

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

Reference Number: CP.PST.14

Effective Date: 03.01.18

Last Review Date: 02.18

Line of Business: Health Insurance Marketplace, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

The following agents are synthetic glucagon-like peptide-1 (GLP-1) receptor agonists: albiglutide (Tanzeum[®]), dulaglutide (Trulicity[®]), exenatide ER (Bydureon[®], Bydureon[®] BCise[™]), exenatide IR (Byetta[®]), liraglutide (Victoza[®]), liraglutide/insulin degludec (Xultophy[®]), lixisenatide (Adlyxin[®]), and lixisenatide/insulin glargine (Soliqua[®]). Formulary status and requirement for step therapy vary by line of business.

FDA Approved Indication(s)

GLP-1 receptor agonists are indicated as adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Victoza is also indicated to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease.

Soliqua and Xultophy should be used in those inadequately controlled on basal insulin (< 60 units daily for Soliqua; < 50 units daily for Xultophy), lixisenatide (for Soliqua only), or liraglutide ≤ 1.8 mg daily (for Xultophy only).

Limitation(s) of use:

- GLP-1 receptor agonists are not recommended as a first-line therapy for patients inadequately controlled on diet and exercise.
- Other than Soliqua and Xultophy which contain insulin, GLP-1 receptor agonists are not a substitute for insulin. They should not be used for the treatment of type 1 diabetes or diabetic ketoacidosis.
- Concurrent use with prandial insulin has not been studied and cannot be recommended.
- GLP-1 receptor agonists have not been studied in patients with a history of pancreatitis. Other antidiabetic therapies should be considered.
- Tanzeum and Trulicity are not for patients with pre-existing severe gastrointestinal disease.
- Adlyxin has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis.

Policy/Criteria

Provider must submit documentation (which may include office chart notes and lab results) 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

A. Electronic Step Therapy for GLP-1 Receptor Agonists (must meet all):

1. Age \geq 18 years;
2. Previous use of \geq 3 consecutive months of metformin, unless contraindicated or clinically significant adverse effects are experienced;
3. If request is for a non-preferred GLP-1 receptor agonist, previous use of \geq 3 consecutive months of a preferred GLP-1 receptor agonist, unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed the FDA approved maximum recommended dose.

Approval duration: 12 months

B. Other diagnoses/indications: Not applicable

II. Continued Therapy

A. Electronic Step Therapy for GLP-1 Receptor Agonists (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. If request is for a dose increase, new dose does not exceed the FDA approved maximum recommended dose.

Approval duration: 12 months

B. Other diagnoses/indications: Not applicable

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

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AACE: American Association of Clinical Endocrinologists	FDA: Food and Drug Administration
ACE: American College of Endocrinology	GLP-1: glucagon-like peptide-1
ADA: American Diabetes Association	HbA1c: glycated hemoglobin
ER: extended-release	IR: immediate-release

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
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:	Regular-release: 2550 mg/day Extended-release • Fortamet: 2500 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	<ul style="list-style-type: none"> Fortamet, Glumetza: 1000 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 	<ul style="list-style-type: none"> Glucophage XR, Glumetza: 2000 mg/day

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: General Information

- A double-blind, placebo-controlled dose-response trial by Garber et al. found the maximal efficacy of metformin to occur at doses of 2000 mg. However, the difference in adjusted mean change in HbA1c between the 1500 and 2000 mg doses was 0.3%, suggesting that the improvement in glycemic control provided by the additional 500 mg may be insufficient when HbA1c is > 7%.
- Per the American Diabetes Association (ADA) and American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) 2017 guidelines:
 - Metformin is recommended for all patients with type 2 diabetes. Monotherapy is recommended for most patients; however:
 - Starting with dual therapy (i.e., metformin plus another agent, such as a sulfonylurea, thiazolidinedione, dipeptidyl peptidase-4 inhibitor, sodium-glucose co-transporter inhibitor, GLP-1 receptor agonist, or basal insulin) may be considered for patients with baseline HbA1c ≥ 9% per the ADA (≥ 7.5% per the AACE/ACE).
 - Starting with combination injectable therapy (i.e., with GLP-1 receptor agonist or insulin) may be considered for patients with baseline HbA1c ≥ 10% per the ADA (≥ 9% if symptoms are present per the AACE/ACE).
 - 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 injectable therapy should be initiated. Each non-insulin agent added to initial therapy can lower HbA1c by 0.9-1.1%.

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Adlyxin (lixisenatide)	Initial dose: 10 mcg SC daily for 14 days Maintenance dose: 20 mcg SC daily	20 mcg/day
Bydureon (exenatide ER)	2 mg SC once weekly	2 mg/week
Bydureon BCise (exenatide ER)	2 mg SC once weekly	2 mg/week
Byetta (exenatide IR)	5 mcg to 10 mcg SC twice daily	20 mcg/day
Soliqua (lixisenatide/insulin glargine)	15 units (15 units insulin/5 mcg lixisenatide) or 30 units (30 units insulin/10 mcg lixisenatide) SC QD	60 units (60 units insulin/20 mcg lixisenatide)/day

Drug Name	Dosing Regimen	Maximum Dose
Tanzeum (liraglutide)	30 mg to 50 mg SC once weekly	50 mg/week
Trulicity (dulaglutide)	0.75 mg to 1.5 mg SC once weekly	1.5 mg/week
Victoza (liraglutide)	Initial: 0.6 mg SC daily for 7 days Maintenance: 1.2 mg to 1.8 mg SC daily	1.8 mg/day
Xultophy (liraglutide/ insulin degludec)	16 units (16 units insulin/0.58 mg liraglutide) SC QD	50 units (50 units insulin/1.8 mg liraglutide)/day

VI. Product Availability

Drug Name	Availability
Adlyxin (lixisenatide)	<ul style="list-style-type: none"> Multi-dose prefilled pen: 50 mcg/mL in 3 mL (14 doses; 10 mcg/dose) Multi-dose prefilled pen: 100 mcg/mL in 3 mL (14 doses; 20 mcg/dose)
Bydureon (exenatide ER)	<ul style="list-style-type: none"> Single-dose tray: 2 mg vial Single-dose prefilled pen: 2 mg pen
Bydureon BCise (exenatide ER)	Single-dose autoinjector: 2 mg
Byetta (exenatide IR)	<ul style="list-style-type: none"> Prefilled pen: 5 mcg/dose (0.02 mL) in 1.2 mL (60 doses) Prefilled pen: 10 mcg/dose (0.04 mL) in 2.4 mL (60 doses)
Soliqua (lixisenatide/ insulin glargine)	Single-patient use pen: 33 mcg/100 units per mL in 3 mL
Tanzeum (liraglutide)	Single dose prefilled pen powder: 30 mg and 50 mg
Trulicity (dulaglutide)	<ul style="list-style-type: none"> Single-dose prefilled pen: 0.75 mg/0.5mL and 1.5 mg/0.5mL Single-dose prefilled syringe: 0.75 mg/0.5mL and 1.5 mg/0.5mL
Victoza (liraglutide)	Multi-dose prefilled pen: 6 mg/mL in 3 mL (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

- American Diabetes Association. Standards of medical care in diabetes—2017. Diabetes Care. 2017; 40(suppl 1): S1-S135.
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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	11.07.17	02.18

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

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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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

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