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 postprandial 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 (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 (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, Fortamet Riomet, 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
Patients who have filled at least one ≥90 day supply of long-acting insulin AND GLP-1 agonist in the past 180 days are exempt from these PA 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 to the use of a GLP-1 receptor agonist and long acting insulin separately
3. Patient must have a HgbA1C greater than 7.0%
4. NOT used for the treatment of diabetic ketoacidosis (DKA)
5. NO dual therapy with other long acting insulins or GLP-1 receptor agonists

AND 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 ≤ 7.0%
3. NOT used for the treatment of diabetic ketoacidosis (DKA)

AND the following for Xultophy only:
1. Prescriber agrees to monitor for signs and symptoms of thyroid tumors
Pre - PA Allowance
None

Prior - Approval Limits

Duration 12 months

Prior – Approval Renewal Limits
Same as above

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

Policy History

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<tr>
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<tbody>
<tr>
<td>May 2017</td>
<td>Addition to PA</td>
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<td>June 2017</td>
<td>Annual review</td>
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Section: Prescription Drugs  Effective Date: January 1, 2020
Subsection: Endocrine and Metabolic Agents  Original Policy Date: May 19, 2017
Subject: Insulin GLP-1 Combinations  Page: 5 of 5

July 2017  Removal of the inadequate treatment response, intolerance, or contraindication to one of the medications from the following categories: sulfonylurea, thiazolidinedione (TZD), DPP-4 inhibitor, SGLT2 inhibitor
September 2017  Annual review
June 2018  Annual editorial review and reference update
September 2018  Addition of patients who have filled at least one ≥90 day supply of long-acting insulin and GLP-1 agonist in the past 180 days are exempt from these PA requirements
November 2018  Annual review
December 2019  Annual editorial review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 6, 2019 and is effective on January 1, 2020.