Insulin GLP-1 Combinations

Description

Soliqua (insulin glargine and lixisenatide), Xultophy (insulin degludec and liraglutide)

Background

Soliqua and Xultophy are injectable antidiabetic agents containing a long-acting human insulin analog (insulin glargine or degludec) and glucagon-like peptide-1 (GLP-1) receptor agonists (lixisenatide or liraglutide). Soliqua and Xultophy are indicated for adults with type 2 diabetes mellitus who have had a suboptimal response to other diabetic agents. Long acting insulin acts via specific membrane-bound receptors on the liver, skeletal muscle, and adipose tissue to regulate metabolism of carbohydrates, proteins, and fats. GLP-1 receptor agonists effects post-prandial blood glucose by binding to the same receptors as endogenous hormone incretin leading to increased glucose-dependent insulin secretion, decreased inappropriate glucagon release, and slowed gastric emptying (1-2).

Regulatory Status

FDA-approved indication:

Soliqua

Soliqua is a combination of a long-acting human insulin analog with a glucagon-like peptide-1 (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus inadequately controlled on basal insulin (less than 60 units daily) or lixisenatide (1).

Xultophy
Xultophy is a combination of insulin degludec, a long-acting human insulin analog, and liraglutide, a glucagon-like peptide 1 (GLP-1) receptor agonist, indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus inadequately controlled on basal insulin (less than 50 units daily) or liraglutide (2).

Limitations of Use: (1-2)
1. Not for treatment of type 1 diabetes mellitus or diabetic ketoacidosis
2. Not recommended for use in combination with any other product containing a GLP-1 receptor agonists or basal insulin
3. Not recommended for use in patients with gastroparesis
4. Has not been studied in people taking short-acting (prandial) insulin
5. Has not been studied in patients with a history of unexplained pancreatitis

Xultophy has a boxed warning and contraindication in patients with a personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 are at high risk of treatment duration-dependent thyroid C-cell tumors. Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC. Significantly elevated serum calcitonin may indicate MTC and patients with MTC usually have calcitonin values >50 ng/L. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated (2).

The safety and effectiveness of Soliqua and Xultophy have not been established in patients under 18 years of age (1-2).

Related policies
Afrezza, Glumetza, SGLT2 Inhibitors

Policy
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Soliqua and Xultophy may be considered medically necessary in patients 18 years of age and older for the treatment of type 2 diabetes mellitus and if the conditions indicated below are met.

Soliqua and Xultophy may be considered investigational in patients less than 18 years of age and for all other indications.
Prior-Approval Requirements

Age  
18 years of age or older

Diagnosis

Type 2 diabetes mellitus (DM)

AND ALL of the following:
1. Inadequate treatment response, intolerance, or contraindication to metformin monotherapy
2. Inadequate treatment response, intolerance, or contraindication to ONE of the medications from the following categories:
   a. Sulfonylurea
   b. Thiazolidinedione (TZD)
   c. DPP-4 inhibitor
   d. SGLT2 inhibitor
3. Inadequate treatment response to the use of a GLP-1 receptor agonist and long acting insulin separately
4. Patient must have a HgbA1C greater than 7.0%
5. NOT used for the treatment of diabetic ketoacidosis (DKA)
6. NO dual therapy with other long acting insulins or GLP-1 receptor agonists

AND ALL of the following for Xultophy only:
1. Prescriber agrees to monitor for signs and symptoms of thyroid tumors

Prior – Approval Renewal Requirements

Age  
18 years of age or older

Diagnosis

Type 2 diabetes mellitus (DM)

AND ALL of the following:
1. NO dual therapy with other long acting insulins or GLP-1 receptor agonists
2. Patient’s HgbA1C must have improved to less than 7.0%
3. NOT used for the treatment of diabetic ketoacidosis (DKA)
AND ALL of the following for **Xultophy** only:

1. Prescriber agrees to monitor for signs and symptoms of thyroid tumors

### Policy Guidelines

#### Pre - PA Allowance

None

#### Prior - Approval Limits

**Duration** 12 months

#### Prior – Approval **Renewal** Limits

**Duration** 12 months

### Rationale

#### Summary

Soliqua and Xultophy are injectable combination products indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus inadequately controlled on basal insulin (1-2). The two active ingredients in Soliqua and Xultophy work to control fasting and post-prandial glucose by regulating carbohydrate metabolism. Long acting insulin acts via specific membrane-bound receptors on the liver, skeletal muscle, and adipose tissue. GLP-1 receptor agonists bind to the same receptors as endogenous hormone incretin leading to increased glucose-dependent insulin secretion, decreased inappropriate glucagon release, and slowed gastric emptying. The safety and effectiveness of Soliqua and Xultophy have not been established in patients under 18 years of age (1-2).

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Soliqua and Xultophy while maintaining optimal therapeutic outcomes.

### References

Section: Prescription Drugs
Subsection: Endocrine and Metabolic Agents
Subject: Insulin GLP-1 Combinations
Effective Date: July 1, 2017
Original Policy Date: May 19, 2017
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Date    Action
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May 2017 Addition to PA
June 2017 Annual review

Keywords

This policy was approved by the FEP® Pharmacy Medical Policy Committee on June 22, 2017 and is effective on July 1, 2017.