Alabama Medicaid DUR Board Meeting Minutes  
January 24, 2018

Members Present: Robert Moon, Rachel Seaman, P.J. Hughes, Bernie Olin, Kelli Littlejohn Newman, Marilyn Bulloch

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

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

Members Absent: Chris Phung, Denyse Thornley-Brown, Dan McConaghy, Donald Kern, Kenny Murray

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

Review and Adoption of Minutes: The minutes of the October 25, 2017 meeting were presented and P.J. Hughes made a motion to approve the minutes. R. Seaman 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 July 2017. She reported 10,139 total manual requests and 18,409 total electronic requests. From the Prior Authorization and Override Response Time Ratio report for July 2017, L. Thomas reported that approximately 69% of all manual PAs and all overrides were completed in less than two hours. Eighty-nine percent of all manual PAs and 91% of all overrides were completed in less than four hours. Ninety-two percent of all manual PAs and 93% of all overrides were completed in less than eight hours. For the month of August 2017, L. Thomas reported 11,965 manual PA requests and 21,033 electronic PA requests were received. She reported that 66% of all manual PAs and 67% of all overrides were completed in less than two hours. Eighty-five percent of all manual PAs and overrides were completed in less than four hours. Eighty-six percent of all manual PAs and 87% of all overrides were completed in less than eight hours. For the month of September 2017, L. Thomas reported 10,671 manual PA requests and 18,998 electronic PA requests. L. Thomas reported that approximately 67% of all manual PAs and 65% of all overrides were completed in less than two hours. Seventy-nine percent of all manual PA requests and all overrides were completed in less than four hours. Eighty-one 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 April 2017 through September 2017. She reported 3,508,752 total prescriptions, 211,241 average recipients per month using pharmacy benefits, and an average paid per prescription of $104.93.

Cost Management Analysis: L. Thomas reported an average cost per claim of $101.85 for September 2017 and emphasized that the table contained the average cost per claim over the past two years. From the 3rd Quarter 2017 Drug Analysis, L. Thomas reported 79.4% generic utilization, 9.3% brand single-source, 7.4% brand multi-source (those requests which required a DAW override), and 3.9% OTC and “other”. From the Top 25 Drugs Based on Number of Claims from 07/01/2017 – 09/30/2017, L. Thomas reported the top five drugs: amoxicillin, cetirizine, hydrocodone-acetaminophen, ProAir® HFA, and montelukast sodium. L. Thomas then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 07/01/2017 – 09/30/2017: Vyvanse®, Focalin XR®, Invega Sustenna®, Lyrica®, and ProAir® HFA. She reminded the Board that Vyvanse® and Focalin XR® are 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, Respiratory and CNS Stimulants, Miscellaneous Anticonvulsants, and Insulins.
Opioid Utilization: K. Newman began the discussion of opioid utilization and emphasized that Dr. Moon tasked the Agency with tackling the use of opioids throughout the state. L. Thomas explained that the top 100 prescribers of opioids throughout the state would be targeted. She explained that pain management specialists would not be excluded, however, oncologist would be excluded. L. Thomas discussed the “Opioid Prescribing Report Cards” that would be hand-delivered by Health Information Designs’ Academic Detailers. L. Thomas shared a list of the top 100 prescribers to the Board. R. Moon reminded the Board that only Medicaid paid claims were used in the report. M. Bulloch asked if the data could be seen in geographical terms and C. Hurst indicated this could be done through Medicaid’s statistical department.

RDUR Intervention Report: L. Thomas presented the RDUR Activity Report for July 2017. She reported 545 profiles reviewed and 581 letters sent with 113 responses received as of the date of the report. She reported 59 of 86 physicians indicated that they found the RDUR letters “useful” or “extremely useful”. The criteria for the cycle of intervention letters included Drug-Disease Precaution (narcotic/opioid use in patients with a history of drug abuse); Hepatitis C SVR Response Rates; Appropriate Use (appropriate use of immediate-release opioids); Appropriate Use (concurrent use of buprenorphine and pure opiate agonists).

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

Medicaid Update: T. Minnifield reminded the Board members that all updated Medicaid drug lists provided are also available online and that the next DUR Meeting would be April 25th.

P & T Committee Update: C. Hurst began the P & T Update by informing the Board that the last meeting was held on January 8, 2018, and covered the Antihypertensive Agents and the Hepatitis C Agents. The next P & T meeting is scheduled for February 21, 2018, at 9 a.m. and will cover the Respiratory Agents.

Next Meeting Date: M. Bulloch notified the Board that the next DUR meeting will be held on April 25, 2018. A motion to adjourn the meeting was made by B. Olin. P.J. Hughes seconded the motion and the meeting was adjourned at 2:00 p.m.

Respectfully submitted,

Lori Thomas, PharmD.
1. Cabozantinib / Therapeutic Appropriateness
Alert Message: The safety and effectiveness of Cabometyx (cabozantinib) have not been established in pediatric patients.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases
Util A | Util B | Util C
Cabozantinib Tabs

Age Range: 0 – 17 yoa

References:
Cabometyx Prescribing Information, April 2016, Exelixis, Inc.

2. Cabozantinib / Therapeutic Appropriateness
Alert Message: Based on its mechanism of action, Cabometyx (cabozantinib) can cause fetal harm when administered to a pregnant woman. If used during pregnancy, or if the patient becomes pregnant while taking this drug, she should be apprised of the potential hazard to the fetus. Advise females of reproductive potential to use effective contraception during treatment with caboazatinib and for 4 months after the last dose.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases
Util A | Util B | Util C
Cabozantinib Tabs

Gender: Female
Age Range 11 – 50

References:
Cabometyx Prescribing Information, April 2016, Exelixis, Inc.
3. Cabozantinib / Overuse
Alert Message: Cabometex (cabozantinib) may be over-utilized. The manufacturer’s maximum recommended dose for a patient with renal cell carcinoma is 60 mg once daily.

Conflict Code: ER - Overutilization

Drugs/Diseases

<table>
<thead>
<tr>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cabozantinib Tabs</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Max Dose: 60 mg/day

References:
Cabometex Prescribing Information, April 2016, Exelixis, Inc.

4. Cabozantinib / Hepatic Impairment
Alert Message: Increased exposure to Cabometex (cabozantinib) has been observed in patients with mild to moderate hepatic impairment. Reduce the cabozantinib dose in patients with mild (Child-Pugh score (C-P A) or moderate (C-P B) hepatic impairment. Cabozantinib is not recommended for use in patients with severe hepatic impairment.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

<table>
<thead>
<tr>
<th>Util A</th>
<th>Util B</th>
<th>Util C (Include)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cabozantinib Tabs</td>
<td></td>
<td>Hepatic Impairment</td>
</tr>
</tbody>
</table>

References:
Cabometex Prescribing Information, April 2016, Exelixis, Inc.

5. Cabozantinib / GI Perforations / Fistulas
Alert Message: Cabometex (cabozantinib) has been shown to cause gastrointestinal (GI) perforations and fistulas in patients with renal cell carcinoma. Patients should be monitored for symptoms of fistulas and perforations. Cabozantinib therapy should be permanently discontinued in patients who experience a fistula which cannot be appropriately managed or a GI perforation.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

<table>
<thead>
<tr>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cabozantinib Tabs</td>
<td>GI Perforation</td>
<td>Fistulas</td>
</tr>
</tbody>
</table>

References:
Cabometex Prescribing Information, April 2016, Exelixis, Inc.
6. Cabozantinib / Hemorrhage

Alert Message: Serious and sometimes fatal hemorrhage has occurred with Cabometyx (cabozantinib) therapy. Do not administer cabozantinib to patients who have or are at risk for severe hemorrhage.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases
Util A Util B Util C (Include)
Cabozantinib Tabs GI Hemorrhage
Subarachnoid Hemorrhage
Intracerebral Hemorrhage
Hemorrhage, unspecified

References:
Cabometyx Prescribing Information, April 2016, Exelixis, Inc.

7. Cabozantinib / Thrombotic Events

Alert Message: Cabometyx (cabozantinib) treatment results in an increased incidence of thrombotic events. Cabozantinib should be discontinued in patients who experience an acute myocardial infarction or other clinically significant arterial thromboembolic complications.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases
Util A Util B Util C
Cabozantinib Tabs Cerebral Thrombosis
Arterial Thrombosis
Venous Thrombosis

References:
Cabometyx Prescribing Information, April 2016, Exelixis, Inc.
8. Cabozantinib / CYP3A4 Inhibitors
Alert Message: Concomitant use of Cabometyx (cabozantinib) with strong CYP3A4 inhibitors (e.g., ketoconazole and clarithromycin) may result in increased exposure of cabozantinib and may increase the risk of exposure-related toxicity. If concurrent use cannot be avoided, the dose of cabozantinib should be reduced by 20 mg. Resume the dose that was used prior to initiating the CYP3A4 inhibitor 2 to 3 days after discontinuation of the strong inhibitor.

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

<table>
<thead>
<tr>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cabozantinib Tabs</td>
<td>Ketoconazole</td>
<td>Clarithromycin</td>
</tr>
<tr>
<td></td>
<td>Itraconazole</td>
<td>Atazanavir</td>
</tr>
<tr>
<td></td>
<td>Nefazodone</td>
<td>Saquinavir</td>
</tr>
<tr>
<td></td>
<td>Telithromycin</td>
<td>Ritonavir</td>
</tr>
<tr>
<td></td>
<td>Indinavir</td>
<td>Nelfinavir</td>
</tr>
<tr>
<td></td>
<td>Voriconazole</td>
<td>Cobicistat</td>
</tr>
<tr>
<td></td>
<td>Posaconazole</td>
<td></td>
</tr>
</tbody>
</table>

References:
Cabometyx Prescribing Information, April 2016, Exelixis, Inc.

9. Cabozantinib / CYP3A4 Inducers
Alert Message: Concomitant use of Cabometyx (cabozantinib) with strong CYP3A4 inducers (e.g., phenytoin and carbamazepine) may result in decreased exposure of cabozantinib leading to reduced efficacy. If concurrent use cannot be avoided, the dose of cabozantinib should be increased by 20 mg (i.e., 60 mg to 80 mg daily or 40 mg to 60 mg daily) as tolerated but should not exceed 80 mg daily. Resume the cabozantinib dose that was used prior to initiating the inducer 2 to 3 days after inducer discontinuation.

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

<table>
<thead>
<tr>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cabozantinib Tabs</td>
<td>Phenytoin</td>
<td>Carbamazepine</td>
</tr>
<tr>
<td></td>
<td>Rifampin</td>
<td>Rifabutin</td>
</tr>
<tr>
<td></td>
<td>Rifapentene</td>
<td>Phenobarbital</td>
</tr>
</tbody>
</table>

References:
Cabometyx Prescribing Information, April 2016, Exelixis, Inc.
10. **Cabozantinib / Hypertension**

Alert Message: Patients taking Cabometyx (cabozantinib) show increased incidence of treatment-emergent hypertension. In a randomized trial, hypertension was reported in 37% of cabozantinib-treated patients as compared to 3.1% of everolimus-treated patients. Blood pressure should be monitored prior to and throughout therapy. Cabozantinib should be discontinued if there is evidence of hypertensive crisis or severe hypertension that cannot be controlled with anti-hypertensive therapy.

Conflict Code: DB – Drug-Drug Marker and/or Diagnosis

<table>
<thead>
<tr>
<th>Drugs/Diseases</th>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cabozantinib Tabs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-Hypertensive Drugs</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

References:
Cabometyx Prescribing Information, April 2016, Exelixis, Inc.

11. **Cabozantinib / Palmar-Plantar Erythrodysesthesia Syndrome**

Alert Message: Palmar-plantar erythrodysesthesia syndrome (PPES) has been reported in patients treated with Cabometyx (cabozantinib). Cabozantinib should be withheld in patients who develop intolerable Grade 2 PPES or Grade 3 PPES until improvement to Grade 1, at which time cabozantinib therapy can resume at a reduced dose.

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

<table>
<thead>
<tr>
<th>Drugs/Diseases</th>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cabozantinib Tabs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palmar-Plantar Erythrodysesthesia Syndrome</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

References:
Cabometyx Prescribing Information, April 2016, Exelixis, Inc.

12. **Cabozantinib / Proteinuria**

Alert Message: In clinical trials, proteinuria was observed in 2% of patients receiving Cabometyx (cabozantinib) as compared to <1% of patients receiving everolimus. Cabozantinib should be discontinued in patients who develop nephrotic syndrome.

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

<table>
<thead>
<tr>
<th>Drugs/Diseases</th>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cabozantinib Tabs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteinuria</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nephrotic Syndrome</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

References:
Cabometyx Prescribing Information, April 2016, Exelixis, Inc.
13. Cabozantinib / Reversible Posterior Leukoencephalopathy Syndrome

Alert Message: Reversible Posterior Leukoencephalopathy Syndrome (RPLS) has been reported with Cabometyx (cabozantinib) treatment. An evaluation for RPLS should be performed in any patient presenting with seizures, headaches, visual disturbances, confusion or altered mental function. Cabozantinib should be discontinued if RPLS develops.

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

Drugs/Diseases
Util A Util B Util C
Cabozantinib Tabs Seizures
Headache
Visual Disturbances
Confusion
Altered Mental Function

References:
Cabometyx Prescribing Information, April 2016, Exelixis, Inc.

14. Daclizumab / Overutilization

Alert Message: The recommended dosage of Zinbryta (daclizumab) is 150 mg injected subcutaneously once monthly.

Conflict Code: ER – Overutilization

Drugs/Diseases
Util A Util B Util C
Daclizumab

Max Dose: 1 injection/month

References:
Zinbryta Prescribing Information, May 2016, Biogen.
### 15. Daclizumab / Hepatic Impairment
Alert Message: The use of Zinbryta (daclizumab) is contraindicated in patients with pre-existing hepatic disease, hepatic impairment, including ALT and AST at least 2 times the ULN, history of autoimmune hepatitis or other autoimmune conditions involving the liver. Daclizumab can cause severe liver injury including life-threatening events, liver failure, and autoimmune hepatitis. Liver injury can occur at any time during treatment with daclizumab, with cases reported up to 4 months after the last dose of daclizumab.

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

<table>
<thead>
<tr>
<th>Drugs/Diseases</th>
<th>Util A</th>
<th>Util B</th>
<th>Util C (Include)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daclizumab</td>
<td></td>
<td></td>
<td>Hepatic Impairment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Autoimmune Hepatitis</td>
</tr>
</tbody>
</table>

References:
Zinbryta Prescribing Information, May 2016, Biogen.

### 16. Daclizumab / Depression & Suicidal Ideation
Alert Message: The use of Zinbryta (daclizumab) has been associated with depression-related events, including suicidal ideation or suicide attempt. Daclizumab should be used with caution in patients with previous or current depressive disorders. Advise patients and/or caregivers to immediately report any symptoms of new or worsening depression and/or suicidal ideation to their healthcare provider.

Conflict Code: TA – Therapeutic Appropriateness

<table>
<thead>
<tr>
<th>Drugs/Diseases</th>
<th>Util A</th>
<th>Util B</th>
<th>Util C (Include)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daclizumab</td>
<td></td>
<td></td>
<td>Depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Suicidal Ideation</td>
</tr>
</tbody>
</table>

References:
Zinbryta Prescribing Information, May 2016, Biogen.

### 17. Daclizumab / Therapeutic Appropriateness
Alert Message: Safety and effectiveness of Zinbryta (daclizumab) in patients less than 17 years of age have not been established. Use of daclizumab is not recommended in pediatric patients due to the risk of hepatic injury and immune-mediated disorders.

Conflict Code: TA - Therapeutic Appropriateness

<table>
<thead>
<tr>
<th>Drugs/Diseases</th>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daclizumab</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Age Range: 0 - 16 yoa

References:
Zinbryta Prescribing Information, May 2016, Biogen.
18. Daclizumab / Pregnancy / Pregnancy Negating

Alert Message: There are no adequate studies on the developmental risk associated with the use of Zinbryta (daclizumab) in pregnant women. Daclizumab is a monoclonal antibody and these agents are known to cross the placenta. Administration of daclizumab in monkeys during gestation resulted in embryofetal death and reduced fetal growth at maternal exposures greater than 30 times that expected clinically.

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

<table>
<thead>
<tr>
<th>Util A</th>
<th>Util B</th>
<th>Util C (Negating)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daclizumab</td>
<td>Pregnancy</td>
<td>Miscarriage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Delivery</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abortion</td>
</tr>
</tbody>
</table>

References:
Zinbryta Prescribing Information, May 2016, Biogen.

19. Daclizumab / Nonadherence

Alert Message: Based on refill history, your patient may be under-utilizing Zinbryta (daclizumab). 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

<table>
<thead>
<tr>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daclizumab</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

References:
20. Daclizumab / Hepatotoxic Drugs

Alert Message: Caution should be exercised when administering Zinbryta (daclizumab) with drugs that can cause hepatotoxicity. Daclizumab can cause severe liver injury, including life-threatening events, and the use with other agents that cause liver injury may increase the risk of the adverse effect.

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

<table>
<thead>
<tr>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daciluzumab</td>
<td>Allopurinol</td>
<td>Nevirapine</td>
</tr>
<tr>
<td></td>
<td>Amiodarone</td>
<td>Nitrofurantoin</td>
</tr>
<tr>
<td></td>
<td>Amoxicillin-clavulanate</td>
<td>Phenytoin</td>
</tr>
<tr>
<td></td>
<td>Atorvastatin</td>
<td>Propylthiouracil</td>
</tr>
<tr>
<td></td>
<td>Azathioprine</td>
<td>Quinidine</td>
</tr>
<tr>
<td></td>
<td>Busulfan</td>
<td>Pyrazinamide</td>
</tr>
<tr>
<td></td>
<td>Carbamazepine</td>
<td>Rifampin</td>
</tr>
<tr>
<td></td>
<td>Chlorpromazine</td>
<td>Simvastatin</td>
</tr>
<tr>
<td></td>
<td>Dantrolene</td>
<td>TMP-SMZ</td>
</tr>
<tr>
<td></td>
<td>Diclofenac</td>
<td>Sulfasalazine</td>
</tr>
<tr>
<td></td>
<td>Didanosine</td>
<td>Sulindac</td>
</tr>
<tr>
<td></td>
<td>Disulfiram</td>
<td>Telithromycin</td>
</tr>
<tr>
<td></td>
<td>Efavirenz</td>
<td>Ticlopidine</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>Valproate</td>
</tr>
<tr>
<td></td>
<td>Flutamide</td>
<td>Alectinib</td>
</tr>
<tr>
<td></td>
<td>Ibuprofen</td>
<td>Sunitinib</td>
</tr>
<tr>
<td></td>
<td>Infliximab</td>
<td>Idelalisib</td>
</tr>
<tr>
<td></td>
<td>Interferon</td>
<td>Ixazomib</td>
</tr>
<tr>
<td></td>
<td>Isoniazid</td>
<td>Erlotinib</td>
</tr>
<tr>
<td></td>
<td>Itraconazole</td>
<td>Lenvatinib</td>
</tr>
<tr>
<td></td>
<td>Ketoconazole</td>
<td>Nefazodone</td>
</tr>
<tr>
<td></td>
<td>Methotrexate</td>
<td>Maraviroc</td>
</tr>
<tr>
<td></td>
<td>Methyldopa</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Minocycline</td>
<td></td>
</tr>
</tbody>
</table>

References:
Zinbryta Prescribing Information, May 2016, Biogen.
Bjornsson, ES. Hepatotoxicity by Drugs: The Most Common Implicated Agents. Int J Mol Sci. 2016 Feb; 17(2);244.
21. Panobinostat / Diarrhea
Alert Message: Farydak (panobinostat) can cause severe diarrhea. Monitor patient for symptoms and ensure the patient has adequate hydration prior to and during therapy. Initiate anti-diarrheal treatment medication at the onset of diarrhea. Interrupt panobinostat therapy at the onset of moderate diarrhea (4 to 6 stools/day) or severe diarrhea (>7 stools/day).

Conflict Code: MC – Drug (Actual) Disease Warning (Black Box Warning)
Drugs/Diseases
Util A  Util B  Util C
Panobinostat  Diarrhea

References:
Farydak Prescribing Information, Feb. 2015, Novartis Pharmaceuticals Corporation.

22. Panobinostat / Cardiovascular Events
Alert Message: Severe and fatal cardiac ischemic events, including arrhythmias and ECG changes, have occurred in patients receiving Farydak (panobinostat). Panobinostat may prolong the QT interval. Obtain ECG and electrolytes at baseline and periodically during treatment as clinically indicated. Panobinostat should not be initiated in patients with a QTcF > 450 msec or clinically significant baseline ST-segment or T-wave abnormalities.

Conflict Code: MC – Drug (Actual) Disease Warning (Black Box Warning)
Drugs/Diseases
Util A  Util B  Util C (Include)
Panobinostat  Myocardial Infarction
Angina
QT Prolongation

References:
Farydak Prescribing Information, Feb. 2015, Novartis Pharmaceuticals Corporation.

*QTcF is the Fridericia corrected QT interval formula and was used to calculate the QT interval in the clinical trials for Farydak (panobinostat). More than 30 correction formula have been proposed, of which Bazett’s (QTcB) and Fridericia’s (QTcF) corrections are the most widely used. Fridericia’s formula generates a more accurate correction in this circumstance.
23. **Panobinostat / Hepatic Impairment**

Alert Message: Farydak (panobinostat) can cause hepatic dysfunction. Liver function should be monitored prior to treatment and regularly during treatment. If abnormal liver function tests are observed dose adjustment may be considered. The starting dose of panobinostat should be reduced in patients with mild or moderate hepatic impairment (15 mg and 10 mg, respectively). Avoid use in patients with severe hepatic impairment.

Conflict Code: MC – Drug (Actual) Disease Warning

Drugs/Diseases

<table>
<thead>
<tr>
<th>Util A</th>
<th>Util B</th>
<th>Util C (Include)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panobinostat</td>
<td></td>
<td>Hepatic Impairment</td>
</tr>
</tbody>
</table>

References:
Farydak Prescribing Information, Feb. 2015, Novartis Pharmaceuticals Corporation.

---

24. **Panobinostat / Hemorrhage**

Alert Message: Fatal and serious hemorrhage has been reported during treatment with Farydak (panobinostat). Obtain a baseline platelet count prior to therapy and monitor the CBC weekly during therapy. Interruption of panobinostat therapy, dose adjustment, or drug discontinuation may be necessary if severe toxicity occurs.

Conflict Code: MC – Drug (Actual) Disease Warning

Drugs/Diseases

<table>
<thead>
<tr>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panobinostat</td>
<td>Gastrointestinal Bleed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subarachnoid Hemorrhage</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intracerebral Hemorrhage</td>
<td></td>
</tr>
</tbody>
</table>

References:
Farydak Prescribing Information, Feb. 2015, Novartis Pharmaceuticals Corporation.
25. Panobinostat 15 mg & 20 mg / Strong CYP3A4 Inhibitors

Alert Message: The dose of Farydak (panobinostat) should be reduced to 10 mg when co-administered with strong CYP3A4 inhibitors. Panobinostat is a CYP3A4 substrate and inhibition of its CYP3A4-mediated metabolism may result in significantly increased panobinostat exposure and risk of adverse effects.

Conflict Code: DD – Drug/Drug Interaction

<table>
<thead>
<tr>
<th>Drugs/Diseases</th>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panobinostat 15 &amp; 20mg</td>
<td>Nefazodone</td>
<td>Ketoconazole</td>
<td>Itraconazole</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>Telithromycin</td>
<td>Voriconazole</td>
<td>Saquinavir</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>Nelfinavir</td>
<td>Cobicistat</td>
<td>Indinavir</td>
</tr>
</tbody>
</table>

Max Dose: 10 mg

References:
Farydak Prescribing Information, Feb. 2015, Novartis Pharmaceuticals Corporation.

26. Panobinostat / Strong CYP3A4 Inducers

Alert Message: Concurrent use of Farydak (panobinostat), a CYP3A4 substrate, with strong CYP3A4 inducers should be avoided. While drug interaction studies have not been conducted simulation studies using mechanistic models suggest an approximate 70% decrease in the systemic exposure of panobinostat in the presence of strong inducers of CYP3A4.

Conflict Code: DD – Drug/Drug Interaction

<table>
<thead>
<tr>
<th>Drugs/Diseases</th>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panobinostat</td>
<td>Phenytoin</td>
<td>Rifampin</td>
<td>Phenobarbital</td>
</tr>
<tr>
<td>Primidone</td>
<td>Rifabutin</td>
<td>Rifapentine</td>
<td>Carbamazepine</td>
</tr>
</tbody>
</table>

References:
Farydak Prescribing Information, Feb. 2015, Novartis Pharmaceuticals Corporation.
### Criteria Recommendations

**27. Panobinostat / Sensitive CYP2D6 Substrates**

Alert Message: Concurrent use of Farydk (panobinostat), a CYP2D6 inhibitor, with sensitive CYP2D6 substrates (e.g., atomoxetine, metoprolol, and venlafaxine) should be avoided due to risk of elevated CYP2D6 substrate concentrations. If concomitant use with the CYP2D6 substrate is unavoidable, monitor patient frequently for adverse reactions.

**Conflict Code: DD – Drug/Drug Interaction**

<table>
<thead>
<tr>
<th>Drugs/Diseases</th>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panobinostat</td>
<td>Atomoxetine</td>
<td>Nebivolol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Desipramine</td>
<td>Perphenazine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dextromethorphan</td>
<td>Tolterodine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metoprolol</td>
<td>Venlafaxine</td>
<td></td>
</tr>
</tbody>
</table>

**References:**
Farydk Prescribing Information, Feb. 2015, Novartis Pharmaceuticals Corporation.

### 28. Panobinostat / QT Prolongation Drugs

Alert Message: Farydk (panobinostat) has been shown to increase the QTc interval and therefore use with drugs that are known to prolong the QT interval is not recommended.

**Conflict Code: DD – Drug/Drug Interaction**

<table>
<thead>
<tr>
<th>Drugs/Diseases</th>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panobinostat</td>
<td>Albuterol</td>
<td>Disopyramide</td>
<td>Imipramine</td>
</tr>
<tr>
<td></td>
<td>Alfuzosin</td>
<td>Doxetilide</td>
<td>Indapamide</td>
</tr>
<tr>
<td></td>
<td>Amantadine</td>
<td>Dolasetron</td>
<td>Isradipine</td>
</tr>
<tr>
<td></td>
<td>Amiodarone</td>
<td>Doxepin</td>
<td>Itraconazole</td>
</tr>
<tr>
<td></td>
<td>Amitriptyline</td>
<td>Droperidol</td>
<td>Ketoconazole</td>
</tr>
<tr>
<td></td>
<td>Amphetamine</td>
<td>Droperidol</td>
<td>Kuprinib</td>
</tr>
<tr>
<td></td>
<td>Arsenic Trioxide</td>
<td>Ephedrine</td>
<td>Levalbuterol</td>
</tr>
<tr>
<td></td>
<td>Asenapine</td>
<td>Epinephrine</td>
<td>Levofloxacine</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>Lithium</td>
<td>Loxadoline</td>
</tr>
<tr>
<td></td>
<td>Atomoxetine</td>
<td>Escitalopram</td>
<td>Metaprotenol</td>
</tr>
<tr>
<td></td>
<td>Azithromycin</td>
<td>Felbamat</td>
<td>Methadone</td>
</tr>
<tr>
<td></td>
<td>Chloral Hydrate</td>
<td>Flecainide</td>
<td>Moexipril/HCTZ</td>
</tr>
<tr>
<td></td>
<td>Chloroquine</td>
<td>Fluconazole</td>
<td>Moxifloxacine</td>
</tr>
<tr>
<td></td>
<td>Chlorpromazine</td>
<td>Fluoxetine</td>
<td>Nicardipine</td>
</tr>
<tr>
<td></td>
<td>Ciproflaxacin</td>
<td>Foscarnet</td>
<td>Nilotinin</td>
</tr>
<tr>
<td></td>
<td>Citalopram</td>
<td>Fonofenitoin</td>
<td>Norfloxacin</td>
</tr>
<tr>
<td></td>
<td>Clarithromycin</td>
<td>Galantamine</td>
<td>Nortriptyline</td>
</tr>
<tr>
<td></td>
<td>Clomipramine</td>
<td>Gemifloxacin</td>
<td>Octreotide</td>
</tr>
<tr>
<td></td>
<td>Clozapine</td>
<td>Granisetron</td>
<td>Ofloxacine</td>
</tr>
<tr>
<td></td>
<td>Dasatinib</td>
<td>Haloperidol</td>
<td>Ondansetron</td>
</tr>
<tr>
<td></td>
<td>Desipramine</td>
<td>Isocarboxazid</td>
<td>Paliperoxide</td>
</tr>
<tr>
<td></td>
<td>Diphenhydramine</td>
<td>Iloperidone</td>
<td>Paroxetine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Terbutaline</td>
</tr>
</tbody>
</table>

**References:**
Farydak Prescribing Information, Feb. 2015, Novartis Pharmaceuticals Corporation.
29. **Panobinostat / Therapeutic Appropriateness**

Alert Message: Farydak (panobinostat) can cause fetal harm. Advise females of reproductive potential to avoid becoming pregnant while taking panobinostat and to use effective contraception while taking panobinostat and for at least 1 month after the last dose. Because of the potential risk of male-medicated teratogenicity, advise sexually active men to use condoms while on treatment and for 3 months after their last dose of panobinostat.

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

References:
Farydak Prescribing Information, Feb. 2015, Novartis Pharmaceuticals Corporation.

30. **Saxagliptin - All / Pancreatitis**

Alert Message: There have been post-marketing reports of acute pancreatitis in patients taking saxagliptin-containing products (Onglyza, Kombiglyze XR, and Qtern). After initiation of a saxagliptin-containing agent, the patient should be observed for signs and symptoms of pancreatitis. If pancreatitis is suspected, promptly discontinue the saxagliptin-containing agent and initiate appropriate management.

Conflict Code: MC – Drug (Actual) Disease Precaution/ Warning
Drugs/Diseases
Util A  Util B  Util C
Saxagliptin  Pancreatitis
Saxagliptin/Metformin
Saxagliptin/Dapagliflozin

References:
31. Saxagliptin – All / Heart Failure

Alert Message: Consider the risks and benefits of saxagliptin-containing therapy (Onglyza, Kombiglyze XR, and Qtern) in patients who have a history of or who have increased risk factors for heart failure. An increased risk of hospitalization for heart failure has been reported in patients receiving saxagliptin in a cardiovascular outcomes trial. If heart failure develops, evaluate and manage according to current standards of care and consider discontinuing the saxagliptin-containing agents.

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

<table>
<thead>
<tr>
<th>Drugs/Diseases</th>
<th>Util A</th>
<th>Util B</th>
<th>Util C (Include)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saxagliptin</td>
<td></td>
<td></td>
<td>Heart Failure</td>
</tr>
<tr>
<td>Saxagliptin/Metformin</td>
<td></td>
<td></td>
<td>Dyspnea</td>
</tr>
<tr>
<td>Saxagliptin/ Dapagliflozin</td>
<td></td>
<td></td>
<td>Fatigue</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Edema</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tachycardia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Arrhythmia</td>
</tr>
</tbody>
</table>

References:
Criteria Recommendations

32. Benzodiazepines / Opioids

Alert Message: Co-administration of opioids and benzodiazepines should be done with extreme caution as the combination may result in respiratory depression, hypotension, profound sedation, coma, and death. If concurrent administration is clinically warranted consider dosage reduction of one or both agents. Re-evaluate the patient’s treatment plan on a regular basis to determine the necessity for continued concomitant use of these agents.

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

Drugs/Diseases

<table>
<thead>
<tr>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td>Codeine</td>
<td></td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td>Fentanyl</td>
<td></td>
</tr>
<tr>
<td>Clonazepam</td>
<td>Hydrocodone</td>
<td></td>
</tr>
<tr>
<td>Clorazepate</td>
<td>Hydromorphone</td>
<td></td>
</tr>
<tr>
<td>Diazepam</td>
<td>Levorphanol</td>
<td></td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Meperidine</td>
<td></td>
</tr>
<tr>
<td>Oxazepam</td>
<td>Methadone</td>
<td></td>
</tr>
<tr>
<td>Estazolam</td>
<td>Morphine</td>
<td></td>
</tr>
<tr>
<td>Flurazepam</td>
<td>Oxycodone</td>
<td></td>
</tr>
<tr>
<td>Quazepam</td>
<td>Oxymorphone</td>
<td></td>
</tr>
<tr>
<td>Temazepam</td>
<td>Tapentadol</td>
<td></td>
</tr>
<tr>
<td>Triazolam</td>
<td>Tramadol</td>
<td></td>
</tr>
<tr>
<td>Clobazam</td>
<td>Buprenorphine</td>
<td></td>
</tr>
</tbody>
</table>

References:
Available at: http://www.healthquality.va.gov/guidelines/Pain/cot/COT_312_Full-er.pdf
33. **Synjardy XR / Overutilization**

Alert Message: Synjardy XR (empagliflozin/metformin extended-release) may be over-utilized. The manufacturer's maximum recommended dose of empagliflozin/metformin XR is 25/2000 mg once daily.

Conflict Code: ER - Overutilization

Drugs/Diseases

<table>
<thead>
<tr>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empagliflozin/metformin XR</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Max Dose: 25/2000 mg/day

References:

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

Alert Message: Synjardy XR (empagliflozin/metformin extended-release) use is contraindicated in patients with moderate to severe renal impairment (eGFR below 45 mL/min/1.73m²), end-stage renal disease, or dialysis. Based on its mechanism of action, inhibition of SGLT2 in the proximal renal tubules, the empagliflozin component is not expected to be effective in these patients.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

<table>
<thead>
<tr>
<th>Util A</th>
<th>Util B</th>
<th>Util C (Include)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empagliflozin/metformin XR</td>
<td>CKD Stage 3, 4 &amp; 5</td>
<td>ESRD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dialysis</td>
</tr>
</tbody>
</table>

References:

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

Alert Message: The safety and effectiveness of Synjardy XR (empagliflozin/metformin extended-release) in pediatric patients under 18 years of age have not been established.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

<table>
<thead>
<tr>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empagliflozin/metformin XR</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Age Range 0 - 17 yoa

References:
36. Synjardy XR / Insulin & Sulfonylureas
Alert Message: The concurrent use of Synjardy XR (empagliflozin/metformin extended-release) with insulin or an insulin secretagogue can increase the risk of hypoglycemia. A lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with empagliflozin/metformin XR.

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

<table>
<thead>
<tr>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empagliflozin/metformin XR</td>
<td>Insulins</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chlorpropamide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Glimepiride</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Glipizide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Glyburide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tolazamide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tolbutamide</td>
<td></td>
</tr>
</tbody>
</table>

References:

37. Synjardy XR / Nonadherence
Alert Message: Based on refill history, your patient may be under-utilizing Synjardy XR (empagliflozin extended-release). 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

<table>
<thead>
<tr>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empagliflozin/metformin XR</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

References:
### 38. Codeine - All / Therapeutic Appropriateness

**Alert Message:** Codeine-containing products, used either as an analgesic or an antitussive, are contraindicated in children under 12 years of age and should be prescribed with extreme caution in adolescents 12 to 18 years of age. Codeine is metabolized to morphine and ultra-rapid metabolizers can have excessive morphine formation and toxicity even after normal therapeutic doses. The use of codeine for post-operative pain management in pediatric patients after a tonsillectomy and/or adenoidectomy is contraindicated due to risk of serious respiratory depression.

**Conflict Code:** TA - Therapeutic Appropriateness

<table>
<thead>
<tr>
<th>Drugs/Diseases</th>
<th>Util A</th>
<th>Util B</th>
<th>Util C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Age Range:** < 18 yoa

**References:**

---

### 39. Codeine - All / Obesity & Severe Breathing Problems

**Alert Message:** The use of codeine-containing agents are not recommended in adolescent patients between 12 and 18 years of age who are obese or have conditions such as sleep apnea, or other severe lung disease due to risk of opioid-induced respiratory depression. Codeine is metabolized via CYP2D6 to morphine and ultra-rapid metabolizers of CYP2D6 can have excessive morphine formation and toxicity even after normal therapeutic doses.

**Conflict Code:** TA - Therapeutic Appropriateness (Warning)

<table>
<thead>
<tr>
<th>Drugs/Diseases</th>
<th>Util A</th>
<th>Util B</th>
<th>Util C (Include)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine - All</td>
<td></td>
<td></td>
<td>Obesity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sleep Apnea</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Asthma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cystic Fibrosis</td>
</tr>
</tbody>
</table>

**Age Range:** 12 -18 yoa

**References:**
40. Codeine - All / Lactation

Alert Message: The use of codeine-containing agents is not recommended in nursing mothers. Codeine is metabolized to morphine which is excreted in breastmilk and may cause sedation and respiratory depression in breast-fed infants. Codeine is metabolized via CYP2D6 and if the nursing mother is a CYP2D6 ultra-rapid metabolizer excessive morphine formation can occur increasing the risk for excessive sedation and respiratory depression.

Conflicts Code: MC – Drug (Actual) Disease Precaution
Drugs/Diseases
Util A          Util B          Util C
Codeine - All   Lactation  Other Disorder of Lactation

Age Range: 11-55 yoa
Gender: Female

References:

41. Tramadol - All / Therapeutic Appropriateness

Alert Message: Due to the risk of respiratory depression, the use of tramadol-containing agents is contraindicated for the treatment of pain in pediatric patients younger than 12 years of age and in post-operative pain management after tonsillectomy and/or adenoidectomy in pediatric patients younger than 18 years of age. Children who are ultra-rapid metabolizers of CYP2D6, an enzyme responsible for tramadol metabolism, are at increased risk for severe respiratory depression.

Conflicts Code: TA - Therapeutic Appropriateness
Drugs/Diseases
Util A          Util B          Util C
Tramadol – All

Age Range: < 18 yoa

References:
42. Tramadol - All / Obesity & Severe Breathing Problems

Alert Message: The use of tramadol-containing agents are not recommended in adolescent patients between 12 and 18 years of age who are obese or have conditions such as sleep apnea, or other severe lung disease. Children who are ultra-rapid metabolizers of CYP2D6, an enzyme responsible for tramadol metabolism, are at increased risk for severe respiratory depression.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A Util B Util C (Include)
Tramadol - All Obesity
Sleep Apnea
Asthma
Cystic Fibrosis

Age Range: 12 - 18 yoa

References:

43. Tramadol - All / Lactation

Alert Message: The use of tramadol-containing agents is not recommended in nursing mothers. The parent drug tramadol and its active metabolite (M1) are excreted in breast milk and may cause excessive sedation and respiratory depression, which could result in death in breast-fed infants. Tramadol is a CYP2D6 metabolized drug and if the nursing mother is a CYP2D6 ultra-rapid metabolizer M1 concentrations will be even higher with increased risk for adverse effects.

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

Util A Util B Util C
Tramadol – All Lactation Other Disorder of Lactation

Age Range: 11 - 55 yoa
Gender: Female

References:
44. Plecanatide / Overutilization
Alert Message: Trulance (plecanatide) may be over-utilized. The manufacturer’s recommended maximum adult dosage is 3 mg once daily.

Conflict Code: ER - Overutilization
Drugs/Diseases
Util A  Util B  Util C
Plecanatide

Max Dose: 3 mg per day

References:

45. Plecanatide / Therapeutic Appropriateness (Age 0 – 5 yoa)
Alert Message: Trulance (plecanatide) is contraindicated in patients less than 6 years of age. Due to increased intestinal expression of guanylate cyclase (GC-C), patients less than 6 years of age may be more likely than patients 6 years and older to develop severe diarrhea and its potentially serious consequences. In nonclinical studies, the use of plecanatide in young juvenile mice resulted in mortality in some mice within the first 24 hours of therapy, apparently due to dehydration.

Conflict Code: TA - Therapeutic Appropriateness (Black Box Warning)
Drugs/Diseases
Util A  Util B  Util C
Plecanatide

Age Range: 0 – 5 yoa

References:

46. Plecanatide / Therapeutic Appropriateness – Age 6 – 17 yoa
Alert Message: The safety and effectiveness of Trulance (plecanatide) in patients 6 years of age to less than 18 years of age have not been established and its use should be avoided in this patient population.

Conflict Code: TA - Therapeutic Appropriateness (Black Box Warning)
Drugs/Diseases
Util A  Util B  Util C
Plecanatide

Age Range: 6 – 17 yoa

References:
47. Plecanatide / Gastrointestinal Obstruction
Alert Message: Trulance (plecanatide) is contraindicated in patients with known or suggested gastrointestinal obstruction. Plecanatide is a guanylate cyclase-C (GC-C) agonist which increases intestinal fluid and accelerates transit.

Conflict Code: MC – Drug (Actual) Disease Precaution/Warning
Diseases
Util A  Util B  Util C
Plecanatide  Intestinal Obstruction
Paralytic ileus

References:

48. Plecanatide / Non-adherence
Alert Message: Based on refill history, your patient may be under-utilizing Trulance (plecanatide). Nonadherence 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
Diseases
Util A  Util B  Util C
Plecanatide

References:
Stephanie McGee Azar, Commissioner

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

Kathy Hall, Deputy Commissioner

☐ Approve  ☐ Deny  

☐ Approve  ☐ Deny  

☐ Approve  ☐ Deny  

3-29-18

3/28/18

3/26/18

Date

Date

Date