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

Reference Number: HIM.PA.53
Effective Date: 03.01.18
Last Review Date: 02.18
Line of Business: Health Insurance Marketplace

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 requiring step therapy: albiglutide (Tanzeum®), dulaglutide (Trulicity®), exenatide IR (Byetta®), and liraglutide (Victoza®).

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.

Limitation(s) of use:

- GLP-1 receptor agonists are not recommended as a first-line therapy for patients inadequately controlled on diet and exercise.
- 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.
- Other than Trulicty, 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.

Policy/Criteria

Provider must submit documentation (including 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

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

1. Age ≥ 18 years;
2. Member meets one of the following (a or b):
   a. Previous use of ≥ 3 consecutive months of metformin, unless contraindicated or clinically significant adverse effects are experienced;

b. HbA1c drawn within the past 3 months is ≥ 9%, and concurrent use of metformin unless contraindicated or clinically significant adverse effects are experienced;

3. Dose does not exceed the FDA approved maximum recommended dose.

Approval duration: 12 months

B. Other diagnoses/indications: Not applicable

II. Continued Therapy

A. 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
ACE: American College of Endocrinology
ADA: American Diabetes Association
ER: extended-release
FDA: Food and Drug Administration
GLP-1: glucagon-like peptide-1
HbA1c: glycated hemoglobin
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: • 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	Regular-release: 2550 mg/day Extended-release • Fortamet: 2500 mg/day • 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 2018 American Diabetes Association (ADA) and 2017 American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) 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
Byetta (exenatide IR)	5 mcg to 10 mcg SC twice daily	20 mcg/day
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

VI. Product Availability

Drug Name	Availability
Byetta (exenatide IR)	• 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)
Tanzeum (liraglutide)	Single dose prefilled pen powder: 30 mg and 50 mg
Trulicity (dulaglutide)	• 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)

VII. References

1. American Diabetes Association. Standards of medical care in diabetes—2018. Diabetes Care. 2018; 41(suppl 1): S1-S159.
2. Byetta Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals, LP; February 2015. Available at: www.byetta.com. Accessed November 29, 2017.
3. Tanzeum Prescribing Information. Wilmington, DE: GlaxoSmithKline; August 2017. Available at: www.tanzeum.com. Accessed November 29, 2017.
4. Trulicity Prescribing Information. Indianapolis, IN: Eli Lilly and Company, Inc; August 2017. Available at: www.trulicity.com. Accessed November 29, 2017.
5. Victoza Prescribing Information. Princeton, NJ: Novo Nordisk Inc; August 2017. Available at: www.victoza.com. Accessed November 29, 2017.
6. Garber AJ, Duncan TG, Goodman AM, et al. Efficacy of metformin in type II diabetes: results of a double-blind, placebo-controlled, dose-response trial. Am J Med. 1997; 102: 491-497.
7. Garber AJ, Abrahamson MJ, Barzilay, JI, et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 diabetes management algorithm – 2017 executive summary. Endocr Pract. 2017; 23(2): 207-238.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Changed guideline to new format. Extended approval period from 6 months to 12 months.	08.16	08.16
Removed age restriction. Modified A1c requirement from > 7% to > 6.5% and specified time frame for lab. Added specific dose and duration for metformin trial. Clarified criterion for failure of other anti-diabetic agents to specifically require a sulfonylurea and pioglitazone be used concurrently with metformin for 3 consecutive months. Removed criterion regarding concurrent insulin use as it is not an absolute contraindication. Modified initial approval duration from 12 months to 6 months to allow for earlier assessment of therapeutic response. Added criteria surrounding required therapeutic response for re-auth.	04.17	08.17
Added age restriction as safety and efficacy have not been established in pediatric populations. Removed requirement that metformin must have been used with a sulfonylurea and pioglitazone as GLP-1 agonists are similar place of therapy as these agents, and the guidelines do not prefer one over the other.	08.18.17	11.17
Removed requirement for diagnosis Removed requirement for A1C submission	11.17	02.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Changed requirement for Metformin trial to be for 3 months without mandating a specific dose Allow first line use for members with A1C >= 9% References reviewed and updated		

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.