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

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

## POLICY REVIEW CYCLE

| Effective Date | Date of Origin |
|---|---|
| 04-01-2024 | 07-01-2017 |

## FDA APPROVED INDICATIONS AND DOSAGE

| Agent(s) | FDA Indication(s) | Notes | Ref# |
|---|---|---|---|
| Soliqua® 100/33<br><br>(insulin glargine/lixisenatide)<br><br>Injection | Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.<br><br>Limitations of use:<br>• Has not been studied in patients with a history of pancreatitis Consider other antidiabetic therapies in patients with a history of pancreatitis.<br>• Not recommended for use in combination with any other product containing lixisenatide or another GLP-1 receptor agonist<br>• Not indicated for use in patients with type 1 diabetes mellitus or diabetic ketoacidosis.<br>• Not recommended in patients with gastroparesis.<br>• Has not been studied in combination with prandial insulin. | | 1 |
| Xultophy® 100/3.6<br><br>(insulin degludec/liraglutide)<br><br>Injection | Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus<br><br>Limitations of use:<br>• Not recommended as first-line therapy for patients inadequately controlled on diet and exercise.<br>• Not recommended for use in combination with any other product containing liraglutide or another GLP-1 receptor agonist.<br>• Not for treatment of type 1 diabetes mellitus or diabetic ketoacidosis.<br>• 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)<br><br>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)<br><br>Xultophy has the following contraindications:(2)<br><br>• Patients with a personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2<br>• During episodes of hypoglycemia<br>• Patients with a serious hypersensitivity reaction to insulin degludec, liraglutide, or any of the excipients in Xultophy<br><br>Soliqua has the following contraindications:(1)<br><br>• During episodes of hypoglycemia<br>• 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. |
| 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 | FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx |
| Xultophy 100/3.6 | insulin degludec-liraglutide sol pen-inj | 100-3.6 UNIT-MG/ML | FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx |

## 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 | FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx |
| Xultophy 100/3.6 | insulin degludec-liraglutide sol pen-inj | 100-3.6 UNIT-MG/ML | FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx |

## STEP THERAPY CLINICAL CRITERIA FOR APPROVAL

**Module**

**Clinical Criteria for Approval**

| TARGET AGENT(S) | PREREQUISITE AGENT(S) |
|---|---|
| **Soliqua**<br>**Xultophy** | Any agent containing:<br>metformin or insulin |

**PRIOR AUTHORIZATION 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 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 is currently being treated with the requested agent as indicated by ALL of the following:
   A. A statement by the prescriber that the patient is currently taking the requested agent **AND**
   B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND**
   C. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR**
4. The patient's medication history includes use of an agent containing insulin or an agent containing metformin **OR**
5. BOTH of the following:
   A. The prescriber has stated that the patient has tried an agent containing insulin or an agent containing metformin **AND**
   B. Insulin or an agent containing metformin was discontinued due to lack of effectiveness or an adverse event **OR**
6. The patient has an intolerance or hypersensitivity to metformin or insulin that is not expected to occur with the requested agent **OR**
7. The patient has an FDA labeled contraindication to BOTH metformin AND insulin that is not expected to occur with the requested agent **OR**
8. 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 **OR**
9. The prescriber has provided documentation that BOTH insulins and metformin cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

**Length of Approval:** 12 months

NOTE: If Quantity Limit program also 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:<br><br>1. The requested quantity (dose) does NOT exceed the program quantity limit **OR**<br>2. The requested quantity (dose) exceeds the program quantity limit AND ONE of the following:<br>A. BOTH of the following:<br>1. The requested agent does NOT have a maximum FDA labeled dose for the requested indication **AND**<br>2. Information has been provided to support therapy with a higher dose for the requested indication **OR**<br>B. BOTH of the following:<br>1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND**<br>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**<br>C. BOTH of the following:<br>1. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND**<br>2. Information has been provided to support therapy with a higher dose for the requested indication<br><br>**Length of Approval**: up to 12 months |