CENTENE® Corporation

Clinical Policy: Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists

Reference Number: CP.PMN.183
Effective Date: FDA Approval Date
Last Review Date: 11.25
Line of Business: Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

The following agents contain a synthetic glucagon-like peptide-1 (GLP-1) receptor agonist and require prior authorization: dulaglutide (Trulicity®), exenatide ER (Bydureon BCise®), exenatide IR (Byetta®)†, liraglutide (Victoza®), liraglutide/insulin degludec (Xultophy®), lixisenatide (Adlyxin®), semaglutide (Ozempic®, Rybelsus®), tirzepatide* (Mounjaro™), insulin glargine/ lixisenatide (Soliqua®).

**Tirzepatide is a combination GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptor agonist.*
†The manufacturer of Bydureon BCise and Byetta, AstraZeneca, is discontinuing these products effective January 1st, 2025.

FDA Approved Indication(s)

GLP-1 receptor agonists are indicated as adjunct to diet and exercise to improve glycemic control with type 2 diabetes mellitus. Bydureon BCise, Trulicity, and Victoza are indicated in patients 10 years of age and older, while the other GLP-1 receptor agonists are indicated in adults.

[Pending for Rybelsus] Ozempic, Rybelsus*, Trulicity, and Victoza are also indicated to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and:

- Established cardiovascular disease (*Ozempic, Rybelsus*, Trulicity, Victoza*);
- Cardiovascular risk factors (*Trulicity only*).

Ozempic is additionally indicated:

- To reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end-stage kidney disease and cardiovascular death in adults with type 2 diabetes mellitus and chronic kidney disease.
- [Pending] For the treatment of adults with symptomatic peripheral artery disease (PAD) and type 2 diabetes.*

Limitation(s) of use:

- Bydureon BCise, and Xultophy are not recommended as a first-line therapy for patients inadequately controlled on diet and exercise.
- GLP-1 receptor agonists should not be used for the treatment of type 1 diabetes. Xultophy and Soliqua are not for the treatment of diabetic ketoacidosis.

- Xultophy and Soliqua have not been studied in combination with prandial insulin. In addition, they are not recommended for use in combination with any other product containing a GLP-1 receptor agonist.
- Other than Ozempic, Victoza, and Xultophy, GLP-1 receptor agonists have not been studied in patients with a history of pancreatitis. Other antidiabetic therapies should be considered.
- Trulicity is not for patients with pre-existing severe gastrointestinal disease.
- Adlyxin and Soliqua are not recommended in patients with gastroparesis.
- Bydureon BCise is an extended-release formulation of exenatide. Do not coadminister with other exenatide containing products.
- Victoza and Xultophy contain liraglutide and should not be co-administered with other liraglutide-containing products.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that GLP-1 receptor agonists are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*
**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Type 2 Diabetes Mellitus (must meet all)**:**
1. Diagnosis of type 2 diabetes mellitus;
2. Age is one of the following (a or b):
   a. Bydureon BCise, Trulicity, Victoza: ≥ 10 years;
   b. All other GLP-1 receptor agonists: ≥ 18 years;
3. Member meets one of the following (a, b, c, d, e, or f):
   a. Request is for Soliqua;
   b. Member has metabolic dysfunction-associated steatotic liver disease (MASLD), and (i):
      i. Member is overweight (body mass index [BMI] 25-29.9 kg/m^2) or obese (BMI ≥ 30 kg/m^2);
   c. Member has metabolic dysfunction-associated steatohepatitis (MASH), and (i):
      i. Failure of ≥ 3 consecutive month trial of pioglitazone, unless contraindicated or clinically significant adverse effects are experienced;
   d. Member has PAD, and all of the following (i, ii, iii, and iv):*
      i. Diagnosis is confirmed by ankle-brachial index ≤ 0.90 or toe-brachial index ≤ 0.70;
      ii. Member has intermittent claudication corresponding to Fontaine stage IIa (i.e., member is able to walk > 200 m without pain or stopping);
      iii. Member has demonstrated limitations due to PAD as evidenced by a maximum walking distance of < 600 m;
      iv. Request is for Ozempic;
   e. Member has established atherosclerotic cardiovascular disease (ASCVD), indicators of high ASCVD risk (*see Appendix D*), heart failure with preserved ejection fraction, or chronic kidney disease, and both of the following (i and ii):

i. Request is for an agent with proven cardiovascular or renal benefit (Ozempic, Rybelsus*, Trulicity, Victoza);
ii. Failure of ≥ 3 consecutive months of a sodium-glucose co-transporter 2 (SGLT2) inhibitor or SGLT2 inhibitor-containing product (*see Appendix B*), unless clinically significant adverse effects are experienced or all are contraindicated;

f. For members without PAD, established ASCVD, indicators of high ASCVD risk (*see Appendix D*), heart failure with preserved ejection fraction, chronic kidney disease, MASLD, or MASH: Failure of ≥ 3 consecutive month trial of two agents from any of the following classes, unless clinically significant adverse effects are experienced or all are contraindicated: biguanides, sulfonylureas (SU), thiazolidinediones (TZD), dipeptidyl peptidase-4 inhibitors (DPP-4), or SGLT2 inhibitor or SGLT2 inhibitor-containing product (*see Appendix B*);

4. Member meets one of the following (a, b, c, or d):
   a. If request is for Trulicity: Failure of liraglutide (Victoza), unless contraindicated or clinically significant adverse effects are experienced;
   b. If request is for Soliqua: Member was prescribed one of the following within the past 180 days (i or ii):
      i. Basal insulin (*see Appendix B*);
      ii. GLP-1 receptor agonist;
   c. If request is for brand Victoza: Member must use liraglutide (Victoza), unless contraindicated or clinically significant adverse effects are experienced;
   d. If request is for a non-preferred GLP-1 receptor agonist, one of the following (i or ii):
      i. Failure of both of the following preferred GLP-1 receptor agonists (1 and 2), each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or both are contraindicated:
         1) Liraglutide (Victoza);
         2) If member has failed liraglutide (Victoza), then failure of Trulicity;
      ii. Member has chronic kidney disease or symptomatic PAD (as defined in criterion 3.d above), and request is for Ozempic;
5. Requested product is not prescribed concurrently with another GLP-1 receptor agonist;
6. Dose does not exceed the FDA-approved maximum recommended dose (*see Section V*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Type 2 Diabetes Mellitus (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. Requested product is not prescribed concurrently with another GLP-1 receptor agonist;
4. If request is for a dose increase, new dose does not exceed the FDA-approved maximum recommended dose (*see Section V*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AACE: American Association of Clinical Endocrinologists
ACE: American College of Endocrinology
ADA: American Diabetes Association
ASCVD: atherosclerotic cardiovascular disease
BMI: body mass index
DPP-4: dipeptidyl peptidase-4
eGFR: estimated glomerular filtration rate
ER: extended-release
FDA: Food and Drug Administration
GIP: glucose-dependent insulinotropic polypeptide
GLP-1: glucagon-like peptide-1
HbA1c: glycated hemoglobin
IR: immediate-release
MASH: metabolic dysfunction-associated steatohepatitis
MASLD: metabolic dysfunction-associated steatotic liver disease
PAD: peripheral artery disease
SGLT2: sodium-glucose co-transporter 2
SU: sulfonylureas
TZD: thiazolidinediones

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Biguanide		
metformin (Fortamet®, Glucophage®, Glucophage® XR, Glumetza®)	Regular-release (Glucophage): 500 mg PO BID or 850 mg PO QD; increase as needed in increments of 500 mg/week or 850 mg every 2 weeks Extended-release: • Fortamet, Glumetza: 1,000 mg PO QD; increase as needed in increments of 500 mg/week • Glucophage XR: 500 mg PO QD; increase as needed in increments of 500 mg/week	Regular-release: 2,550 mg/day Extended-release: 2,000 mg/day
SGLT2 Inhibitors		
Brenzavvy™ (bexagliflozin)	20 mg PO QD	20 mg/day
Farxiga® (dapagliflozin)	5 mg PO QD To reduce the risk of hospitalization for heart failure, the recommended dose is 10 mg PO QD	10 mg/day
Glyxambi® (empagliflozin/linagliptin)	One 10/5 mg tablet PO QD	25/5 mg/day
Invokamet® (canagliflozin/metformin)	One 50/500 mg tablet PO BID	300/2,000 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Invokamet® XR (canagliflozin/metformin)	Two 50/500 mg tablets PO QD	300/2,000 mg/day
Invokana® (canagliflozin)	100 mg PO QD	300 mg/day
Jardiance® (empagliflozin)	10 mg PO QD	25 mg/day
Qtern® (dapagliflozin/saxagliptin)	One 5/5 mg tablet PO QD	10/5 mg/day
Segluromet™ (ertugliflozin/ metformin)	Individualized dose PO BID	15/2,000 mg/day
Steglatro™ (ertugliflozin)	5 mg PO QD	15 mg/day
Steglujan™ (ertugliflozin/sitagliptin)	One 5/100 mg tablet PO QD	15/100 mg/day
Synjardy® (empagliflozin/metformin)	Individualized dose PO BID	25/2,000 mg/day
Synjardy® XR (empagliflozin/metformin)	Individualized dose PO QD	25/2,000 mg/day
Trijardy™ XR (empagliflozin/linagliptin/ metformin)	Individualized dose PO QD	25/5/2,000 mg/day
Xigduo® XR (dapagliflozin/metformin)	Individualized dose PO QD	IR: 40mg/day XR: 20 mg/day
SUs		
glipizide	Instant-release, extended-release: 5 mg tablet PO QD	10 mg/day
glimepiride (Amaryl®)	1-2 mg tablet PO QD	8 mg/day
glyburide, Micronized glyburide (Glynase®)	2.5- 5 mg tablet PO QD	20 mg/day
TZDs		
pioglitazone (Actos™)	15-30 mg tablet PO QD	45 mg/day
DPP-4 Inhibitors		
Jentadueto® (linagliptin/metformin)	Individualized dose PO BID	5/2,000 mg/day
Jentadueto® XR (linagliptin/metformin)	Individualized dose PO QD	5/2,000 mg/day
Kazano® (alogliptin/metformin)	Individualized dose PO BID	25/2,000 mg/day
Kombiglyze XR® (saxagliptin/metformin)	Individualized dose PO QD	5/2,000 mg/day
Nesina® (alogliptin)	25 mg tablet PO QD	25 mg/day
Onglyza® (saxagliptin)	2.5 or 5 mg tablet PO QD	5 mg/day
Oseni® (alogliptin/pioglitazone)	Individualized dose PO QD	25/45 mg/day
Tradjenta® (linagliptin)	5 mg tablet PO QD	5 mg/day
pioglitazone (Actos™)	15-30 mg tablet PO QD	45 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Basal Insulins		
Insulin determine (Levemir®)	Individualized dose SC QD or BID	Not applicable
Insulin glargine (Lantus®, Toujeo®, Basaglar®, Semglee®)	Individualized dose SC QD	Not applicable
Insulin degludec (Tresiba®)	Individualized dose SC QD	Not applicable

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Hypersensitivity to any product components
  - Personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2 (*all GLP-1 receptor agonists other than Byetta, Adlyxin, and Soliqua*)
  - Use during episodes of hypoglycemia (*Xultophy and Soliqua only*)
  - History of drug-induced immune-mediated thrombocytopenia from exenatide products (*Bydureon BCise and Byetta only*)
- Boxed warning(s): thyroid C-cell tumors (*all GLP-1 receptor agonists other than Byetta, Adlyxin, and Soliqua*)

Appendix D: General Information

- Per the American Diabetes Association (ADA) and American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) guidelines:
  - Metformin is recommended for all patients with type 2 diabetes. It is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death. Monotherapy is recommended for most patients; however:
    - Starting with dual therapy (i.e., metformin plus another agent, such as a SU, TZD, DPP-4 inhibitor, SGLT2 inhibitor, GLP-1 receptor agonist, or basal insulin) may be considered for patients with baseline HbA1c ≥ 1.5% above their target. According to the ADA, a reasonable HbA1c target for many non-pregnant adults is < 7% (≤ 6.5% per the AACE/ACE).
    - Starting with combination therapy with insulin may be considered for patients with baseline HbA1c > 10% or if symptoms of hyperglycemia are present.
    - For patients with established ASCVD or indicators of high ASCVD risk, heart failure, or chronic kidney disease, use of an SGLT2 inhibitor or GLP-1 receptor agonist with demonstrated cardiovascular benefit is recommended as part of the glucose-lowering regimen independent of HbA1c and metformin use. For heart failure, GLP-1 receptor agonists are specifically recommended for obese patients with preserved ejection fraction, while SGLT2 inhibitors are recommended regardless of ejection fraction or presence of obesity.
    - For patients with MASLD, GLP-1 receptor agonists are recommended for glycemic management due to potential beneficial effects on MASLD.

        - For patients with MASH, GLP-1 receptor agonists, pioglitazone, or a combination of the two are recommended for glycemic management due to potential beneficial effects on MASH.
    - If the target HbA1c is not achieved after approximately 3 months of monotherapy, dual therapy should be initiated. If dual therapy is inadequate after 3 months, triple therapy should be initiated. Finally, if triple therapy fails to bring a patient to goal, combination therapy with insulin should be initiated. Each non-insulin agent added to initial therapy can lower HbA1c by 0.7-1%.
- Although Trulicity is currently the only GLP-1 receptor agonist that is FDA approved for use in patients with multiple cardiovascular risk factors, the ADA guidelines recognize Ozempic, Trulicity, and Victoza as agents that confer cardiovascular benefit and recommend the use of any of the three in patients at high risk of ASCVD, without preference for any one over the other. In addition, patients with multiple cardiovascular risk factors were included in each drug's cardiovascular outcomes trial.
- Examples of cardiovascular risk factors may include but are not limited to: dyslipidemia, hypertension, obesity, a family history of premature coronary disease, smoking, chronic kidney disease, and presence of albuminuria.
- According to the ADA, ASCVD includes coronary heart disease, cerebrovascular disease, or PAD presumed to be of atherosclerotic origin. Per American College of Cardiology, indicators of high ASCVD risk are age ≥ 55 years with coronary, carotid, or lower-extremity artery stenosis > 50%; left ventricular hypertrophy; retinopathy; and other end organ damage.
- Ozempic is the only GLP-1 receptor agonist with an FDA approved indication for use in diabetic patients with chronic kidney disease. Although Victoza and Trulicity have both shown benefit for renal end points in their cardiovascular outcomes trials in diabetic patients with established or high risk of cardiovascular disease, Ozempic is the only GLP-1 receptor agonist that has demonstrated benefit for progression of chronic kidney disease in a chronic kidney disease-specific trial evaluating diabetic patients with chronic kidney disease. Of note, the ADA guidelines recommend use of GLP-1 receptor agonist with proven chronic kidney disease benefit in patients with chronic kidney disease.
- [Pending] Ozempic is the only GLP-1 receptor agonist with an FDA approved indication for use in diabetic patients with symptomatic PAD. In this population, it has demonstrated both cardiovascular and functional benefit (i.e., improvement in walking distance) in its cardiovascular outcomes and PAD-specific trials, respectively. On the other hand, while Victoza and Trulicity have also demonstrated cardiovascular benefit in their cardiovascular outcomes studies which included diabetic patients with PAD (12.5% and 8.7%, respectively), there is insufficient evidence that either of these agents offers comparable, if any, functional benefit.

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Adlyxin (lixisenatide)	Initial dose: 10 mcg SC QD for 14 days Maintenance dose: 20 mcg SC QD	20 mcg/day
Bydureon BCise (exenatide ER)	2 mg SC once weekly	2 mg/week
Byetta (exenatide IR)	5 mcg to 10 mcg SC BID	20 mcg/day

Drug Name	Dosing Regimen	Maximum Dose
Mounjaro (tirzepatide)	Initial dose: 2.5 mg SC once weekly. May increase by 2.5 mg every 4 weeks up to 15 mg once weekly	15 mg/week
Ozempic (semaglutide)	0.25 mg to 2 mg SC once weekly, increased no more frequently than every 4 weeks For patients with type 2 diabetes and chronic kidney disease, the dosage should be increased to the maintenance dose of 1 mg once weekly after at least 4 weeks on the 0.5 mg dosage [Pending] For patients with type 2 diabetes and symptomatic PAD, the dosage should be increased to the maintenance dose of 1 mg once weekly after 4 weeks on the 0.25 mg dosage and 4 weeks on the 0.5 mg dosage*	2 mg/week
Rybelsus (semaglutide)	Formulation R1:* Initial dose: 3 mg PO QD. After 30 days on the 3 mg dose, increase to 7 mg PO QD. May increase to 14 mg PO QD if needed after at least 30 days on the 7 mg dose [Pending] For patients with type 2 diabetes and established cardiovascular disease, the dosage should be increased to the maintenance dose of 14 mg PO QD* Formulation R2:* Initial dose: 1.5 mg PO QD. After 30 days on the 1.5 mg dose, increase to 4 mg PO QD. May increase to 9 mg PO QD if needed after at least 30 days on the 4 mg dose **Formulations R1 and R2 are not substitutable on a mg per mg basis. Use either formulation, but do not use both formulations at the same time. Patients may switch between formulations after 30 days of treatment (i.e., after the initiation phase). When switching between the formulations, initiate the other formulation the day after discontinuing the previous formulation.*	Formulation R1: 14 mg/day Formulation R2: 9 mg/day

Drug Name	Dosing Regimen	Maximum Dose
Soliqua (insulin glargine/ lixisenatide)	Treatment naïve to basal insulin or GLP-1 receptor agonist, currently on a GLP-1 receptor agonist, or currently on less than 30 units of basal insulin daily: 15 units (15 units insulin/5 mcg lixisenatide) SC QD Currently on 30 to 60 units of basal insulin daily, with or without GLP-1 receptor agonist: 30 units (30 units insulin/10 mcg lixisenatide) SC QD	60 units insulin/ 20 mcg lixisenatide/ day
Trulicity (dulaglutide)	0.75 mg to 1.5 mg SC once weekly For adults only: May increase to 3 mg once weekly if needed after at least 4 weeks on 1.5 mg dose. May further increase to 4.5 mg once weekly if needed after at least 4 weeks on 3 mg dose.	Pediatrics: 1.5 mg/week Adults: 4.5 mg/week
Victoza (liraglutide)	Initial: 0.6 mg SC QD for 7 days Maintenance: 1.2 mg to 1.8 mg SC QD	1.8 mg/day
Xultophy (liraglutide/ insulin degludec)	Treatment naïve to basal insulin or GLP-1 receptor agonist: 10 units (10 units of insulin/0.36 mg liraglutide) SC QD Treatment experienced to basal insulin or GLP-1 receptor agonist: 16 units (16 units insulin/0.58 mg liraglutide) SC QD	50 units insulin/1.8 mg liraglutide/day

VI. Product Availability

Drug Name	Availability
Adlyxin (lixisenatide)	Multi-dose prefilled pen: 50 mcg/mL in 3 mL (14 doses; 10 mcg/dose), 100 mcg/mL in 3 mL (14 doses; 20 mcg/dose)
Bydureon BCise (exenatide ER)	Single-dose autoinjector: 2 mg
Byetta (exenatide IR)	Prefilled pen: 5 mcg/dose (0.02 mL) in 1.2 mL (60 doses), 10 mcg/dose (0.04 mL) in 2.4 mL (60 doses)
Mounjaro (tirzepatide)	• Single-dose prefilled pen: 2.5 mg/0.5 mL, 5 mg/0.5 mL, 7.5 mg/0.5 mL, 10 mg/0.5 mL, 12.5 mg/0.5 mL, 15 mg/0.5 mL • Single-dose vial: 2.5 mg/0.5 mL, 5 mg/0.5 mL, 7.5 mg/0.5 mL, 10 mg/0.5 mL, 12.5 mg/0.5 mL, 15 mg/0.5 mL

Drug Name	Availability
Ozempic (semaglutide)	Prefilled pen: • 2 mg/3 mL (0.68 mg/mL); delivers 0.25 mg or 0.5 mg per injection • 4 mg/3 mL (1.34 mg/mL); delivers 1 mg per injection • 8 mg/3 mL (2.68 mg/mL); delivers 2 mg per injection
Rybelsus (semaglutide)	• Tablets (formulation R1): 3 mg, 7 mg, 14 mg • Tablets (formulation R2): 1.5 mg, 4 mg, 9 mg
Soliqua (insulin glargine/ lixisenatide)	Single-patient-use pen: 100 units/33mcg per mL in 3 mL
Trulicity (dulaglutide)	Single-dose prefilled pen: 0.75 mg/0.5 mL, 1.5 mg/0.5 mL, 3 mg/0.5 mL, 4.5 mg/0.5 mL
Victoza (liraglutide)	Multi-dose prefilled pen: 18 mg/3 mL (6 mg/mL; delivers doses of 0.6 mg, 1.2 mg, or 1.8 mg)
Xultophy (liraglutide/ insulin degludec)	Single-patient use pen: 3.6 mg/100 units per mL in 3 mL

VII. References

1. American Diabetes Association. Standards of medical care in diabetes—2025. Diabetes Care. December 2024; 48(suppl 1): S1-S352. Accessed December 17, 2024.
2. Blonde L, Umpierrez GE, Reddy SS, et al. American Association of Clinical Endocrinology clinical practice guideline: Developing a diabetes mellitus comprehensive care plan – 2022 update. Endocrine Practice. 2022; 28(10): 923-1049.
3. Samson SL, Vellanki P, Blonde L, et al. American Association of Clinical Endocrinology Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm - 2023 Update. Endocr Pract. 2023 May;29(5):305-340. doi: 10.1016/j.eprac.2023.02.001.
4. de Boer IH, Khunti K, Sadusky T, et al. Diabetes management in chronic kidney disease: A consensus report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). Diabetes Care. 2022; dci220027. Available at: https://diabetesjournals.org/care/article/doi/10.2337/dci22-0027/147614/Diabetes-Management-in-Chronic-Kidney-Disease-A. Accessed November 25, 2024.
5. Adlyxin Prescribing Information. Bridgewater, NJ: Sanofi-aventis US LLC; September 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/208471s007lbl.pdf. Accessed October 21, 2024.
6. Bydureon BCise Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals, LP; May 2023. Available at: https://www.astrazeneca-us.com/medicines/astrazeneca-medications.html. Accessed October 21, 2024.
7. Byetta Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals, LP; December 2022. Available at: www.byetta.com. Accessed October 21, 2024.
8. Trulicity Prescribing Information. Indianapolis, IN: Eli Lilly and Company, Inc; November 2022. Available at: www.trulicity.com. Accessed October 21, 2024.
9. Victoza Prescribing Information. Princeton, NJ: Novo Nordisk Inc; July 2023. Available at: www.victoza.com. Accessed October 21, 2024.
10. Xultophy Prescribing Information. Bagsvaerd, Denmark: Novo Nordisk A/S; July 2023. Available at: www.xultophy.com. Accessed October 21, 2024.

11. Ozempic Prescribing Information. Bagsvaerd, Denmark: Novo Nordisk A/S; January 2025. Available at: www.ozempic.com. Accessed February 12, 2025.
12. Rybelsus Prescribing Information. Bagsvaerd, Denmark: Novo Nordisk A/S; December 2024. Available at: www.rybelsuspro.com. Accessed December 17, 2024.
13. Mounjaro Prescribing Information. Indianapolis, IN: Lilly USA, LLC; July 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/215866Orig1s002s006lbl.pdf. Accessed October 21, 2024.
14. Soliqua Prescribing Information. Bridgewater, NJ: Sanofi-aventis US LLC; September 2023. Available at: www.soliqua.com. Accessed October 21, 2024.
15. McGuire DK, Marx N, Mulvagh SL, et al. Oral semaglutide and cardiovascular outcomes in high-risk type 2 diabetes. N Engl J Med. 2025; 392: 2001-2012.*
16. Bonaca MP, Catarig A, Houlind K, et al. Semaglutide and walking capacity in people with symptomatic peripheral artery disease and type 2 diabetes (STRIDE): a phase 3b, double-blind, randomised, placebo-controlled trial. Lancet. 2025; 405(10489): 1580-1593.*
17. Gornik HL, Aronow HD, Goodney PP, et al. 2024 ACC/AHA/AACVPR/APMA/ABC/ SCAI/ SVM/SVN/SVS/SIR/VESS guideline for the management of lower extremity peripheral artery disease: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2024;149:e1313–e1410. DOI: 10.1161/CIR.0000000000001251*

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: no significant changes; added new dosage strength (4 mg/3 mL) form for Ozempic; references reviewed and updated.	10.26.20	02.21
Removed Trulicity step-wise dose escalation criteria based on cost/PA analysis and low anticipation for inappropriate usage.	03.11.21	
Per March SDC, removed Victoza as a preferred agent.	03.09.21	05.21
RT4: updated indication and age limits down to 10 years of age for Bydureon and Bydureon BCise per updated prescribing information.	08.03.21	
1Q 2022 annual review: per November SDC removed Soliqua from criteria and added reference to CP.PST.01 step therapy criteria for Soliqua requests; WCG.CP.PMN.183 to be retired; references reviewed and updated.	11.30.21	02.22
RT4: added new dosage strength (2 mg) form for Ozempic.	04.13.22	
RT4: added newly FDA approved drug, Mounjaro.	05.31.22	
Template changes applied to other diagnoses/indications and continued therapy section.	10.04.22	
1Q 2023 annual review: RT4: added new dosage strength (2 mg/3 mL pen) for Ozempic; RT4: added pediatric expansion for age ≥ 10 years for Trulicity; references reviewed and updated. Per November SDC, updated redirections from requiring metformin + SGLT2 to requiring two agents from any of the following classes: biguanides, SU, TZD, DPP-4 inhibitors, SGLT2 inhibitors; added bypass of	01.17.23	02.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
required trial agents for members with ASCVD, indicators of high ASCVD risk, or chronic kidney disease per ADA guidelines; for non-preferred GLP-1 agents added criteria to require preferred GLP-1 products (e.g., Bydureon, Bydureon BCise, Byetta, Trulicity, Adlyxin). RT4: removed limitation of use regarding first line use for Rybelsus per updated PI.		
Per February SDC, added Soliqua requiring use of either basal insulin or GLP-1 receptor agonist within the past 180 days.	02.21.23	05.23
Added the following requirement to both initial and continued therapy: requested product is not prescribed concurrently with another GLP-1 receptor agonist.	07.31.23	
RT4: Added newly approved Mounjaro vial formulations.	09.12.23	
1Q 2024 annual review: no significant changes; for Ozempic, removed 2 mg/1.5 mL (1.34 mg/mL) from section VI as strength is not currently marketed; updated Appendix D; references reviewed and updated. Per December SDC, removed Adlyxin as an example of a preferred GLP-1 receptor agonist.	12.06.23	02.24
Per March SDC, added Victoza as a preferred agent for Ozempic in member established cardiovascular disease or multiple cardiovascular risk factors added Victoza as an additional required step; removed Bydureon from criteria as product has been discontinued.	03.12.24	05.24
Per SDC, modified step therapy requirement for non-preferred agents from one preferred agent to all preferred agents; added bypass of step therapy requirements for preferred agents.	07.01.24	
Per September SDC: removed redirection to Bydureon BCise and Byetta; removed redirection to brand Victoza and added redirection to liraglutide (Victoza authorized generic); revised redirection of preferred agents in a stepwise fashion, first requiring liraglutide (Victoza authorized generic), then if member has failed liraglutide, member must fail Trulicity; removed redirection criterion for Ozempic in members with established cardiovascular disease or multiple cardiovascular risk factors as redirection through liraglutide and Trulicity now align with all non-preferred products; added disclaimer that manufacturer AstraZeneca has discontinued Bydureon BCise and Byetta products.	09.25.24	12.24
1Q 2025 annual review: no significant changes; added Brenzavvy to Appendix B; references reviewed and updated. RT4: added new Rybelsus formulation (R2 tablets: 1.5 mg, 4 mg, and 9 mg); per 2025 ADA guidelines, added bypass of required non-GLP-1 trial agents for members with MASLD, MASH, and heart failure with preserved ejection fraction.	12.17.24	02.25

Reviews, Revisions, and Approvals	Date	P&T Approval Date
RT4: updated criteria to reflect Ozempic's new FDA indication for use in diabetic patients with chronic kidney disease; added "renal" benefit to criterion I.A.3.d.i. Per SDC, revised "liraglutide (Victoza authorized generic)" to "liraglutide (Victoza)".	02.12.25	
Clarified for Bydureon BCise age should be ≥ 10 years.	05.27.25	
Added pre-emptive criteria for Rybelsus (diabetic patients with established cardiovascular disease) and Ozempic (diabetic patients with symptomatic PAD).	08.26.25	11.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to

recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.