Theida P, et.al., An Economic Review of Compliance with Medication Therapy in the Treatment of Schizophrenia, Psychiatric Services, 2003;54:508-516.

Acsher-Svanum H, Zhu B, Faries DE, et al., The Cost of Relapse and the Predictors of Relapse in the Treatment of Schizophrenia. BMC Psychiatry 2010, 10:2.

Berger A, Edelsberg J, Sanders KN, et al., Medication Adherence and Utilization in Patients with Schizophrenia or Bipolar Disorder Receiving Aripiprazole, Quetiapine, or Ziprasidone at Hospital Discharge: A Retrospective Cohort Study. BMC Psychiatry 2012,12:99.

Stephenson JJ, Tuncelli O, Gu T, et al., Adherence to Oral Second-Generation Antipsychotic Medications in Patients with Schizophrenia and Bipolar Disorder: Physicians' Perceptions of Adherence vs. Pharmacy Claims. Int J Clin Pract, June 2012, 66, 6, 565-573.

Morken G, Widen JH, Grawe RW. Non-adherence to Antipsychotic Medication, Relapse and Rehospitalisation in Recent-Onset Schizophrenia. BMC Psychiatry. 2008, 8:32.

**23. Elbasvir+Grazoprevir**

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Alert Message: The manufacturer's recommended dose of Zepatier (elbasvir/grazoprevir) is one tablet once daily (total 50 mg elbasvir/100 mg grazoprevir).

Conflict Code: ER - Overutilization

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Elbasvir/Grazoprevir		

Max Dose: 1 Tablet per day

References:

Zepatier Prescribing Information, Jan. 2016, Merck Sharp & Dohme Corp. Clinical Pharmacology, 2016 Elsevier/Gold Standard.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**24. Elbasvir+Grazoprevir / Hepatic Impairment**

Alert Message: Zepatier (elbasvir/grazoprevir) is contraindicated in patients with moderate to severe hepatic impairment (Child-Pugh B or C) due to the expected significantly increased grazoprevir plasma concentration and the increased risk of alanine aminotransferase (ALT) elevations.

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

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

References:  
Zepatier Prescribing Information, Jan. 2016, Merck Sharp & Dohme Corp.  
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

**25. Elbasvir+Grazoprevir / OATP1B1/3 Inhibitors**

Alert Message: Concurrent use of Zepatier (elbasvir/grazoprevir) with organic anion transporting polypeptide (OATP1B1/3) inhibitors (e.g., atazanavir, saquinavir, and cyclosporine) is contraindicated. The grazoprevir component of the combination antiviral is a OATP1B1/3 substrate and co-administration of these agents may increase grazoprevir plasma concentrations increasing the risk of ALT elevations.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Elbasvir/Grazoprevir	Atazanavir Darunavir Lopinavir Saquinavir Tipranavir Cyclosporine	

References:  
Zepatier Prescribing Information, Jan. 2016, Merck Sharp & Dohme Corp.  
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

**26. Elbasvir+Grazoprevir / Strong 3A4 Inducers & Efavirenz**

Alert Message: Concurrent use of Zepatier (elbasvir/grazoprevir) with a strong CYP3A inducer (e.g., carbamazepine, phenobarbital, and enzalutamide) or an efavirenz-containing agent is contraindicated. Both components of the combination antiviral are CYP3A substrates and co-administration with CYP3A inducers may lead to loss of virologic response due to significant decreases in the elbasvir/grazoprevir 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>
Elbasvir/Grazoprevir	Carbamazepine Phenytoin Primidone Phenobarbital Rifampin Efavirenz Enzalutamide	

References:  
Zepatier Prescribing Information, Jan. 2016, Merck Sharp & Dohme Corp.  
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**27. Elbasvir+Grazoprevir / Moderate CYP3A Inducers**

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Alert Message: Concurrent use of Zepatier (elbasvir/grazoprevir) with a moderate CYP3A inducer (e.g., etravirine, modafinil, and dexamethasone) is not recommended. Both components of the combination antiviral are CYP3A substrates and co-administration with CYP3A inducers may lead to reduced virologic response due to decreases in the elbasvir/grazoprevir plasma concentrations.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Elbasvir/Grazoprevir	Bosentan Etravirine Nevirapine Modafinil Armodafinil Dexamethasone Bexarotene Dabrafenib Deferasirox Eslicarbazepine Oxcarbazepine Rifapentine Rifabutin	

References:  
Zepatier Prescribing Information, Jan. 2016, Merck Sharp & Dohme Corp.  
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

**28. Elbasvir+Grazoprevir / Certain Strong CYP3A Inhibitors**

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Alert Message: Concurrent use of Zepatier (elbasvir/grazoprevir) with a strong CYP3A inhibitor (e.g., ketoconazole, nefazodone, and clarithromycin) is not recommended. Both components of the combination antiviral are CYP3A substrates and co-administration with strong CYP3A inhibitors may lead to increased plasma concentration of elbasvir/grazoprevir and risk of adverse effects.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>
Elbasvir/Grazoprevir	Nefazodone Ketoconazole Itraconazole Cobicistat Indinavir Nelfinavir Ritonavir Clarithromycin Telithromycin Boceprevir	Atazanavir Darunavir

References:  
Zepatier Prescribing Information, Jan. 2016, Merck Sharp & Dohme Corp.  
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**29. Elbasvir+Grazoprevir / Tacrolimus**

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Alert Message: Concurrent use of Zepatier (elbasvir/grazoprevir) with systemic tacrolimus, a narrow therapeutic index drug, may result in increased tacrolimus concentrations due to inhibition, by the grazoprevir component of the antiviral agent, of tacrolimus CYP3A4-mediated metabolism. Frequent monitoring of tacrolimus whole blood concentrations, changes in renal function, and tacrolimus-related adverse events is recommended.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A

Util B

Util C

Elbasvir/Grazoprevir

Tacrolimus

References:

Zepatier Prescribing Information, Jan. 2016, Merck Sharp & Dohme Corp.  
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

**30. Elbasvir+Grazoprevir / Atorvastatin 40 & 80 mg**

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Alert Message: The dose of an atorvastatin-containing product should not exceed a daily dose of 20 mg when co-administered with Zepatier (elbasvir/grazoprevir). The grazoprevir component of the antiviral agent is a CYP3A4 inhibitor and co-administration with atorvastatin, a CYP3A4 substrate, may result in elevated atorvastatin concentrations and increased risk of statin-related myopathy and rhabdomyolysis.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A

Util B

Util C

Elbasvir/Grazoprevir

Atorvastatin 40 & 80mg

References:

Zepatier Prescribing Information, Jan. 2016, Merck Sharp & Dohme Corp.  
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

**31. Elbasvir+Grazoprevir / Rosuvastatin 20 & 40 mg**

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Alert Message: The dose of Crestor (rosuvastatin) should not exceed a daily dose of 10 mg when co-administered with Zepatier (elbasvir/grazoprevir). Both elbasvir and grazoprevir are breast cancer resistance protein (BCRP) transport inhibitors and co-administration with rosuvastatin, a BCRP substrate, may result in elevated rosuvastatin concentrations and increased risk of statin-related myopathy and rhabdomyolysis.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A

Util B

Util C

Elbasvir/Grazoprevir

Rosuvastatin 20 & 40mg

References:

Zepatier Prescribing Information, Jan. 2016, Merck Sharp & Dohme Corp.  
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**32. Elbasvir+Grazoprevir / Higher Strengths of Fluvastatin, Lovastatin & Simvastatin**

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Alert Message: Caution should be exercised when co-administering Zepatier (elbasvir/grazoprevir) with fluvastatin, lovastatin, or simvastatin. Concomitant use may result in elevated statin concentrations increasing the risk of statin-related myopathy and rhabdomyolysis. The lowest necessary dose of the statin should be used and the patient should be closely monitored for statin-associated adverse effects.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Elbasvir/Grazoprevir	Lovastatin Fluvastatin Simvastatin	

References:

Zepatier Prescribing Information, Jan. 2016, Merck Sharp & Dohme Corp.  
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

**33. Elbasvir+Grazoprevir / Pediatric Use**

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Alert Message: The safety and efficacy of Zepatier (elbasvir/grazoprevir) in pediatric patients less than 18 years of age have not been established.

Conflict Code: TA – Therapeutic Appropriateness  
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Elbasvir/Grazoprevir		

Age Range: 0 – 17 yoa

References:

Zepatier Prescribing Information, Jan. 2016, Merck Sharp & Dohme Corp.  
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

**34. Rolapitant / BCRP Substrates with Narrow Therapeutic Indices**

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Alert Message: Caution should be exercised when Varubi (rolapitant) is used concurrently with a drug that is a BCRP substrate with a narrow therapeutic index. Rolapitant is an inhibitor of BCRP transport and concomitant use with a BCRP substrate may result in increased BCRP substrate concentrations and potential for adverse effects. Monitor patient for adverse reactions if concomitant use with a BCRP substrate with a narrow therapeutic index cannot be avoided.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Rolapitant	Methotrexate Topotecan Irinotecan	

References:

Varubi Prescribing Information, September 2015, Tesaro.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**35. Rolapitant / P-gp Substrates with Narrow Therapeutic Indices**

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Alert Message: Caution should be exercised when Varubi (rolapitant) is used concurrently with a drug that is a P-gp substrate with a narrow therapeutic index. Rolapitant is a P-gp efflux inhibitor and concomitant use with a P-gp substrate may result in increased P-gp substrate concentrations and risk of adverse reactions. If concomitant therapy cannot be avoided monitor patient for P-gp-related adverse reactions.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Rolapitant	Digoxin Cyclosporine Quinidine Tacrolimus	

References:

Varubi Prescribing Information, September 2015, Tesaro.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**36. Rolapitant / Strong CYP3A4 Inducers**

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Alert Message: Avoid the use of Varubi (rolapitant) in patients who require chronic administration of a strong CYP3A4 inducer. Rolapitant is a CYP3A4 substrate and concomitant use with a CYP3A4 inducer may result in significantly reduced rolapitant plasma concentrations and decreased efficacy.

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

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

References:

Varubi Prescribing Information, September 2015, Tesaro.  
Clinical Pharmacology, 2015 Elsevier/Gold Standard.

**37. Buprenorphine Buccal / Overutilization**

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Alert Message: Belbuca (buprenorphine buccal) may be over-utilized. The manufacturer's maximum recommended daily dose of buprenorphine buccal is 900 mcg every 12 hours. Exceeding the maximum daily dose increases the potential for QTc interval prolongation.

Conflict Code: ER - Overutilization  
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Buprenorphine Buccal		

Max Dose: 1,800 mcg/day

References:

Belbuca Prescribing Information, Oct. 2015, Endo Pharmaceuticals, Inc.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**38. Buprenorphine Buccal / CYP3A4 Inhibitors**

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Alert Message: Concurrent use of Belbuca (buprenorphine buccal), a CYP3A4 substrate, with a CYP3A4 inhibitor can increase buprenorphine plasma concentrations resulting in prolonged opioid effects.

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

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

References:

Belbuca Prescribing Information, Oct. 2015, Endo Pharmaceuticals, Inc.

**39. Buprenorphine Buccal / CYP3A4 Inducers**

\_\_\_ ✓ \_\_\_ \_\_\_

Alert Message: Concurrent use of Belbuca (buprenorphine buccal), a CYP3A4 substrate with a CYP3A4 inducer can decrease buprenorphine plasma concentrations resulting in decreased efficacy or onset of withdrawal syndrome in patients who have developed physical dependence to buprenorphine.

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

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

References:

Belbuca Prescribing Information, Oct. 2015, Endo Pharmaceuticals, Inc.

**Criteria Recommendations**

**Accepted Approved Rejected  
As  
Amended**

**40. Buprenorphine Buccal / Class 1A & III Antiarrhythmics & Other QT Prolonging Drugs**

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Alert Message: Belbuca (buprenorphine buccal) has been observed to prolong the QTc interval therefore its use should be avoided in patients with long QT syndrome, family history of long QT syndrome, or if taking Class 1A or Class III antiarrhythmics or other medications that prolong the QTc interval.

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

<u>Util A</u>	<u>Util B</u>				
Buprenorphine Buccal	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	Rasagiline
	Chlorpromazine	Fluoxetine	Nicardipine	Saquinavir	Phenelzine
	Ciprofloxacin	Foscarnet	Nilotinib	Sertraline	Tranlycypromine
	Citalopram	Fosphenytoin	Norfloxacin	Solifenacin	Linezolid
	Clarithromycin	Galantamine	Nortriptyline	Sotalol	
	Clomipramine	Gemifloxacin	Octreotide	Sunitinib	
	Clozapine	Granisetron	Ofloxacin	Tacrolimus	
	Dasatinib	Haloperidol	Ondansetron	Tamoxifen	
	Desipramine	Isocarboxazid	Paliperidone	Telithromycin	
	Diphenhydramine	lloperidone	Paroxetine	Terbutaline	

References:  
Belbuca Prescribing Information, Oct. 2015, Endo Pharmaceuticals, Inc.

**41. Buprenorphine Buccal / QT Prolongation**

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Alert Message: Belbuca (buprenorphine buccal) has been observed to prolong the QTc interval therefore its use should be avoided in patients with long QT syndrome, family history of long QT syndrome, or if taking Class 1A or Class III antiarrhythmics or other medications that prolong the QT interval.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Buprenorphine Buccal	QT Prolongation	

References:  
Belbuca Prescribing Information, Oct. 2015, Endo Pharmaceuticals, Inc.

**42. Buprenorphine Buccal / Hepatic Impairment**

Alert Message: Belbuca (buprenorphine buccal) is extensively metabolized in the liver and its use in patients with moderate or severe hepatic impairment has been shown to result in higher plasma concentrations and longer half-life. In patients with severe hepatic impairment, reduce the starting dose and the titration dose by half that of patients with normal liver functions, from 150 to 75 mcg. Patients with moderate to severe hepatic impairment should be monitored for signs and symptoms of toxicity or overdose.

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

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

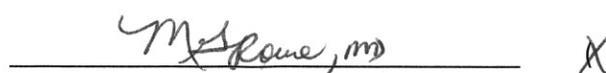
References:

Belbuca Prescribing Information, Oct. 2015, Endo Pharmaceuticals, Inc.

  
Stephanie McGee Azar, Commissioner

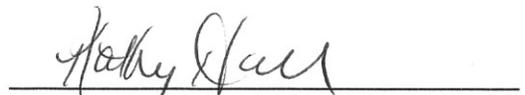
Approve    ( ) Deny

1-30-17  
Date

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

Approve    ( ) Deny

1/17/2017  
Date

  
Kathy Hall, Deputy Commissioner

Approve    ( ) Deny

Jan 17, 2017  
Date