Clinical Policy: Non-Preferred Dipeptidyl Peptidase-4 (DPP-4) Inhibitors

Reference Number: CP.CPA.343
Effective Date: 11.16.16
Last Review Date: 02.20
Line of Business: Commercial

Revision Log

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

Description

The following agents contain a dipeptidyl peptidase-4 (DPP-4) inhibitor and require prior authorization: linagliptin (Tradjenta®), linagliptin/metformin (Jentadueto®, Jentadueto® XR), saxagliptin (Onglyza®), saxagliptin/metformin (Kombiglyze® XR), alogliptin/metformin (Kazano®), alogliptin (Nesina™), and alogliptin/pioglitazone (Oseni®).

FDA Approved Indication(s)

DPP-4 inhibitors are indicated as adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitation(s) of use:

- DPP-4 inhibitors should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.
- DPP-4 inhibitors have not been studied in patients with a history of pancreatitis.

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 DPP-4 inhibitors are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of type 2 diabetes mellitus;
2. Age ≥ 18 years;
3. Member meets one of the following (a or b):
   a. Failure of ≥ 3 consecutive months of metformin, unless contraindicated or clinically significant adverse effects are experienced;
   b. HbA1c drawn within the past 3 months is ≥ 8.5%, and concurrent use of metformin unless contraindicated or clinically significant adverse effects are experienced;
4. Failure of a sitagliptin-containing product (e.g., sitagliptin [Januvia®], sitagliptin/metformin [Janumet®, Janumet® XR]), unless all are contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed the FDA approved maximum recommended dose (*see Section V*).

Approval duration: Length of Benefit

B. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

II. Continued Therapy

A. Type 2 Diabetes Mellitus (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed the FDA approved maximum recommended dose (*see Section V*).

Approval duration: Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

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 policy – CP.CPA.09 for commercial or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DPP-4: dipeptidyl peptidase-4
FDA: Food and Drug Administration
HbA1c or A1c: glycated hemoglobin test

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 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: 2,550 mg/day Extended-release: 2,000 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	• 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	
Janumet® (sitagliptin/metformin)	Individualized dose PO BID	100/2,000 mg/day
Janumet XR® (sitagliptin/metformin)	Individualized dose PO QD	100/2,000 mg/day
Januvia® (sitagliptin)	100 mg PO QD	100 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: Contraindications/Boxed Warnings

- Contraindication(s):
  - History of serious hypersensitivity reaction to the requested drug product
  - Severe renal impairment (*metformin-containing products*)
  - Metabolic acidosis, including diabetic ketoacidosis (*metformin-containing products only*)
  - NYHA Class III or IV heart failure (*Oseni only*)
- Boxed warning(s): lactic acidosis (*metformin-containing products only*), congestive heart failure (*Oseni only*)

Appendix D: General Information

- Both the American Diabetes Association guideline and the American Association of Clinical Endocrinologist/American College of Endocrinology algorithm recommend metformin as an initial first line agent due to its safety and efficacy profile. 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 ≥ 1.5% above their target per the ADA (≥ 7.5% per the AACE/ACE). According to the ADA, a reasonable HbA1c target for many non-pregnant adults is < 7% (≤ 6.5% per the AACE/ACE).
- There are warning of acute pancreatitis, hepatic failure (fatal), and severe and disabling arthralgia in post marketing reports.

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
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

Drug Name	Dosing Regimen	Maximum Dose
Kombiglyze XR (saxagliptin/metformin)	Individualized dose PO QD	5/2,000 mg/day
Onglyza (saxagliptin)	2.5 or 5 mg PO QD	5 mg/day
Tradjenta (linagliptin)	5 mg PO QD	5 mg/day
Nesina (alogliptin)	25 mg PO QD	25 mg/day
Oseni (alogliptin/pioglitazone)	Individualized dose PO QD	25/45 mg/day
Kazano (alogliptin/metformin)	Individualized dose PO BID	25/2,000 mg/day

VI. Product Availability

Drug Name	Availability
Jentadueto (linagliptin/metformin)	Tablets: 2.5/500 mg, 2.5/850 mg, 2.5/1,000 mg
Jentadueto XR (linagliptin/metformin)	Tablets: 5/1,000 mg, 2.5/1,000 mg
Kombiglyze XR (saxagliptin/metformin)	Tablets: 5/500 mg, 5/1,000 mg, 2.5/1,000 mg
Onglyza (saxagliptin)	Tablets: 2.5 mg, 5 mg
Tradjenta (linagliptin)	Tablets: 5 mg
Nesina (alogliptin)	Tablets: 6.25 mg, 12.5 mg, 25 mg
Oseni (alogliptin/pioglitazone)	Tablets: 12.5/15 mg, 12.5/30 mg, 12.5/45 mg, 25/15 mg, 25/30 mg, 25/45 mg
Kazano (alogliptin/metformin)	Tablets: 12.5/500 mg, 12.5/1,000 mg

VII. References

1. American Diabetes Association. Standards of medical care in diabetes—2019. Diabetes Care. 2019; 42(suppl 1): S1-S193. Updated July 31, 2019. Accessed October 29, 2019.
2. Jentadueto Prescribing Information Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; July 2019. Available at: www.jentadueto.com. Accessed October 29, 2019.
3. Jentadueto XR Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; July 2019. Available at: www.jentaduetoxr.com. Accessed October 29, 2019.
4. Kombiglyze XR Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; October 2019. Available at: www.kombiglyzexr.com. Accessed October 29, 2019.
5. Onglyza Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; October 2019. Available at: www.onglyza.com. Accessed October 29, 2019.
6. Tradjenta Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; July 2019. Available at: www.tradjenta.com. Accessed October 29, 2019.
7. Nesina Prescribing Information. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; June 2019. Available at: www.nesinafamily.com. Accessed October 29, 2019.
8. Oseni Prescribing Information. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; June 2019. Available at: www.nesinafamily.com. Accessed October 29, 2019.
9. Kazano Prescribing Information. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; June 2019. Available at: www.nesinafamily.com. Accessed October 29, 2019.

10. 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.
11. 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 – 2019 executive summary. Endocr Pract. 2019; 25(1): 69-100.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Minor changes to verbiage and grammar. References updated.	01.13.17	11.17
1Q18 Annual Review Modified metformin trial requirement to have a mandate a specific duration rather than dose and removed specific definition of failure. Added option for members with A1c ≥ 9% to bypass previous use of metformin for 3 months per ADA guidelines (concurrent metformin use is still required). References reviewed and updated.	11.30.17	02.18
1Q 2019 annual review: added age ≥ 18 years; clarified metformin trial required to be consecutive months; modified minimum A1c related for concurrent use of metformin from 9% to 8.5% based on 2019 ADA guidelines; references reviewed and updated.	10.12.18	02.19
Per SDC, added Tradjenta, Jentadueto, Jentadueto XR, Onglyza, Kombiglyze XR, Kazano, and Oseni to policy; added redirection to a sitagliptin-containing product.	06.25.19	
Policy number revised to CP.CPA.343; CP.CPA.126 retired.	08.19.19	
1Q 2020 annual review: no significant changes; references reviewed and updated.	10.29.19	02.20

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.

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