

Alabama Medicaid DUR Board Meeting Minutes
April 26, 2017

Members Present: Kelli Littlejohn Newman, Melinda Rowe, Marilyn Bulloch, Chris Phung, Bernie Olin, Paula Thompson, Denyse Thornley-Brown

Also Present: Tiffany Minnifield, Lori Thomas, Clemice Hurst, Heather Vega, Whitney Hughley

Present via Conference Call: Kristian Testerman, Samir Hadid, Amy Donaldson, Michelle Stiles, Joshua Lee, Elaine Alexander, Lisa Channell, Paul Young

Members Absent: Robert Moon, Christopher Randolph, Dan McConaghy, Donald Kern, P.J. Hughes

Call to Order: The DUR meeting was called to order by M. Bulloch at approximately 1:04p.m.

Review and Adoption of Minutes: The minutes of the January 25, 2017 meeting were presented and P. Thompson made a motion to approve the minutes. C. Phung 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 October 2016. She reported 9,859 total manual requests and 22,118 total electronic requests. From the Prior Authorization and Override Response Time Ratio report for October 2016, L. Thomas reported that approximately 72% of all manual PAs and 74% of all overrides were completed in less than two hours. Eighty-eight percent of all manual PAs and 91% of all overrides were completed in less than four hours. Ninety-four percent of all manual PAs and 95% of all overrides were completed in less than eight hours. For the month of November 2016, L. Thomas reported 9,733 manual PA requests and 20,807 electronic PA requests were received. She reported that 81% of all manual PAs and 83% of all overrides were completed in less than two hours. Ninety-one percent of all manual PAs and 93% of all overrides were completed in less than four hours. Ninety-six percent of all manual PAs and all overrides were completed in less than eight hours. For the month of December 2016, L. Thomas reported 9,382 manual PA requests and 19,887 electronic PA requests. L. Thomas reported that approximately 86% of all manual PAs and 87% of all overrides were completed in less than two hours. Ninety-five percent of all manual PA requests and all overrides were completed in less than four hours. Ninety-seven 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 July 2016 through December 2016. She reported 3,696,585 total prescriptions, 216,955 average recipients per month using pharmacy benefits, and an average paid per prescription of \$99.27.

Cost Management Analysis: L.Thomas reported an average cost per claim of \$99.25 for December 2016 and emphasized that the table contained the average cost per claim over the past two years. From the 4th Quarter 2016 Drug Analysis, L.Thomas reported 79.6% generic utilization, 9.1% brand single-source, 7.5% 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 10/01/2016 – 12/31/2016, L.Thomas reported the top five drugs: amoxicillin, hydrocodone-acetaminophen, cetirizine, ProAir[®] HFA, and montelukast. She informed the Board that this was the same as reported last quarter. L. Thomas then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 10/01/16 – 12/31/2016: Vyvanse[®], Focalin XR[®], Invega[®] Sustenna[®], ProAir[®] HFA, and Adderall XR[®]. L. Thomas reminded the Board that Vyvanse[®], Focalin XR[®], and Adderall XR[®] are preferred agents. She also mentioned that Synagis[®] was in the top 25 and that the Synagis[®] season began on October 1st. 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 Insulins.

Review of Opioid Dependence Treatment Patient Consent Form: K. Newman began the Informed Consent form discussion by introducing the most recent version of the form that included input from AL Medicaid Legal Department. She indicated that it was the Agency's goal to have this form included with the July 3rd updates. The document was reviewed and M. Bulloch added additional medication names to the list of benzodiazepines. Also, additional verbiage was added to indicate the patient would not use prescription medications prescribed to other patients. A motion to approve the additional verbiage was made by D. Thornley-Brown, M. Bulloch seconded the motion, and the motion was approved unanimously. L. Thomas added that the Academic Detailers could go over the form with the top prescribers and let the prescribers know the form must be attached to the PA form when submitted for review. P. Thompson recommended the Board approve the form as amended. D. Thornley-Brown seconded the motion and the motion was approved unanimously.

Review of FDA Guidance on Prescription Codeine Pain and Cough Medicines and Tramadol: C. Hurst and K. Newman began the discussion regarding the Safety Announcement from the FDA surrounding codeine and tramadol pain medication use in children. The Board suggested that HID draft DUR criteria pertaining to the FDA's contraindications and warnings surrounding the use of these medications in children and breastfeeding mothers. K. Newman recommended that the Agency's quarterly newsletter also contain this information. C. Hurst and K. Newman added that the Academic Detailers could visit and deliver the FDA's Guidance to the top prescribers of these medications in children.

RDUR Intervention Report: L. Thomas presented the RDUR Activity Report for October 2016. She reported 755 profiles reviewed and 799 letters sent with 185 responses received as of the date of the report. She reported 71 of 126 physicians indicated that they found the RDUR letters "useful" or "extremely useful". The criteria for the cycle of intervention letters included Drug-Drug Interaction (benzodiazepines and clozapine; methadone and CNS depressants); Therapeutic Duplication of skeletal muscle relaxants; Hepatitis C SVR Response Rates; Appropriate Use (concurrent use of buprenorphine and pure opiate agonists). L. Thomas then presented the RDUR Activity Report for November 2016. She reported 716 profiles reviewed and 516 letters sent with 134 responses received as of the date of the report. She reported 30 of 45 physicians indicated that they found the RDUR letters "useful" or "extremely useful". The criteria for the cycle of intervention letters included Overuse Precaution (appropriate use of immediate-release opioids); Underutilization of aripiprazole; Hepatitis C SVR Response Rates; Appropriate Use (concurrent use of buprenorphine and pure opiate agonists). The December 2016 Activity Report indicated 500 profiles reviewed and 677 letters sent with 76 responses received as of the date of the report. L. Thomas reported 43 of 59 physicians indicated that they found the RDUR letters "useful" or "extremely useful". The criteria for the cycle of intervention letters were Underutilization of quetiapine; Inappropriate therapy (quetiapine 25, 50, and 100mg and possible use as a sedative/hypnotic); Hepatitis C SVR Response Rates; Appropriate Use (concurrent use of buprenorphine and pure opiate agonists).

Proposed Criteria: L.Thomas presented the proposed set of 57 criteria to the Board. T.Minnifield instructed the Board members to mark their ballots. Of the 57 criteria, results from the criteria vote returned 54 approved and 3 approved as amended.

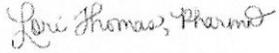
Medicaid Update: T. Minnifield reminded the Board members that all updated Medicaid drug lists provided are also available online and that the next DUR Meeting would be July 26th.

P & T Committee Update: C. Hurst began the P & T Update by informing the Board that the last meeting was held on February 8, 2017, and covered the remaining anti-infectives and new drug reviews for Xeljanz[®] and Entresto[™]. The next P & T meeting is scheduled for May 10, 2017, at 9 a.m. and will

cover First Generation Antihistamines, Estrogens, Antidiabetic Agents, Prenatal Vitamins, and a drug class review for Multiple Sclerosis Agents.

Next Meeting Date: A motion to adjourn the meeting was made by D. Thornley-Brown. P. Thompson seconded the motion and the meeting was adjourned at 2:21 p.m.

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. Naloxegol / Therapeutic Appropriateness

_____✓_____

Alert Message: The review did not reveal current use of opioid medication.
Movantik (naloxegol) is approved for the treatment of opioid-induced constipation.
Naloxegol should be discontinued if treatment with the opioid pain medication is discontinued.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

| | | |
|---------------|---------------|--------------------------|
| <u>Util A</u> | <u>Util B</u> | <u>Util C (Negating)</u> |
| Naloxegol | | Opioids |

References:

Movantik Prescribing Information, Sept. 2014, AstraZeneca.
Clinical Pharmacology, 2016, Elsevier/Gold Standard.
Facts& Comparisons, 2016 Updates, Wolters Kluwer Health.

2. Brivaracetam / Overutilization

_____✓_____

Alert Message: The manufacturer's maximum recommended daily dose of Briviact (brivaracetam) is 200 mg (100 mg twice daily).

Conflict Code: ER - Overutilization

Drugs/Diseases

| | | |
|---------------|---------------|--------------------------|
| <u>Util A</u> | <u>Util B</u> | <u>Util C (Negating)</u> |
| Brivaracetam | | Hepatic Impairment |

Max Dose: 200mg/day

References:

Briviact Prescribing Information, Feb. 2016, UCB, Inc.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

3. Brivaracetam / Overutilization - Hepatic Impairment

_____✓_____

Alert Message: For all stages of hepatic impairment, the manufacturer's maximum recommended daily dose of Briviact (brivaracetam) is 150 mg (75 mg twice daily).

Conflict Code: ER - Overutilization

Drugs/Diseases

| | | |
|---------------|---------------|-------------------------|
| <u>Util A</u> | <u>Util B</u> | <u>Util C (Include)</u> |
| Brivaracetam | | Hepatic Impairment |

Max Dose: 150mg/day

References:

Briviact Prescribing Information, Feb. 2016, UCB, Inc.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

4. Brivaracetam / Psychiatric Adverse Reactions

_____ ✓ _____

Alert Message: Briviact (brivaracetam) can cause psychiatric adverse reactions.
Counsel patients concerning possible behavioral changes.

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

| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
|---------------|---|---------------|
| Brivaracetam | Hallucinations Paranoia Acute Psychosis Anxiety Nervousness Agitation Irritability/Anger Hostility Depression | |

References:
Briviact Prescribing Information, Feb. 2016, UCB, Inc.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

5. Brivaracetam / Rifampin

_____ ✓ _____

Alert Message: Concurrent use of Briviact (brivaracetam) with rifampin can decrease brivaracetam plasma concentrations by 45%. If the agents are co-administered the manufacturer recommends that the brivaracetam dose should be increased by 100% (i.e., double the dose) while receiving concomitant treatment with rifampin.

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

| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
|---------------|---------------|---------------|
| Brivaracetam | Rifampin | |

References:
Briviact Prescribing Information, Feb. 2016, UCB, Inc.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

6. Brivaracetam / Carbamazepine

_____ ✓ _____

Alert Message: Concurrent use of Briviact (brivaracetam) with carbamazepine may result in increased exposure to carbamazepine-epoxide, the active metabolite of carbamazepine. Though available data did not reveal any safety concerns, if carbamazepine-related tolerability issues arise when the agents are co-administered consider carbamazepine dose reduction.

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

| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
|---------------|---------------|---------------|
| Brivaracetam | Carbamazepine | |

References:
Briviact Prescribing Information, Feb. 2016, UCB, Inc.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

7. Brivaracetam / Phenytoin

 ✓

Alert Message: Concurrent use of Briviact (brivaracetam) with phenytoin may increase phenytoin plasma concentrations by 20%. Phenytoin has a narrow therapeutic index and monitoring of phenytoin levels is recommended when brivaracetam is added to or discontinued from ongoing phenytoin therapy.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A

Util B

Util C

Brivaracetam

Phenytoin

References:

Briviact Prescribing Information, Feb. 2016, UCB, Inc.

8. Brivaracetam / Levetiracetam

 ✓

Alert Message: In two clinical studies the co-administration of Briviact (brivaracetam) with a levetiracetam-containing product did not provide additional benefit. Brivaracetam is an analog of levetiracetam and concurrent use may result in increased adverse effects.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A

Util B

Util C

Brivaracetam

Levetiracetam

References:

Briviact Prescribing Information, Feb. 2016, UCB, Inc.

9. Brivaracetam / Nonadherence

 ✓

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

Conflict Code: LR – Nonadherence

Drugs/Diseases

Util A

Util B

Util C

Brivaracetam

References:

Hodges JC, Treadwell J, Malphrus AD, et al., Identification and Prevention of Antiepileptic Drug Noncompliance: The Collaborative Use of State-Supplied Pharmaceutical Data. ISRN Pediatr. 2014 Feb 19;1-8.

Viswanathan M, Golin CE, Jones DC, et al., Interventions to Improve Adherence to Self-administered Medications for Chronic Disease in the United States: A Systematic Review. Ann Intern Med.2012;157:785-792.

Faught E, Duh MS, Weiner JR, et al. Nonadherence to Antiepileptic Drugs and Increased Mortality, Findings from the RANSOM Study. Neurology 2008;71(20): 1572-1578.

Faught ER, Weiner JR, Guerin A, et al. Impact of Nonadherence to Antiepileptic Drugs on Health Care Utilization and Costs: Findings from the RANSOM Study. Epilepsia 2009;50(3):501-509.

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.

12. Daclatasvir 60 mg / Strong CYP3A4 Inhibitors

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Alert Message: The dosage of Daklinza (daclatasvir) should not exceed 30 mg once daily when daclatasvir is co-administered with strong CYP3A4 inhibitors (e.g., ketoconazole, nefazodone, and cobicistat). Daclatasvir is a CYP3A4 substrate and use with a strong CYP3A4 inhibitor may result in increased daclatasvir plasma levels.

Conflict Code: ER - Overutilization

Drugs/Diseases

| <u>Util A</u> | <u>Util B</u> | | <u>Util C</u> |
|------------------|----------------|--------------|---------------|
| Daclatasvir 60mg | Nefazodone | Voriconazole | Saquinavir |
| | Clarithromycin | Posaconazole | Ritonavir |
| | Telithromycin | Boceprevir | Indinavir |
| | Itraconazole | Cobicistat | Nelfinavir |
| | Ketoconazole | | |

Max Dose: 30mg/day

References:

Daklinza Prescribing Information, Feb. 2016, Bristol-Myers Squibb.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

13. Daclatasvir / Moderate CPY3A4 Inducers

___√___

Alert Message: The dosage of Daklinza (daclatasvir) should be increased to 90 mg once daily when co-administered with moderate CYP3A4 inducers. Daclatasvir is a CYP3A4 substrate and co-administration with moderate CYP3A4 inducers may decrease daclatasvir plasma concentrations potentially resulting in loss of virologic response and possible development of resistance.

Conflict Code: ER - Overutilization

Drugs/Diseases

| <u>Util A</u> | <u>Util B</u> | <u>Util C (Negate)</u> |
|------------------|---------------|------------------------|
| Daclatasvir 60mg | Bosentan | Daclatasvir 30mg |
| | Dexamethasone | |
| | Efavirenz | |
| | Etravirine | |
| | Modafinil | |
| | Rifapentine | |

Minimum Dose: 90mg/day

References:

Daklinza Prescribing Information, Feb. 2016, Bristol-Myers Squibb.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

14. Daclatasvir / Amiodarone / Sofosbuvir ___√___

Alert Message: The concurrent use of amiodarone with Daklinza (daclatasvir) in combination with Sovaldi (sofosbuvir) is not recommended due to the risk of serious symptomatic bradycardia. Patients taking amiodarone who have no alternative treatment options other than daclatasvir with sofosbuvir should be counseled about the risk of serious bradycardia and have cardiac monitoring conducted according to manufacturer's recommendations.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

| <u>Util A</u> | <u>Util B</u> | <u>Util C (Include)</u> |
|---------------|---------------|-------------------------|
| Daclatasvir | Amiodarone | Sofosbuvir |

References:

Daklinza Prescribing Information, Feb. 2016, Bristol-Myers Squibb.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

15. Daclatasvir / Moderate CYP3A4 Inhibitors ___√___

Alert Message: Concurrent use of Daklinza (daclatasvir), a CYP3A4 substrate, with moderate CYP3A4 inhibitors (e.g., diltiazem, verapamil, and erythromycin) may result in elevated daclatasvir plasma levels. The patient should be monitored for daclatasvir-related adverse effects (e.g., headache, fatigue, and diarrhea).

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

| <u>Util A</u> | <u>Util B</u> | <u>Util C (Negating)</u> |
|---------------|---------------------|--------------------------|
| Daclatasvir | Atazanavir | Ritonavir |
| | Fosamprenavir | Cobicistat |
| | Ciprofloxacin | |
| | Diltiazem | |
| | Verapamil | |
| | Erythromycin | |
| | Darunavir/ritonavir | |
| | Fluconazole | |
| | Aprepitant | |

References:

Daklinza Prescribing Information, Feb. 2016, Bristol-Myers Squibb.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

16. Daclatasvir / Digoxin

 √

Alert Message: Concurrent use of Daklinza (daclatasvir) with digoxin may result in elevated digoxin plasma levels due to inhibition, by daclatasvir, of digoxin P-gp mediated transport. If initiating digoxin in a patient receiving daclatasvir, start digoxin at the lowest appropriate dosage, monitor digoxin concentrations, adjust digoxin dose if necessary, and continue monitoring. When initiating daclatasvir in a patient receiving digoxin, measure serum digoxin concentrations before initiating daclatasvir and reduce digoxin dose by 30% to 50%. Alternatively, the digoxin dose may be reduced by prolonging the dosing interval.

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

| | | |
|---------------|---------------|---------------|
| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
| Daclatasvir | Digoxin | |

References:

Daklinza Prescribing Information, Feb. 2016, Bristol-Myers Squibb.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

17. Daclatasvir / Statins

 √

Alert Message: Caution should be used when Daklinza (daclatasvir) is co-administered with an HMG CoA reductase inhibitor (statin) as they are substrates of OATP1B1, P-gp, and BCRP transporters. Daclatasvir is an inhibitor of these transporters and concurrent use with transporter substrates can result in increased statin plasma concentrations and increased risk for adverse events (e.g., myopathy and rhabdomyolysis). Patients should be monitored closely for statin-related adverse effects.

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

| | | |
|---------------|---|---------------|
| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
| Daclatasvir | Lovastatin Fluvastatin Pravastatin Simvastatin Atorvastatin Rosuvastatin Pitavastatin | |

References:

Daklinza Prescribing Information, Feb. 2016, Bristol-Myers Squibb.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Hirano M, Maeda K, Matsushima S, et al. Involvement of BCRP (ABCG2) in the Biliary Excretion of Pitavastatin. Molecu Pharmaco. 2005 Vol. 68(3):800 – 807.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

18. Daclatasvir / Pregnancy / Pregnancy Negating

 ✓

Alert Message: No data are available for Daklinza (daclatasvir) use in pregnant women. Consider the benefits and risks of daclatasvir when prescribing it for use in a pregnant woman.

Conflict Code: MC – Drug (Actual) Disease Precaution

Drugs/Diseases

| <u>Util A</u> | <u>Util B</u> | <u>Util C (Negating)</u> |
|---------------|---------------|-------------------------------------|
| Daclatasvir | Pregnancy | Miscarriage Abortion Delivery |

References:

Daklinza Prescribing Information, Feb. 2016, Bristol-Myers Squibb.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

19. Daclatasvir / Pediatric

 ✓

Alert Message: The safety and effectiveness of Daklinza (daclatasvir) in pediatric patients younger than 18 years of age have not been established.

Conflict Code: TA - Therapeutic Effectiveness

Drugs/Diseases

| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
|---------------|---------------|---------------|
| Daclatasvir | | |

Age Range; 0-17 yoa

References:

Daklinza Prescribing Information, Feb. 2016, Bristol-Myers Squibb.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

20. Ixazomib / Strong CYP3A4 Inducers

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Alert Message: Concurrent user of Ninlaro (ixazomib), a CYP3A4 substrate, with strong CYP3A inducers should be avoided due to the potential for decreased ixazomib efficacy.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
|---------------|---------------|---------------|
| Ixazomib | Carbamazepine | Rifampin |
| | Phenytoin | Rifapentine |
| | Phenobarbital | Rifabutin |
| | Primidone | Enzalutamide |

References:

Ninlaro Prescribing Information, Nov. 2015, Takeda Pharmaceuticals America.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

21. Ixazomib / Pregnancy / Pregnancy Negating

_____√_____

Alert Message: Ninlaro (ixazomib) can cause fetal harm in a pregnant woman based on its mechanism of action and findings in animals. Females of reproductive potential should avoid becoming pregnant while taking ixazomib. Male and female patients of childbearing potential must use effective contraceptive measures during and for 90 days following the final ixazomib dose. If the patient becomes pregnant while taking ixazomib, apprise them of the potential hazard to the fetus.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

| <u>Util A</u> | <u>Util B</u> | <u>Util C (Negating)</u> |
|---------------|---------------|--------------------------|
| Ixazomib | | Miscarriage |
| | | Delivery |
| | | Abortion |

Age Range 11-50

References:

Ninlaro Prescribing Information, Nov. 2015, Takeda Pharmaceuticals America.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

22. Selexipag / Overutilization

 ✓

Alert Message: Upravi (selexipag) may be over-utilized. The manufacturer's recommended maximum dose is 1600 mcg twice daily (total 3200 mcg daily).

Conflict Code: ER - Overutilization

Drugs/Diseases

Util A

Util B

Util C

Selexipag

Max Dose: 3200 mcg/day

References:

Upravi Prescribing Information, Dec. 2015, Actelion Pharmaceuticals US, Inc.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

23. Selexipag / Nonadherence

 ✓

Alert Message: Based on the refill history, your patient may be underutilizing Upravi (selexipag). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects which may lead to decreased patient outcomes and additional healthcare costs. If treatment is missed for 3 days or more, selexipag should be restarted at a lower dose and then re-titrated.

Conflict Code: LR - Nonadherence

Drugs/Diseases

Util A

Util B

Util C

Selexipag

References:

Upravi Prescribing Information, Dec. 2015, Actelion Pharmaceuticals US, Inc.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Stewart T. Facilitating Pulmonary Arterial Hypertension Medication Adherence: Patient-centered Management. *Adv Pulm Hypertens.* 2010;8(4):228–231.

24. Selexipag / Hepatic Impairment

 ✓

Alert Message: A once-daily regimen is recommended in patients with moderate hepatic impairment (Child-Pugh class B) due to the increased exposure to Upravi (selexipag) and its active metabolite. The starting dose in these patients should be 200 mcg once daily, increasing the dose by 200 mcg once daily at weekly intervals to the highest tolerated dose up to 1600 mcg daily. The use of selexipag should be avoided in patients with severe hepatic impairment. No dosage adjustment is necessary for patients with mild hepatic impairment.

Conflict Code: ER – Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C (Include)

Selexipag

Hepatic Impairment

Max Dose: 1600 mcg/day

References:

Upravi Prescribing Information, Dec. 2015, Actelion Pharmaceuticals US, Inc.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

31. Quillichew ER / Therapeutic Appropriateness

___√___ ___ ___

Alert Message: The safety and efficacy of Quillichew ER (methylphenidate extended-release) in pediatric patients younger than 6 years old with ADHD have not been established.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C

Methylphenidate ER Chewable

Age Range: 0-5 yoa

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Quillichew ER Prescribing Information, Dec. 2015, Pfizer, Inc.

32. Hydroxyzine / QT Prolongation

___√___ ___ ___

Alert Message: Hydroxyzine is contraindicated in patients with prolonged QT interval. Post-marketing data indicate that hydroxyzine causes QT prolongation and torsade de pointes

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C (Include)

Hydroxyzine

QT Prolongation

References:

Vistaril Prescribing Information, Jan. 2016, Pfizer.

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

33. IR Opioids / LA Opioid (Negating)

_____√_____

Alert Message: Immediate-release opioids should be reserved for pain severe enough to require opioid treatment and for which alternative treatment options such as non-opioid analgesics are inadequate or not tolerated. These agents expose patients to the risks of opioid addiction, abuse and misuse, potentially harmful drug interactions, and adverse effects on the endocrine system. Prolonged use of immediate-release opioids in pregnant women can also result in NOWS (neonatal opioid withdrawal syndrome).

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

| <u>Util A</u> | <u>Util B</u> | <u>Util C (Negating)</u> |
|------------------|---------------|--------------------------|
| Codeine | | Morphine ER |
| Hydromorphone-IR | | Oxycodone ER |
| Levorphanol | | Fentanyl ER |
| Meperidine | | Methadone |
| Hydrocodone-IR | | Oxymorphone ER |
| Morphine-IR | | Hydromorphone ER |
| Oxycodone-IR | | Hydrocodone ER |
| Oxymorphone – IR | | Tapentadol ER |
| Pentazocine | | Tramadol ER |
| Fentanyl-IR | | |
| Tapentadol-IR | | |
| Tramadol-IR | | |

References:

FDA MEDWATCH Safety Alerts for Human Medical Products. Opioid Pain Medicines: Drug Safety Communications – New Safety Warnings Added to Prescription Opioid Medications [Posted 3/22/2016]. Available at: <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm491715.htm>

34. IR Opioids / Pregnancy / LA Opioid (Negating)

____√____ _____ _____

Alert Message: Chronic maternal use of immediate-release opioid analgesics during pregnancy can result in NOWS (neonatal opioid withdrawal syndrome), which may be life-threatening and require management by neonatology experts. Symptoms associated with NOWS include tachycardia, trembling, poor feeding, and excessive or high-pitched crying. These agents should be prescribed to pregnant women only if clearly needed.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

| <u>Util A</u> | <u>Util B</u> | <u>Util C (Negating)</u> |
|------------------|---------------|--------------------------|
| Codeine | Pregnancy | Morphine ER |
| Hydromorphone-IR | | Oxycodone ER |
| Levorphanol | | Fentanyl ER |
| Meperidine | | Methadone |
| Hydrocodone-IR | | Oxymorphone ER |
| Morphine-IR | | Hydromorphone ER |
| Oxycodone-IR | | Hydrocodone ER |
| Oxymorphone – IR | | Tapentadol ER |
| Pentazocine | | Tramadol ER |
| Fentanyl-IR | | |
| Tapentadol-IR | | |
| Tramadol-IR | | |

References:

FDA MEDWATCH Safety Alerts for Human Medical Products. Opioid Pain Medicines: Drug Safety Communications – New Safety Warnings Added to Prescription Opioid Medications [Posted 3/22/2016]. Available at: <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm491715.htm>

FDA News Release FDA Announces Enhanced Warnings for Immediate-Release Opioid Pain Medications Related to Risks of Misuse, Abuse, Addiction, Overdose and Death. [Release 03/22/2016].

35. Reslizumab / Helminth Infection

____√____ _____ _____

Alert Message: The patient has a diagnosis of a helminth infection and is receiving Cinqair (reslizumab) which may adversely influence a patient’s response against parasitic infections. Treat patients with pre-existing helminth infections before initiating therapy with reslizumab. If patients become infected while receiving treatment with reslizumab and do not respond to anti-helminth treatment, discontinue reslizumab treatment until infection resolves. Reslizumab is an interleukin-5 antagonist (IL-5) which reduces the production and survival of eosinophils.

Conflict Code: MC – Drug (Actual) Disease Precaution

Drugs/Diseases

| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
|---------------|--------------------------|---------------|
| Reslizumab | Helminth Infection (B83) | |

References:

Cinqair Prescribing Information, March 2016, Teva Pharmaceuticals.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

36. Tofacitinib / Overutilization

 ✓

Alert Message: Xeljanz XR (tofacitinib) may be over-utilized. The manufacturer’s recommended daily dose is one 11 mg tablet once daily.

Conflict Code: ER - Overutilization

Drugs/Diseases

Util A Util B Util C

Tofacitinib XR

Max dose: 11 mg/day

References:

Xeljanz/Xeljanz XR Prescribing Information, Feb. 2016, Pfizer, Inc.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

37. Pimavanserin / Over-utilization

 ✓

Alert Message: Nuplazid (pimavanserin) may be over-utilized. The manufacturer's maximum recommended daily dose is 34 mg once daily.

Conflict Code: ER - Overutilization

Drugs/Diseases

Util A Util B Util C

Pimavanserin

Max Dose: 34 mg/day

References:

Nuplazid Prescribing Information, April 2016, Acadia Pharmaceuticals Inc.

38. Pimavanserin / Strong CYP3A4 Inhibitors

 ✓

Alert Message: The recommended dose of Nuplazid (pimavanserin) is 17 mg once daily in patients receiving concurrent therapy with a strong CYP3A4 inhibitor (e.g., nefazodone, clarithromycin, and boceprevir). Pimavanserin is a CYP3A4 substrate and concomitant use with a strong CYP3A4 inhibitor may result in increased pimavanserin exposure and risk of adverse effects.

Conflict Code: ER - Overutilization

Drugs/Diseases

| | | | | |
|---------------|---------------|-------------------------|--------------|--------------|
| <u>Util A</u> | <u>Util B</u> | <u>Util C (Include)</u> | | |
| Pimavanserin | | Nefazodone | Indinavir | Itraconazole |
| | | Clarithromycin | Nelfinavir | Posaconazole |
| | | Telithromycin | Boceprevir | Voriconazole |
| | | Saquinavir | Cobicistat | |
| | | Ritonavir | Ketoconazole | |

Max Dose: 17 mg/day

References:

Nuplazid Prescribing Information, April 2016, Acadia Pharmaceuticals Inc.

39. Pimavanserin / Strong CYP3A4 Inducers

Alert Message: Concurrent use of Nuplazid (pimavanserin) with a strong CYP3A4 inducer (e.g., carbamazepine, phenytoin, and rifampin) may result in reduced pimavanserin exposure and potential for decreased pimavanserin efficacy. The patient should be monitored for reduced pimavanserin efficacy and the dosage may need to be increased.

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

| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
|---------------|--|---------------|
| Pimavanserin | Carbamazepine Phenytoin Phenobarbital Primidone Rifampin Rifapentine Rifabutin | |

References:
Nuplazid Prescribing Information, April 2016, Acadia Pharmaceuticals Inc.

40. Pimavanserin / Severe Renal Impairment

Alert Message: Use of Nuplazid (pimavanserin) is not recommended in patients with severe renal impairment (CrCL < 30 ml/min, Cockcroft-Gault). Pimavanserin has not been evaluated in this patient population. In clinical trials, patients with mild to moderate renal impairment showed similar exposure to pimavanserin as patients with normal renal function, therefore no dosage adjustment is required.

Conflict Code: MC - Drug Disease Precaution
Drugs/Diseases

| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
|---------------|-------------------|---------------|
| Pimavanserin | CKD 4 & 5 ESRD | |

References:
Nuplazid Prescribing Information, April 2016, Acadia Pharmaceuticals Inc.

41. Pimavanserin / Hepatic Impairment

Alert Message: Use of Nuplazid (pimavanserin) is not recommended in patients with hepatic impairment. Pimavanserin has not been evaluated in this patient population.

Conflict Code: MC - Drug Disease Precaution
Drugs/Diseases

| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
|---------------|--------------------|---------------|
| Pimavanserin | Hepatic Impairment | |

References:
Nuplazid Prescribing Information, April 2016, Acadia Pharmaceuticals Inc.

42. Pimavanserin / QT Prolongation

____√____

Alert Message: Nuplazid (pimavanserin) prolongs the QT interval and its use should be avoided in patients with known QT prolongation or in combination with other drugs known to prolong the QT interval (e.g., procainamide, quinidine, amiodarone, and ziprasidone). Pimavanserin should also be avoided in patients with a history of cardiac arrhythmias as well as circumstances that increase the risk of occurrence of torsade de pointes and/or sudden death (e.g., bradycardia, hypokalemia, or hypomagnesemia), and in the presence of congenital prolongation of the QT interval.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C (Include)

Pimavanserin

QT Prolongation

Bradycardia

Hypokalemia

Hypomagnesemia

Cardiac Arrhythmias

References:

Nuplazid Prescribing Information, April 2016, Acadia Pharmaceuticals Inc.

43. Pimavanserin / Drugs that Prolong the QT Interval

Alert Message: Concurrent use of Nuplazid (pimavanserin) with drugs known to prolong the QT interval should be avoided. Pimavanserin has been shown to prolong the QT interval and co-administration with another agent that prolongs the QT interval may have additive QT effects and increase the risk of cardiac arrhythmia.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

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

References:

Nuplazid Prescribing Information, April 2016, Acadia Pharmaceuticals Inc.

46. Lenvatinib / Hypertension

___√___

Alert Message: In clinical trials, hypertension was reported in 73% of Lenvima (lenvatinib) treated patients compared to 10% in the placebo group. Blood pressure should be controlled prior to treatment with lenvatinib. Withhold lenvatinib for Grade 3 hypertension despite optimal hypertensive therapy; resume at a reduced dose when hypertension is controlled at Grade 2 or less. Discontinue for Grade 4 hypertension and do not resume.

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

| | | |
|---------------|---------------|------------------------------|
| <u>Util A</u> | <u>Util B</u> | <u>Util C (Negating)</u> |
| Lenvatinib | Hypertension | Antihypertensive Medications |

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Facts & Comparisons, 2016 Updates, Wolters Kluwer Health, Inc.
Lenvima Prescribing Information, May 2016, Eisai Inc.

47. Lenvatinib / Cardiac Failure

___√___

Alert Message: In clinical studies, cardiac dysfunction was reported in 7% of Lenvima (lenvatinib) treated patients compared to 2% in the placebo group. Monitor patient for clinical symptoms or signs of cardiac decompensation. Withhold lenvatinib for development of Grade 3 cardiac dysfunction until improved to Grade 0 or 1 or baseline. Either resume lenvatinib at a reduced dose (per adjustments in official prescribing information) or discontinue depending on the severity and persistence of cardiac dysfunction. Discontinue for Grade 4 cardiac dysfunction.

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

| | | |
|---------------|-----------------|---------------|
| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
| Lenvatinib | Heart Failure | |
| | Pulmonary Edema | |
| | Orthopnea | |
| | Dyspnea | |

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Facts & Comparisons, 2016 Updates, Wolters Kluwer Health, Inc.
Lenvima Prescribing Information, May 2016, Eisai Inc.

48. Lenvatinib / Arterial Thromboembolic Event

___/___ ___

Alert Message: In clinical studies, arterial thromboembolic events were reported in 5% of Lenvima (lenvatinib) treated patients compared to 2% in the placebo group. Discontinue lenvatinib following an arterial thrombotic event. The safety of resuming lenvatinib has not been established.

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

| | | |
|---------------|----------------------------------|---------------|
| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
| Lenvatinib | Arterial Embolism and Thrombosis | |

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Facts & Comparisons, 2016 Updates, Wolters Kluwer Health, Inc.
Lenvima Prescribing Information, May 2016, Eisai Inc.

49. Lenvatinib / Hepatic Impairment

___/___ ___

Alert Message: In clinical studies, Lenvima (lenvatinib) has been shown to cause increases in ALT (4%) and AST (5%) that were Grade 3 or greater as compared to placebo (0%). Withhold lenvatinib for development of Grade 3 or greater liver impairment until resolved to Grade 0 or 1 or baseline. Either resume lenvatinib at a reduced dose (per adjustments in official prescribing information) or discontinue depending on the severity and persistence of hepatotoxicity. Discontinue lenvatinib for hepatic failure.

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

| | | |
|---------------|-----------------|--------------------|
| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
| Lenvatinib | Hepatic Failure | Hepatic Impairment |

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Facts & Comparisons, 2016 Updates, Wolters Kluwer Health, Inc.
Lenvima Prescribing Information, May 2016, Eisai Inc.

50. Lenvatinib / Proteinuria

____√____

Alert Message: In clinical studies, proteinuria was reported in 34% of Lenvima (lenvatinib) treated patients as compared to 3% in the placebo group. Monitor patient for proteinuria before initiation of and periodically during treatment. If urine dipstick proteinuria greater than or equal to 2+ is detected, obtain a 24 hour urine protein. Withhold lenvatinib for greater or equal to 2 grams of proteinuria/24 hours and resume at a reduced dose (per adjustments in official prescribing information) when proteinuria is less than 2 gm/24 hours. Discontinue lenvatinib for nephrotic syndrome.

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

| | | |
|---------------|---------------|---------------|
| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
| Lenvatinib | Proteinuria | |

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Facts & Comparisons, 2016 Updates, Wolters Kluwer Health, Inc.
Lenvima Prescribing Information, May 2016, Eisai Inc.

51. Lenvatinib / Renal Failure & Renal Impairment

____√____

Alert Message: In clinical studies, renal impairment was reported in 14% of Lenvima (lenvatinib) treated patients as compared to 2% in the placebo group. Withhold lenvatinib for development of Grade 3 or 4 renal failure/impairment until resolved to Grade 0 to 1 or baseline. Either resume lenvatinib at a reduced dose (per adjustments in official prescribing information) or discontinue depending on the severity and persistence of renal impairment.

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

| | | |
|---------------|------------------|--------------------------|
| <u>Util A</u> | <u>Util B</u> | <u>Util C (Negating)</u> |
| Lenvatinib | Renal Impairment | CKD 4 & 5 ESRD |

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Facts & Comparisons, 2016 Updates, Wolters Kluwer Health, Inc.
Lenvima Prescribing Information, May 2016, Eisai Inc.

52. Lenvatinib / Gastrointestinal Perforation & Fistula Formation

______ ___ ___

Alert Message: In clinical studies, gastrointestinal perforation or fistula were reported in 2% of Lenvima (lenvatinib) treated patients as compared to 0.8% in the placebo group. Discontinue lenvatinib in patients who develop gastrointestinal perforation or life-threatening fistula.

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

| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
|---------------|---|---------------|
| Lenvatinib | Perforation of Intestine Gastrointestinal ulcer w/ perforation Fistula of stomach or duodenum Fistula of intestine | |

References:
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Facts & Comparisons, 2016 Updates, Wolters Kluwer Health, Inc.
Lenvima Prescribing Information, May 2016, Eisai Inc.

53. Lenvatinib / QT Interval Prolongation

______ ___ ___

Alert Message: Lenvima (lenvatinib) can cause QT interval prolongation. Monitor ECGs in patients with congenital long QT syndrome, heart failure, bradyarrhythmias, or those taking drugs known to prolong the QT interval. Also monitor and correct electrolyte abnormalities in all patients. Withhold lenvatinib for the development of QTc interval prolongation greater than 500 ms. Resume lenvatinib at a reduced dose (per adjustments in official prescribing information) when QTc prolongation resolves to baseline.

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

| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
|---------------|--|---------------|
| Lenvatinib | QT Long Syndrome Heart Failure Bradycardia | |

References:
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Facts & Comparisons, 2016 Updates, Wolters Kluwer Health, Inc.
Lenvima Prescribing Information, May 2016, Eisai Inc.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

54. Lenvatinib / Hypocalcemia

______ ___ ___

Alert Message: In clinical studies, hypocalcemia, Grade 3 or greater, was reported in 9% of Lenvima (lenvatinib) treated patients as compared to 2% in the placebo group. Monitor blood calcium at least monthly and replace calcium as necessary during treatment. Interrupt and adjust lenvatinib dose as necessary (per adjustments in official prescribing information) depending on severity and persistence of hypocalcemia.

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

| | | |
|---------------|---------------|---------------|
| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
| Lenvatinib | Hypocalcemia | |

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Facts & Comparisons, 2016 Updates, Wolters Kluwer Health, Inc.
Lenvima Prescribing Information, May 2016, Eisai Inc.

55. Lenvatinib / Reversible Posterior Leukoencephalopathy Syndrome

______ ___ ___

Alert Message: Reversible Posterior Leukoencephalopathy Syndrome (RPSL) has been reported in patients receiving Lenvima (lenvatinib). If the diagnosis of RPSL is confirmed withhold lenvatinib until fully resolved. Upon resolution, resume at a reduced dose (per adjustments in official prescribing information) or discontinue depending on severity and persistence of neurologic symptoms.

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

| | | |
|---------------|---|---------------|
| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
| Lenvatinib | Reversible Posterior Leukoencephalopathy Syndrome | |

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Facts & Comparisons, 2016 Updates, Wolters Kluwer Health, Inc.
Lenvima Prescribing Information, May 2016, Eisai Inc.

56. Lenvatinib / Hemorrhagic Event

___√___ ___ ___

Alert Message: In clinical studies, hemorrhagic events occurred in 35% of Lenvima (lenvatinib) treated patients as compared to 18% in the placebo group. Withhold lenvatinib for development of Grade 3 hemorrhage until resolved to Grade 0 to 1. Either resume at a reduced dose (per adjustments in official prescribing information) or discontinue depending on severity and persistence of hemorrhage. Discontinue lenvatinib in patients who experience Grade 4 hemorrhage.

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

| <u>Util A</u> | <u>Util B</u> | <u>Util C</u> |
|---------------|--|---------------|
| Lenvatinib | Epistaxis Intracranial Hemorrhage Intracerebral Hemorrhage Subdural Hemorrhage Gastrointestinal Hemorrhage | |

References:
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Facts & Comparisons, 2016 Updates, Wolters Kluwer Health, Inc.
Lenvima Prescribing Information, May 2016, Eisai Inc.

57. Lenvatinib / Pregnancy / Pregnancy Negating

___√___ ___ ___

Alert Message: *Based on its mechanism of action, Lenvima (lenvatinib) can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with Lenvima (lenvatinib) and for at least 2 weeks following completion of therapy.*

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

| <u>Util A</u> | <u>Util B</u> | <u>Util C (Negating)</u> |
|---------------|---------------|-------------------------------------|
| Lenvatinib | Pregnancy | Delivery Miscarriage Abortion |

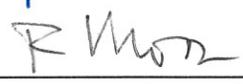
Age Range: 11-50 yoa
Gender: Female

References:
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Facts & Comparisons, 2016 Updates, Wolters Kluwer Health, Inc.
Lenvima Prescribing Information, May 2016, Eisai Inc.


Stephanie McGee Azar, Commissioner

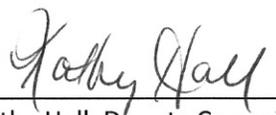
Approve Deny

6-22-17
Date


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

Approve Deny

6-20-17
Date


Kathy Hall, Deputy Commissioner

Approve Deny

June 19, 2017
Date