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

POLICY REVIEW CYCLE

Effective Date **Date of Origin**
4/1/2023

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Soliqua® 100/33 (insulin glargine/lixisenatide) Injection	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Limitations of use: • 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 diabetic ketoacidosis. • Not recommended in patients with gastroparesis. • Has not been studied in combination with prandial insulin.		1
Xultophy® 100/3.6 (insulin degludec/liraglutide) Injection	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus Limitations of use: • Not recommended as first-line therapy for patients inadequately controlled on diet and exercise. • 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		2

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Guidelines	The American Diabetes Association (ADA) states that first-line therapy for type 2 diabetes depends on comorbidities, patient-centered treatment factors, and management needs but will generally include metformin and comprehensive lifestyle modification. When A1c is greater than or equal to 1.5% above the glycemic target, many patients will require dual combination therapy to achieve their target A1c level. Insulin has the advantage of being effective where other agents are not and

	should be considered as part of any combination regimen when hyperglycemia is severe, especially if catabolic features are present. If basal insulin has been titrated to an acceptable fasting blood glucose level (or if the dose is greater than 0.5 units/kg/day with indications of need for other therapy) and A1c remains above target, consider advancing to combination injectable therapy. This approach can use a GLP-1 added to basal insulin or multiple doses of insulin. The combination of basal insulin and GLP-1 has potent glucose-lowering actions and less weight gain and hypoglycemia compared with intensified insulin regimens. For patients with established atherosclerotic cardiovascular disease (ASCVD) or indicators of high ASCVD risk (such as patients greater than or equal to 55 years of age with coronary, carotid, or lower-extremity artery stenosis greater than 50% or left ventricular hypertrophy), heart failure, or chronic kidney disease, an SGLT2 inhibitor or GLP-1 with demonstrated CVD benefit is recommended as part of the glucose-lowering regimen independent of the A1C, independent of metformin use, and in consideration of other patient-specific factors.(3)
Safety	Xultophy carries a black box warning. Liraglutide, one of the components of Xultophy, causes thyroid C-cell tumors at clinically relevant expression in both genders of rats and mice. It is unknown whether Xultophy causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC) in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined. Xultophy is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk of MTC and the symptoms of thyroid tumors.(2)

REFERENCES

Number	Reference
1	Soliqua prescribing information. Sanofi-Aventis US LLC. June 2022.
2	Xultophy prescribing information. Novo Nordisk Inc. June 2022.
3	American Diabetes Association. Standards of medical care in diabetes-2022. Available at: https://diabetesjournals.org/care/issue/45/Supplement_1
4	Garber AJ, Handelsman Y, Grunberger G et, al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm-2020 Executive Summary. Endocrine Practice, 26 (1) January 2020. 107-139.

POLICY AGENT SUMMARY STEP THERAPY

Agent Names	Strength	Targeted MSC	Available MSC	Preferred Status	Effective Date
SOLIQUA*insulin glargine-lixisenatide sol pen-inj	100 UNT-MCG/ML	M ; N ; O	N		
XULTOPHY*insulin degludec-liraglutide sol pen-inj	100 UNIT-MG/ML	M ; N ; O	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist	Effective Date
Soliqua 100/33	Insulin Glargine-Lixisenatide Sol Pen-Inj 100-33 Unit-MCG/ML	100 UNT-MCG/ML	6	PENS	30	Days				
Xultophy 100/3.6	Insulin Degludec-Liraglutide Sol Pen-Inj 100-3.6 Unit-MG/ML	100 UNIT-MG/ML	5	PENS	30	Days				

CLIENT SUMMARY – STEP THERAPY

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Soliqua 100/33	insulin glargine-lixisenatide sol pen-inj	100 UNT-MCG/ML	Commercial ; HIM ; ResultsRx
Xultophy 100/3.6	insulin degludec-liraglutide sol pen-inj	100 UNIT-MG/ML	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Soliqua 100/33	Insulin Glargine-Lixisenatide Sol Pen-Inj 100-33 Unit-MCG/ML	100 UNT-MCG/ML	Commercial ; HIM ; ResultsRx
Xultophy 100/3.6	Insulin Degludec-Liraglutide Sol Pen-Inj 100-3.6 Unit-MG/ML	100 UNIT-MG/ML	Commercial ; HIM ; ResultsRx

STEP THERAPY CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Target Agent(s) will be approved when ONE of the following is met: 1. Information has been provided that indicates the patient is currently being treated with the requested agent within the past 90 days **OR** 2. The prescriber states the patient is currently being treated with the requested agent within the past 90 days AND is at risk if therapy is changed **OR** 3. The patient's medication history includes use of an agent containing insulin or an agent containing metformin within the past 90 days **OR** 4. The patient has an intolerance or hypersensitivity to metformin or insulin that is not expected to occur with the requested agent **OR**

Module	Clinical Criteria for Approval
	5. The patient has an FDA labeled contraindication to BOTH metformin AND insulin that is not expected to occur with the requested agent **OR** 6. The patient has a diagnosis of type 2 diabetes with or at high risk for atherosclerotic cardiovascular disease, heart failure, and/or chronic kidney disease **Length of approval:** 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria section below.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. The requested quantity (dose) is greater than the program quantity limit AND ONE of the following: A. BOTH of the following: 1. The requested agent does not have a maximum FDA labeled dose for the requested indication **AND** 2. Information has been provided to support therapy with a higher dose for the requested indication **OR** B. BOTH of the following: 1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** 2. Information has been provided to support why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **OR** C. BOTH of the following: 1. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication **AND** 2. Information has been provided to support therapy with a higher dose for the requested indication **Length of Approval**: up to 12 months