

**Alabama Medicaid DUR Board Meeting Minutes
July 26, 2017**

Members Present: Melinda Rowe, Marilyn Bulloch, Chris Phung, Bernie Olin, Paula Thompson, Denyse Thornley-Brown, Rachel Seaman, P.J. Hughes, Dan McConaghy

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

Present via Conference Call: Kelli Littlejohn Newman, Kristian Testerman, Lauren Ward, Tammy Dubac

Members Absent: Robert Moon, Donald Kern

Call to Order: The DUR meeting was called to order by M. Bulloch at approximately 1:03p.m.

Review and Adoption of Minutes: The minutes of the April 26, 2017 meeting were presented and P. Thompson made a motion to approve the minutes. D. Thornley-Brown seconded the motion and the motion was approved unanimously.

Prior Authorization and Overrides Update: L. Thomas began the Prior Authorization and Overrides Update with the Monthly Manual Prior Authorizations and Overrides Report for the month of January 2017. She reported 10,505 total manual requests and 25,881 total electronic requests. From the Prior Authorization and Override Response Time Ratio report for January 2017, L. Thomas reported that approximately 82% of all manual PAs and 83% of all overrides were completed in less than two hours. Ninety-three percent of all manual PAs and 97% of all overrides were completed in less than four hours. Ninety-five percent of all manual PAs and 96% of all overrides were completed in less than eight hours. For the month of February 2017, L. Thomas reported 10,093 manual PA requests and 24,320 electronic PA requests were received. She reported that 74% of all manual PAs and 76% of all overrides were completed in less than two hours. Eighty-eight percent of all manual PAs and 90% of all overrides were completed in less than four hours. Ninety-three percent of all manual PAs and all overrides were completed in less than eight hours. For the month of March 2017, L. Thomas reported 11,310 manual PA requests and 25,829 electronic PA requests. L. Thomas reported that approximately 59% of all manual PAs and 54% of all overrides were completed in less than two hours. Eighty-five percent of all manual PA requests and 84% of all overrides were completed in less than four hours. Ninety-three percent of all manual PA requests and all overrides were completed in less than eight hours.

Program Summary Review: L. Thomas briefly reviewed the Alabama Medicaid Program Summary for the months of October 2016 through March 2017. She reported 3,777,029 total prescriptions, 230,052 average recipients per month using pharmacy benefits, and an average paid per prescription of \$99.83.

Cost Management Analysis: L. Thomas reported an average cost per claim of \$101.69 for March 2017 and emphasized that the table contained the average cost per claim over the past two years. L. Thomas reminded the Board that the Prescription Limit and Maintenance Supply was mandatory starting January 2014. From the 1st Quarter 2017 Drug Analysis, L. Thomas reported 79.2% generic utilization, 9.7% brand single-source, 7.4% brand multi-source (those requests which required a DAW override), and 3.8% OTC and "other". From the Top 25 Drugs Based on Number of Claims from 01/01/2017 – 03/31/2017, L. Thomas reported the top five drugs: amoxicillin, cetirizine, hydrocodone-acetaminophen, ProAir[®] HFA, and azithromycin. L. Thomas then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 01/01/2017 – 03/31/2017: Vyvanse[®], Focalin XR[®], Invega[®] Sustenna[®], Tamiflu[®], and ProAir[®] HFA. L. Thomas mentioned that Tamiflu[®] was not in the top 25 of the previous quarter. 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.

Ingredient Duplication Edit: L. Thomas introduced a new edit that the Agency would like to implement that would limit the simultaneous use of drug products containing one or more identical generic chemical entity. Initially, this edit would be implemented for gabapentin and pregabalin products. A review of 2016 claims found a total of 770 patients on 2 or more strengths of gabapentin and 132 patients on 2 or more strengths of pregabalin. The Ingredient Duplication Edit would require medical justification for patients to be on 2 strengths of the same medication at the same time. D. Thornley-Brown asked if other medications would be included. C. Hurst indicated that once the edit was implemented, the Agency may review additional medications to add to the edit. P.J. Hughes asked if the edit would be triggered by someone using gabapentin and pregabalin simultaneously. L. Thomas indicated that the edit would only be triggered if the patient was simultaneously using one or more medications with the same generic chemical entity.

Review of Palivizumab Utilization for the 2016-2017 Season: The 2016-2017 RSV season ended March 31, 2017. L. Thomas provided an update which compared the results of the 2016-2017 season to previous seasons. L. Thomas referred to Alabama RSV data from the CDC which supported Alabama Medicaid's policy of limiting the Synagis® timeframe to October 2016 – March 2017. L. Thomas reminded the Board that each recipient could receive a maximum of 5 doses per season and that all policies relating to Synagis® were based on clinical literature and recommendations. For the 2016-17 season, there were 2,574 claims for 522 recipients. The average cost per claim was \$2,382 while the average cost per recipient was \$11,748. L. Thomas pointed out that there were 1,407 prior authorizations requested over the course of the season, with an approval rate of 72%. L. Thomas briefly reviewed the top dispensing pharmacies and the top PA denial reasons. L. Thomas reviewed the graphs comparing the total spend of all drugs compared to the total spend of Synagis® per RSV season.

RDUR Intervention Report: L. Thomas presented the RDUR Activity Report for January 2017. She reported 503 profiles reviewed and 771 letters sent with 130 responses received as of the date of the report. She reported 62 of 89 physicians indicated that they found the RDUR letters "useful" or "extremely useful". The criteria for the cycle of intervention letters included Drug-Drug Interaction (concurrent use of opioids and benzodiazepines); Hepatitis C SVR Response Rates; Appropriate Use (concurrent use of buprenorphine and pure opiate agonists).

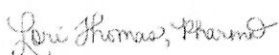
Proposed Criteria: L. Thomas presented the proposed set of 50 criteria to the Board. T. Minnifield instructed the Board members to mark their ballots. Of the 50 criteria, results from the criteria vote returned 46 approved and 4 approved as amended.

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 October 25th.

P & T Committee Update: C. Hurst began the P & T Update by informing the Board that the last meeting was held on May 10, 2017, and covered the First Generation Antihistamines, Estrogens, Antidiabetic Agents, Prenatal Vitamins, and a drug class review of Multiple Sclerosis Agents. C. Hurst mentioned that the PDL updates went into effect on July 3, 2017. The next P & T meeting is scheduled for August 9, 2017, at 9 a.m. and will cover the Cardiac Agents, Antihyperlipidemic Agents, and Anticoagulants.

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 1:55 p.m.

Respectfully submitted,



Lori Thomas, PharmD.

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

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

1. Lixisenatide / Over-utilization

Alert Message: The manufacturer's recommended maximum daily dose of Adlyxin (lixisenatide) is 20 mcg per day.

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Conflict Code: ER – Overuse

Drug/Disease

Util A

Util B

Util C

Lixisenatide

Max Dose: 1, 2 pen pack per month

References:

Adlyxin Prescribing Information, July 2016, Sanofi-Aventis U.S.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

2. Lixisenatide / Pancreatitis

Alert Message: In clinical trials, there were more cases of pancreatitis-related adverse reactions among patients treated with Adlyxin (lixisenatide) than placebo-treated. If pancreatitis is suspected, promptly discontinue lixisenatide and, if confirmed, lixisenatide should not be restarted.

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Conflict Code: MC – Drug Disease Warning/Contraindication

Drugs/Diseases:

Util A

Util B

Util C

Lixisenatide

Pancreatitis

References:

Adlyxin Prescribing Information, July 2016, Sanofi-Aventis U.S.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

3. Lixisenatide / Basal Insulin & Insulin Secretagogues

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

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Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases:

Util A

Util B

Util C

Lixisenatide

Insulin Glargine, Detemir & Degludec
Chlorpropamide
Glimepiride
Glipizide
Glyburide
Tolazamide
Tolbutamide

References:

Adlyxin Prescribing Information, July 2016, Sanofi-Aventis U.S.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

4. Lixisenatide / Renal Impairment

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

Conflict Code: MC – Drug Disease Warning/Contraindication
Drugs/Diseases:

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

References:

Adlyxin Prescribing Information, July 2016, Sanofi-Aventis U.S.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

5. Lixisenatide / Severe Gastrointestinal Disorders

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

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

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

References:

Adlyxin Prescribing Information, July 2016, Sanofi-Aventis U.S.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

6. Lixisenatide / Therapeutic Appropriateness < 18 years of age

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Alert Message: Safety and effectiveness of Adlyxin (lixisenatide) have not been established in pediatric patients younger than 18 years of age.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

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

Age Range: 0-17 yoa

References:

Adlyxin Prescribing Information, July 2016, Sanofi-Aventis U.S.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

7. Lixisenatide / Pregnancy / Delivery, Miscarriage & Abortion

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Alert Message: There are no adequate and well-controlled studies of Adlyxin (lixisenatide) use in pregnant women. Lixisenatide should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus.

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

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

Age Range: 11-55 yoa
Gender: Female

References:
Adlyxin Prescribing Information, July 2016, Sanofi-Aventis U.S.
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

8. Lixisenatide / Non-adherence

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

Conflict Code: LR – Non-adherence
Drugs/Diseases

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

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

9. Methylnaltrexone Tabs / Overutilization

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Alert Message: Relistor (methylnaltrexone) may be over-utilized. The manufacturer's recommended dosage of oral methylnaltrexone, for the treatment of opioid-induced constipation in patients with chronic non-cancer pain, is 450 mg once daily in the morning.

Conflict Code: ER - Overutilization
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>
Methylnaltrexone tabs		Hepatic Impairment CKD Stage 4 & 5

Max Dose: 450mg/day

References:
Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Relistor Prescribing Information, July 2016, Valeant Pharmaceuticals North America.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

10. Methylnaltrexone Tabs / Overutilization Renal Impairment

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Alert Message: Relistor (methylnaltrexone) may be over-utilized. The manufacturer's recommended dosage of oral methylnaltrexone, for the treatment of opioid-induced constipation in patients with chronic non-cancer pain with moderate to severe renal impairment (e.g., CrCl < 60 mL/min as estimated by Cockcroft-Gault) is 150 mg once daily in the morning.

Conflict Code: ER - Overutilization
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Methylnaltrexone tabs		CKD Stage 4 & 5

Max Dose: 150mg/day

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Relistor Prescribing Information, July 2016, Valeant Pharmaceuticals North America.

11. Methylnaltrexone Tabs / Overutilization Hepatic Impairment

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Alert Message: Relistor (methylnaltrexone) may be over-utilized. The manufacturer's recommended dosage of oral methylnaltrexone for the treatment of opioid-induced constipation in patients with chronic non-cancer pain with moderate to severe hepatic impairment (Child-Pugh Class B or C) is 150 mg daily in the morning.

Conflict Code: ER - Overutilization
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Methylnaltrexone tabs		Hepatic Impairment

Max Dose: 150mg/day

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Relistor Prescribing Information, July 2016, Valeant Pharmaceuticals North America.

12. Methylnaltrexone / Overutilization

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Alert Message: Relistor (methylnaltrexone) may be over-utilized. The manufacturer's recommended dosage of methylnaltrexone injection, for the treatment of opioid-induced constipation in patients with chronic non-cancer pain, is 12 mg subcutaneously once daily.

Conflict Code: ER - Overutilization
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>
Methylnaltrexone injection		Hepatic Impairment CKD Stage 4 & 5

Max Dose: 12mg/day

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Relistor Prescribing Information, July 2016, Valeant Pharmaceuticals North America.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

13. Methylnaltrexone / Overutilization Mod to Severe Renal Impairment

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Alert Message: Relistor (methylnaltrexone) may be over-utilized. The manufacturer's recommended dosage of methylnaltrexone injection, for the treatment of opioid-induced constipation in patients with chronic non-cancer pain with chronic non-cancer pain with moderate to severe renal impairment (e.g., CrCl < 60 mL/min as estimated by Cockcroft-Gault), is 6 mg subcutaneously once daily.

Conflict Code: ER - Overutilization
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Methylnaltrexone injection		CKD Stage 4 & 5

Max Dose: 6mg/day

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Relistor Prescribing Information, July 2016, Valeant Pharmaceuticals North America.

14. Methylnaltrexone / Overutilization Severe Hepatic Impairment

_____ ✓ _____

Alert Message: Relistor (methylnaltrexone) has not been studied in patients with severe hepatic impairment. Patients with severe hepatic impairment receiving methylnaltrexone should be monitored for methylnaltrexone-related adverse reactions. If considering dosage adjustment for patients with severe hepatic impairment follow the official product labeling weight-based daily dosing recommendation: < 38 kg give 0.075 mg/kg subQ, 38 to < 62 kg give 4 mg subQ, 62 to 114 kg give 6 mg, more than 114 kg give 0.075 mg/kg subQ.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Methylnaltrexone Injection		Severe Hepatic Impairment

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Relistor Prescribing Information, July 2016, Valeant Pharmaceuticals North America.

15. Methylnaltrexone / Opioid Agonists (Negating)

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Alert Message: The review of the patient's drug history did not reveal current use of opioid medication. Relistor (methylnaltrexone) is approved for the treatment of opioid-induced constipation (OIC) in adults with chronic non-cancer pain and OIC in patients with advanced illness who are receiving palliative care with insufficient response to laxative therapy. Methylnaltrexone 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>
Methylnaltrexone		Opioid Agonists

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Relistor Prescribing Information, July 2016, Valeant Pharmaceuticals North America.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

16. Methylnaltrexone / Gastrointestinal Obstruction

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Alert Message: Relistor (methylnaltrexone) use is contraindicated in patients with known or suspected gastrointestinal obstruction and patients at increased risk of recurrent obstruction, due to the potential for gastrointestinal perforation. Monitor patients for development of severe, persistent, or worsening abdominal pain and discontinue methylnaltrexone in patients who develop these symptom.

Conflict Code: TA – Therapeutic Appropriateness (Contraindication)

Drugs/Diseases

Util A

Util B

Util C (Include)

Methylnaltrexone

Gastrointestinal Obstruction

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Relistor Prescribing Information, July 2016, Valeant Pharmaceuticals North America.

17. Methylnaltrexone / Reduction in GI Wall Integrity

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Alert Message: Cases of gastrointestinal perforation have been reported in patients receiving Relistor (methylnaltrexone) who had conditions associated with localized or diffuse reduction of structural integrity in the wall of the gastrointestinal tract (e.g., peptic ulcer disease, Ogilvie's syndrome, diverticular disease, infiltrative gastrointestinal tract malignancies or peritoneal metastases). Monitor patients for the development of severe, persistent, or worsening abdominal pain, and discontinue methylnaltrexone in patients who develop this symptoms.

Conflict Code: TA – Therapeutic Appropriateness (Warning)

Drugs/Diseases

Util A

Util B

Util C (Include)

Methylnaltrexone

Crohn's Disease

Peptic, Gastric, Duodenal & Gastrojejunal Ulcer Disease

Perforation of Intestine

Diverticular Disease of Intestine

Malignant Neoplasm of Intestine

Malignant Neoplasm of Stomach

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Relistor Prescribing Information, July 2016, Valeant Pharmaceuticals North America.

18. Methylnaltrexone / Therapeutic Appropriateness

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Alert Message: Safety and effectiveness of Relistor (methylnaltrexone) tablets and injection have not been established in pediatric patients.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C (Negating)

Methylnaltrexone

Age Range: 0-17 yoa

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Relistor Prescribing Information, July 2016, Valeant Pharmaceuticals North America.

Criteria Recommendations

Accepted Approved Rejected

**As
Amended**

19. Vandetanib / Overutilization

Alert Message: Caprelsa (vandetanib) may be over-utilized. The manufacturer's recommended maximum daily dose is 300 mg once daily.

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Conflict Code: ER - Overutilization

Drugs/Diseases

Util A

Util B

Util C

Vandetanib

Max Dose: 300mg/day

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Caprelsa Prescribing Information, July 2016, AstraZeneca.

20. Vandetanib / QT Prolongation

Alert Message: Caprelsa (vandetanib) is contraindicated in patients with congenital long QT syndrome. Vandetanib can prolong the QT interval in a concentration-dependent manner. Do not start vandetanib in patients whose QTcF interval is greater than 450 ms or in patients with a history of torsades de pointes, bradyarrhythmias, or uncompensated heart failure.

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

Drugs/Diseases

Util A

Util B

Util C

Vandetanib

Long QT Syndrome

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Caprelsa Prescribing Information, July 2016, AstraZeneca.

21. Vandetanib / Strong CYP3A4 Inducers

Alert Message: The concurrent use of Caprelsa (vandetanib) with known strong CYP3A4 inducers should be avoided. Vandetanib is a CYP3A4 substrate and concomitant use with a strong CYP3A4 inducer may result in decreased vandetanib plasma concentrations.

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Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A

Util B

Util C

Vandetanib

Carbamazepine

Phenytoin

Phenobarbital

Primidone

Rifampin

Rifapentine

Rifabutin

References:

Caprelsa Prescribing Information, July 2016, AstraZeneca.

Facts & Comparisons, 2016 Wolters Kluwer Health.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

22. Vandetanib / Digoxin

Alert Message: Caution should be exercised when co-administering Caprelsa (vandetanib) with digoxin. Concurrent use of vandetanib with digoxin has been shown to increase digoxin plasma concentrations and exposure. Closely monitor patients for digoxin toxicities.

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Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vandetanib	Digoxin	

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Caprelsa Prescribing Information, July 2016, AstraZeneca.

23. Vandetanib / Interstitial Lung Disease

Alert Message: Interstitial lung disease (ILD) or pneumonitis, including fatalities, has occurred in patients treated with Caprelsa (vandetanib). Consider a diagnosis of ILD if the patient presents with new or worsening of breathlessness, persistent cough, or fever. Interrupt vandetanib treatment for acute or worsening pulmonary symptoms. Discontinue vandetanib if ILD is confirmed.

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

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vandetanib	Interstitial Lung Disease Breathlessness Cough Fever	

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Caprelsa Prescribing Information, July 2016, AstraZeneca.

24. Vandetanib / Pregnancy / Pregnancy Negating

Alert Message: Based on its mechanism of action, Caprelsa (vandetanib) can cause fetal harm when administered to a pregnant women. Vandetanib is embryotoxic, fetotoxic, and teratogenic in rats at exposures less than or equal to those expected at the recommended human dose of 300 mg/day. If vandetanib is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

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

Drugs/Diseases

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

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Caprelsa Prescribing Information, July 2016, AstraZeneca.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

25. Vandetanib / Ischemic Cerebrovascular Event

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Alert Message: Ischemic cerebrovascular events, including fatalities, occurred in patients treated with Caprelsa (vandetanib). In the randomized medullary thyroid cancer (MTC) study, ischemic cerebrovascular events occurred more frequently with vandetanib compared to placebo (1.3% compared to 0%). The safety of resumption of vandetanib therapy after resolution of an ischemic cerebrovascular event has not been studied. Discontinue vandetanib in patients who experience a severe ischemic cerebrovascular event.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vandetanib	Cerebral infarction	

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Caprelsa Prescribing Information, July 2016, AstraZeneca.

26. Vandetanib / Hemorrhage

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Alert Message: Serious hemorrhagic events, including fatalities, occurred in patients treated with Caprelsa (vandetanib). Discontinue vandetanib in patients with severe hemorrhage. Do not administer vandetanib to patients with a recent history of hemoptysis of greater than or equal to 1/2 teaspoon of red blood.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vandetanib	Cerebrovascular Hemorrhage Gastrointestinal Hemorrhage	

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Caprelsa Prescribing Information, July 2016, AstraZeneca.

27. Vandetanib / Heart Failure

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Alert Message: Heart failure, including fatalities, occurred in patients treated with Caprelsa (vandetanib). Monitor for signs and symptoms of heart failure. Consider discontinuation of vandetanib in patients with heart failure. Heart failure may not be reversible upon stopping vandetanib.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Vandetanib	Heart Failure	

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Caprelsa Prescribing Information, July 2016, AstraZeneca.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

28. Soliqua / Overutilization

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Alert Message: The manufacturers' recommended maximum daily dose of Soliqua (insulin glargine/lixisenatide) is 60 units per day. Administration of more than 60 units of insulin glargine/lixisenatide can result in overdose of the lixisenatide (> 20 mcg lixisenatide) component.

Conflict Code: ER - Overutilization

ER - Overutilization

Drugs/Diseases

Util A

Util B

Util C

Insulin Glargine/Lixisenatide

Max Dose: 60 units per day

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Soliqua 100/33 Prescribing Information, Nov. 2016, Sanofi-Aventis.

29. Soliqua / GLP-1 Receptor Agonists

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Alert Message: Soliqua (insulin glargine/lixisenatide) is not recommended for use in combination with any other products containing lixisenatide or another GLP-1 receptor agonist. Concurrent use of these agents represents an unnecessary duplication of therapy.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A

Util B

Util C

Insulin Glargine/Lixisenatide

Lixisenatide

Albiglutide

Dulaglutide

Exenatide

Liraglutide

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Soliqua 100/33 Prescribing Information, Nov. 2016, Sanofi-Aventis.

30. Soliqua / Gastroparesis

___√___ ___ ___

Alert Message: Soliqua (insulin glargine/lixisenatide) has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis. The lixisenatide component of the combination product slows gastric emptying, therefore, use of the product is not recommended in patients with severe gastroparesis.

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

Drugs/Diseases

Util A

Util B

Util C

Insulin Glargine/Lixisenatide

Gastroparesis

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Soliqua 100/33 Prescribing Information, Nov. 2016, Sanofi-Aventis.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

31. Soliqua / Therapeutic Appropriateness

_____√_____

Alert Message: The safety and effectiveness of Soliqua (insulin glargine/lixisenatide) have not been established in pediatric patients below 18 years of age.

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C

Insulin Glargine/Lixisenatide

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Soliqua 100/33 Prescribing Information, Nov. 2016, Sanofi-Aventis.

32. Soliqua / Pancreatitis

_____√_____

Alert Message: Soliqua (insulin glargine/lixisenatide) has not been studied in patients with a history of pancreatitis. The lixisenatide component of the combination product is a GLP-1 receptor agonists and these agents have been associated with acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis. Consider alternative antidiabetic therapy in patients with a history of pancreatitis. If pancreatitis is suspected, promptly discontinue use. If pancreatitis is confirmed, restarting insulin glargine/lixisenatide is not recommended.

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C (Include)

Insulin Glargine/Lixisenatide

Pancreatitis

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Soliqua 100/33 Prescribing Information, Nov. 2016, Sanofi-Aventis.

33. Soliqua / Renal Impairment

_____√_____

Alert Message: Soliqua (insulin glargine/lixisenatide) should be used with caution in patients with renal impairment. The lixisenatide component is a GLP-1 receptor agonist and these agents have been associated with acute kidney injury and worsening of chronic renal failure. Monitor renal function in patients with renal impairment and in those with severe GI adverse reactions (majority of reported renal events occurred in patients who experienced nausea, vomiting, diarrhea, or dehydration). Insulin glargine/lixisenatide use is not recommended in patients with ESRD.

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C (Include)

Insulin Glargine/Lixisenatide

Renal Impairment

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Soliqua 100/33 Prescribing Information, Nov. 2016, Sanofi-Aventis.

34. Soliqua / Hypokalemia

_____√_____

Alert Message: All insulin-containing products, including Soliqua (insulin glargine/lixisenatide), cause a shift in potassium from extracellular to intracellular space, possibly leading to hypokalemia. Monitor potassium levels in patients at risk for hypokalemia if indicated.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Insulin Glargine/Lixisenatide	Hypokalemia	

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Soliqua 100/33 Prescribing Information, Nov. 2016, Sanofi-Aventis.

35. Soliqua / Pregnancy / Pregnancy Negating

_____√_____

Alert Message: There are no adequate and well-controlled studies of Soliqua (insulin glargine/lixisenatide) in pregnant women. Lixisenatide-containing agents should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus.

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

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>
Insulin Glargine/Lixisenatide	Pregnancy	Delivery Miscarriage Abortion

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Soliqua 100/33 Prescribing Information, Nov. 2016, Sanofi-Aventis.

36. Soliqua / Nonadherence

_____√_____

Alert Message: Non-adherence to Soliqua (insulin glargine/lixisenatide) therapy may result in loss of glycemic control and an increased risk of developing diabetic-related complications.

Conflict Code: LR - Nonadherence
Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Insulin Glargine/Lixisenatide		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Ho PM, Rumsfeld JS, Masoudi FA, et al., Effect of Medication Nonadherence on Hospitalization and Mortality Among Patients with Diabetes Mellitus. Arch Intern Med. 2006;166:1836-1841.
Currie CJ, Peyrot M, Morgan CL, et al. The Impact of Treatment Noncompliance on Mortality in People with Type 2 Diabetes. Diabetes Care 35:1279-1284, June 2012.
Butler RJ, Davis TK, Johnson WL, et al. Effects of Non Adherence with Prescription Drugs Among Older Adults. Am J Manag Care. 2011 Feb; 17(2):153-60.

37. Soliqua / Drugs That Increase Risk of Hypoglycemia

_____ ✓ _____

Alert Message: Caution should be exercised when Soliqua (insulin glargine/lixisenatide) is co-administered with drugs that can enhance the hypoglycemic effect of the antidiabetic agent. The patient may be at an increased risk for hypoglycemia. Dose reduction of insulin glargine/lixisenatide and increased frequency of glucose monitoring may be required when co-administering these drugs.

Conflict Code: DD – Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Insulin Glargine/Lixisenatide	ACEIs ARBs Disopyramide Fibrates MAOIs Fluoxetine Pentoxifylline Pramlintide Salicylates Sulfamethoxazole Sulfasalazine Sulfadiazine Sulfisoxazole	

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Soliqua 100/33 Prescribing Information, Nov. 2016, Sanofi-Aventis.

38. Soliqua / Drugs That Decrease Blood Glucose Lowering Effect

_____ ✓ _____

Alert Message: Caution should be exercised when Soliqua (insulin glargine/lixisenatide) is co-administered with drugs that can decrease the blood glucose lowering effect of insulin glargine/lixisenatide. The patient may be at risk for decreased therapeutic effect of antidiabetic agent. Dosage increase of insulin glargine/lixisenatide and increased frequency of glucose monitoring may be required when co-administering these drugs.

Conflict Code: DD – Drug Interaction

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Insulin Glargine/Lixisenatide	Atypical Antipsychotics Danazol Isoniazid Niacin Oral Contraceptives Estrogens Protease Inhibitors Somatropin Thyroid Hormones	

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Soliqua 100/33 Prescribing Information, Nov. 2016, Sanofi-Aventis.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

39. Xultophy / Overutilization

___√___ ___ ___

Alert Message: The manufacturer's recommended maximum daily dose of Xultophy (insulin degludec/liraglutide) is 50 units once daily. Administration of more than 50 units of insulin degludec/liraglutide can result in overdose of the liraglutide (> 1.8 mg liraglutide).

Conflict Code: ER - Overutilization

Drugs/Diseases

Util A

Util B

Util C

Insulin degludec/Liraglutide

Max Dose: 50 units per day

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Xultophy 100/3.6 Prescribing Information, Nov. 2016, Novo Nordisk Inc.

40. Xultophy / GLP-1 Receptor Agonists

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Alert Message: Xultophy (insulin degludec/liraglutide) is not recommended for use in combination with any other product containing liraglutide or another GLP-1 receptor agonist. Concurrent use of these agents represents an unnecessary duplication of therapy.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A

Util B

Util C

Insulin degludec/Liraglutide

Liraglutide

Lixisenatide

Albiglutide

Dulaglutide

Exenatide

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Xultophy 100/3.6 Prescribing Information, Nov. 2016, Novo Nordisk Inc.

41. Xultophy / Gastroparesis

___√___ ___ ___

Alert Message: Xultophy (insulin degludec/liraglutide) has not been studied in patients with gastroparesis and should be used with caution in this patients population. The liraglutide component of the combination product slows gastric emptying and may exacerbate existing gastroparesis.

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

Drugs/Diseases

Util A

Util B

Util C

Insulin degludec/Liraglutide

Gastroparesis

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Xultophy 100/3.6 Prescribing Information, Nov. 2016, Novo Nordisk Inc.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

42. Xultophy / Therapeutic Appropriateness

___√___ ___ ___

Alert Message: The safety and effectiveness of Xultophy (insulin degludec/liraglutide) have not been established in pediatric patients.

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C

Insulin degludec/Liraglutide

Age Range: 0 – 17 yoa

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Xultophy 100/3.6 Prescribing Information, Nov. 2016, Novo Nordisk Inc.

43. Xultophy / Pancreatitis

___√___ ___ ___

Alert Message: Xultophy (insulin degludec/liraglutide) has not been studied in patients with a history of pancreatitis. The liraglutide component of the combination product is a GLP-1 receptor agonist and these agents have been associated with acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis. Consider alternative antidiabetic therapy in patient with a history of pancreatitis. If pancreatitis is suspected, promptly discontinue use. If pancreatitis is confirmed, restarting insulin degludec/liraglutide is not recommended.

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C (Include)

Insulin degludec/Liraglutide

Pancreatitis

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Xultophy 100/3.6 Prescribing Information, Nov. 2016, Novo Nordisk Inc.

44. Xultophy / Renal Impairment

___√___ ___ ___

Alert Message: Xultophy (insulin degludec/liraglutide) should be used with caution in patients with renal impairment as the liraglutide component of the combination product is a GLP-1 receptor agonist and these agents have been associated with acute kidney injury and worsening of chronic renal failure. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. Advise patients of the potential risk of dehydration due to gastrointestinal adverse reactions and take precautions to avoid fluid depletion.

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

Util A

Util B

Util C (Include)

Insulin degludec/Liraglutide

Renal Impairment

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Xultophy 100/3.6 Prescribing Information, Nov. 2016, Novo Nordisk Inc.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

45. Xultophy / Hypokalemia

____√____

Alert Message: All insulin-containing products, including Xultophy (insulin degludec/liraglutide), cause a shift in potassium from extracellular to intracellular space, possibly leading to hypokalemia. Monitor potassium levels in patients at risk for hypokalemia if indicated.

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

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C</u>
Insulin degludec/Liraglutide	Hypokalemia	

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Xultophy 100/3.6 Prescribing Information, Nov. 2016, Novo Nordisk Inc.

46. Xultophy / Pregnancy / Pregnancy Negating

____√____

Alert Message: There are not adequate and well-controlled studies of Xultophy (insulin degludec/liraglutide) in pregnant women. Liraglutide-containing agents should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus.

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

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Negating)</u>
Insulin degludec/Liraglutide	Pregnancy	Delivery Miscarriage Abortion

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Xultophy 100/3.6 Prescribing Information, Nov. 2016, Novo Nordisk Inc.

47. Xultophy / Medullary Thyroid Carcinoma

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Alert Message: The use of Xultophy (insulin degludec/liraglutide) is contraindicated in patients with a personal or family history of Medullary Thyroid Carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia Syndrome Type 2. Cases of MTC have been reported in patients treated with liraglutide a component of the combination product. In clinical trials, there were 7 reported cases of papillary thyroid carcinomas in liraglutide-treated patients.

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

<u>Util A</u>	<u>Util B</u>	<u>Util C (Include)</u>
Insulin degludec/Liraglutide		Medullary Thyroid Carcinoma Multiple Endocrine Neoplasia Syndrome Type 2

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.
Xultophy 100/3.6 Prescribing Information, Nov. 2016, Novo Nordisk Inc.

Criteria Recommendations

**Accepted Approved Rejected
As
Amended**

48. Xultophy / Nonadherence

____√____ _____ _____

Alert Message: Non-adherence to Xultophy (insulin degludec/liraglutide) therapy may result in loss of glycemic control and an increased risk of developing diabetic-related complications.

Conflict Code: LR - Nonadherence

Drugs/Diseases

Util A

Util B

Util C

Insulin degludec/Liraglutide

References:

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

Ho PM, Rumsfeld JS, Masoudi FA, et al., Effect of Medication Nonadherence on Hospitalization and Mortality Among Patients with Diabetes Mellitus. Arch Intern Med. 2006;166:1836-1841.

Currie CJ, Peyrot M, Morgan CL, et al. The Impact of Treatment Noncompliance on Mortality in People with Type 2 Diabetes. Diabetes Care 35:1279-1284, June 2012.

Butler RJ, Davis TK, Johnson WL, et al. Effects of Non Adherence with Prescription Drugs Among Older Adults. Am J Manag Care. 2011 Feb; 17(2):153-60.

49. Xultophy / Drugs That Increase Risk of Hypoglycemia

____√____ _____ _____

Alert Message: Caution should be exercised when Xultophy (insulin degludec/liraglutide) is co-administered with drugs that can enhance the hypoglycemic effect of the antidiabetic agent. The patient may be at an increased risk for hypoglycemia. Dose reduction of insulin degludec/liraglutide and increased frequency of glucose monitoring may be required when co-administering these drugs.

Conflict Code: DD – Drug Interaction

Drugs/Diseases

Util A

Util B

Util C

Insulin degludec/Liraglutide

- ACEIs
- ARBs
- Disopyramide
- Fibrates
- MOAIs
- Fluoxetine
- Pentoxifylline
- Pramlintide
- Salicylates
- Sulfamethoxazole
- Sulfasalazine
- Sulfadiazine
- Sulfisoxazole

References:

Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Xultophy 100/3.6 Prescribing Information, Nov. 2016, Novo Nordisk Inc.

50. Xultophy / Drugs That Decrease blood Glucose Lowering Effect

Alert Message: Caution should be exercised when Xultophy (insulin degludec/liraglutide) is co-administered with drugs that can decrease the blood glucose lowering effect of insulin degludec/liraglutide. The patient may at risk for decreased therapeutic effect of the antidiabetic agent. Dosage increase of insulin degludec/liraglutide and increased frequency of glucose monitoring may be required when co-administering these drugs.

Conflict Code: DD – Drug Interaction

Drugs/Diseases

Util A

Insulin degludec/Liraglutide

Util B

- Atypical Antipsychotics
- Danazol
- Isoniazid
- Niacin
- Oral Contraceptives
- Estrogens
- Protease Inhibitors
- Somatropin
- Thyroid Hormones

Util C

References:

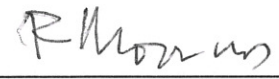
Clinical Pharmacology, 2016 Elsevier/Gold Standard.

Xultophy 100/3.6 Prescribing Information, Nov. 2016, Novo Nordisk Inc.


Stephanie McGee Azar, Commissioner

Approve () Deny

9-25-17
Date


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

Approve () Deny

9-21-17
Date


Kathy Hall, Deputy Commissioner

Approve () Deny

9/20/17
Date