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

POLICY REVIEW CYCLE

Effective Date 04-01-2024 **Date of Origin**

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) Basal with or without prandial insulin treatment may be needed as initial therapy if the A1C is >10% and/or glucose values are >300 mg/dL, combined with catabolic symptoms, such as weight loss. If symptomatic hyperglycemia is present, a GLP-1 RA alone is not recommended as it requires titration and may delay glucose control. The goal of initial intensive insulin therapy for symptomatic hyperglycemia is to reduce glucose levels safely and promptly. After improved glycemic control is achieved with short-term insulin therapy, especially with a new diagnosis of DM, a role for noninsulin antihyperglycemic agents could be considered. For most persons who need intensification of glycemic control and who are already undergoing 3 to 4 oral therapies, a GLP-1 RA or GIP/GLP-1 RA should be the initial choice, if not already in use. If glycemic targets are not achieved with these therapies, basal insulin should be added alone or as a basal insulin/GLP-1 RA combination injection. Stepwise addition of prandial insulin at 1 to 3 meals is recommended if additional glycemic control is required. The dose of basal insulin can be based on A1C levels at the time of initiation. For an A1C <8%, basal insulin can be started at 0.1 to 0.2 U/kg/day and for an A1C >8%, 0.2 to 0.3 U/kg/day can be considered. Analog insulins, including detemir, glargine, or degludec are preferred over human insulins such as neutral protamine Hagedorn (NPH) to reduce hypoglycemia.(4)
Safety (1,2)	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.(2) Xultophy has the following contraindications:(2) • Patients with a personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2 • During episodes of hypoglycemia • Patients with a serious hypersensitivity reaction to insulin degludec, liraglutide, or any of the excipients in Xultophy Soliqua has the following contraindications:(1) • During episodes of hypoglycemia • Serious hypersensitivity to insulin glargine, lixisenatide, or any of the excipients in Soliqua

REFERENCES

Number	Reference
1	Soliqua prescribing information. Sanofi-Aventis US LLC. June 2022.

Number	Reference
2	Xultophy prescribing information. Novo Nordisk Inc. July 2023.
3	American Diabetes Association. Standards of medical care in diabetes-2022. Available at: https://diabetesjournals.org/care/issue/45/Supplement_1.
4	American Diabetes Association, 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2023. Diabetes Care 1 January 2023; 46 (Supplement_1): S140–S157. https://doi.org/10.2337/dc23-S009.

POLICY AGENT SUMMARY STEP THERAPY

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Soliqua 100/33	insulin glargine-lixisenatide sol pen-inj	100-33 UNT-MCG/ML	M ; N ; O	N		
Xultophy 100/3.6	insulin degludec-liraglutide sol pen-inj	100-3.6 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
Soliqua 100/33	insulin glargine-lixisenatide sol pen-inj	100-33 UNT-MCG/ML	6	Pens	30	DAYS			
Xultophy 100/3.6	insulin degludec-liraglutide sol pen-inj	100-3.6 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	100-33 UNT-MCG/ML	Commercial ; HIM 5 and 6 Tiers ; HIM 7 Tiers
Xultophy 100/3.6	insulin degludec-liraglutide sol pen-inj	100-3.6 UNIT-MG/ML	Commercial ; HIM 5 and 6 Tiers ; HIM 7 Tiers

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 UNT-MCG/ML	Commercial ; HIM 5 and 6 Tiers ; HIM 7 Tiers
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STEP THERAPY CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval

TARGET AGENT(S)	PREREQUISITE AGENT(S)
Soliqua Xultophy	Any agent containing: metformin or insulin

Target Agent(s) will be approved when ONE of the following is met:

1. Information has been provided that indicates the patient has been treated with the requested agent within the past 90 days **OR**
2. The prescriber states the patient has been 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**
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: If Quantity Limit applies, please refer to Quantity Limit Criteria.

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) exceeds 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) exceeds 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