Insulin Combination Agents (Soliqua, Xultophy) Step Therapy and Quantity Limit Criteria Program Summary

This program applies to Commercial and Health Insurance Marketplace formularies.

OBJECTIVE

The intent of the Insulin Combination (Soliqua, Xultophy) Step Therapy (ST) program is to ensure appropriate selection of patients based on product labeling, and/or clinical guidelines, and/or clinical studies. The program will approve for patients who have tried an agent containing metformin and an agent containing either basal insulin or GLP-1. The step edit allows continuation of therapy. Patients without prerequisite agents in claims history or those who are unable to take a prerequisite agent due to documented intolerance, FDA labeled contraindication, or hypersensitivity will be reviewed when patient-specific documentation has been provided.

TARGET AGENTS

Soliqua (insulin glargine/lixisenatide)
Xultophy (insulin degludec/liraglutide)

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Insulin Combination Agents will be approved when ONE of the following is met:

1. There is documentation that the patient is currently using the requested agent
   OR
2. The prescriber states the patient is using the requested agent AND is at risk if therapy is changed
   OR
3. BOTH of the following:
   a. ONE of the following:
      i. The patient's medication history includes an agent containing metformin in the past 180 days
         OR
      ii. The patient has a documented intolerance, FDA labeled contraindication, hypersensitivity to metformin, or the patient has failed metformin therapy

   AND

   b. ONE of the following:
      i. The patient's medication history includes the use of at least one of the agents included as a combination in the requested agent (e.g. basal insulin, GLP-1 for diabetes) in the past 180 days

Length of approval: 12 months

NOTE: If Quantity Limit program also applies, please refer to Quantity Limit documents.

FDA APPROVED INDICATIONS AND DOSAGE[1,2]

Agent	Indication	Important limitations for use	Dosage and Administration
Soliqua™ 100/33 (insulin glargine/ lixisenatide)	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.	• Has not been studied in patients with a history of pancreatitis Consider other antidiabetic therapies in patients with a history of pancreatitis. • Not recommended for use in combination with any other product containing lixisenatide or another GLP-1 receptor agonist • Not indicated for use in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. • Has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis. • Has not been studied in combination with prandial insulin.	• In patients inadequately controlled on less than 30 units of basal insulin or on lixisenatide, the starting dosage is 15 units (15 units insulin glargine/5 mcg lixisenatide) given subcutaneously once daily. • In patients inadequately controlled on 30 to 60 units of basal insulin, the starting dosage is 30 units (30 units insulin glargine/10 mcg lixisenatide) given subcutaneously once daily. • Maximum daily dosage is 60 units (60 units of insulin glargine and 20 mcg of lixisenatide). • Use alternative antidiabetic products if patients require a Soliqua 100/33 daily dosage below 15 units or over 60 units

Agent	Indication	Important limitations for use	Dosage and Administration
Xultophy® 100/3.6 (insulin degludec/ liraglutide)	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 (less than or equal to 1.8 mg daily)	• Not recommended as first-line therapy for patients inadequately controlled on diet and exercise. • Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis. • Not recommended for use in combination with any other product containing liraglutide or another GLP-1 receptor agonist. • Not for treatment of type 1 diabetes mellitus or diabetic ketoacidosis. • Has not been studied in combination with prandial insulin	• Recommended starting dosage is 16 units (16 units of insulin degludec and 0.58 mg of liraglutide) given subcutaneously once daily • Maximum daily dosage is 50 units (50 units of insulin degludec and 1.8 mg of liraglutide) • Use alternative antidiabetic products if patients require a Xultophy 100/3.6 daily dosage: ○ Persistently below 16 units, or ○ Over 50 units

CLINICAL RATIONALE

Guidelines

Both the American Diabetes Association (ADA) and American Association of Clinical Endocrinologists (AACE) recommend metformin as the optimal non-insulin first-line drug in type II diabetes mellitus.[3,4] Initial dual non-insulin therapy or insulin therapy may be considered to reduce time to goal treatment targets when A1C is >9%.[3] The AACE recommends metformin plus a second agent when A1C is >7.5%. Guidelines support sulfonylurea (SU), thiazolidinedione (TZD), dipeptidyl peptidase-4 inhibitor (DPP-4), sodium glucose transporter 2 inhibitor (SGLT2), glucagon-like peptide-1 receptor agonist (GLP-1), or insulin (usually basal e.g., NPH, insulin glargine, or insulin detemir) as first line alternatives when metformin cannot be used.[3,4]

Beyond first-line therapy pharmacotherapy choice is based on patient and drug characteristics in order to improve glycemic control and minimize side effects.[3,4] Dual-therapy optimally include combining metformin with either a SU, TZD, DPP-4, SGLT2, GLP-1, or basal insulin.[3] If the goal is not met with two-drugs, a third agent may be added albeit combination of complementary mechanisms of action is essential. Notably, insulin is likely to be more effective than most other agents as a third-line therapy, especially symptomatic patients when A1C is very high (e.g., >9.0%).[4]

REFERENCES

1. Soliqua prescribing information. Sanofi-Aventis US LLC. November 2016
2. Xultophy prescribing information. Novo Nordisk Inc. November 2016

3. American Diabetes Association. Standards of medical care in diabetes-2016. *Diabetes Care* 2016; 39(Supp 1): S1-S112.
4. Garber, A, Abrahamson, M, Barzilay, J et al. Consensus statement by the American association of clinical endocrinologists and American college of endocrinology on the comprehensive type 2 diabetes management algorithm – 2016 executive summary. Endocrin Pract 2015; 22 (No. 1): 84-113.