

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

Reference Number: AZ.CP.PHAR.26

Effective Date: 09.04.18

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Line of Business: Arizona Medicaid

[Revision Log](#)

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

Description

The following are dipeptidyl peptidase-4 (DPP-4) inhibitors requiring prior authorization: alogliptin (Nesina[®]), alogliptin/metformin (Kazano[®]), alogliptin/pioglitazone (Oseni[®]), linagliptin (Tradjenta[®]), linagliptin/empagliflozin (Glyxambi[®]), linagliptin/metformin (Jentaduet[®], Jentaduet[®] XR), saxagliptin (Onglyza[®]), saxagliptin/metformin (Kombiglyze[®] XR), sitagliptin (Januvia[®]), ertugliflozin/sitagliptin (Steglujan[®]), and sitagliptin/metformin (Janumet[®], Janumet[®] XR).

AHCCCS preferred drugs in this class include Januvia, Janumet, Janumet XR, Jentaduet, Tradjenta, Glyxambi, Onglyza and Kombigylze.

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 (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 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 \geq 18 years;
3. Member meets one of the following (a or b):
 - a. Failure of \geq 3 consecutive months of metformin, unless contraindicated or clinically significant adverse effects are experienced;
 - b. HbA1c drawn within the past 3 months is \geq 9%, and concurrent use of metformin unless contraindicated or clinically significant adverse effects are experienced;
4. Request meets one of the following (a, or b):

- a. Request is for a preferred DPP-4 inhibitor;
 - b. Request is for a non-preferred DPP-4 inhibitor: failure of ≥ 3 consecutive months of all preferred DPP-4 inhibitors, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed the FDA approved maximum recommended dose (*see Section V*).

Approval duration: 12 months

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.PMN.53 for Medicaid.

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: 12 months

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.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

DPP-4: dipeptidyl peptidase-4

FDA: Food and Drug Administration

GLP-1: glucagon-like peptide-1

HbA1c: glycated hemoglobin

SGLT2: sodium-glucose co-transporter 2

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: <ul style="list-style-type: none"> • Fortamet: 500 or 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: <ul style="list-style-type: none"> • Fortamet: 2500 mg/day • Glucophage XR: 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: Contraindications/Boxed Warnings

- Contraindication(s):
 - History of serious hypersensitivity reaction to the requested drug product
 - Severe renal impairment (*metformin-containing products and Glyxambi*)
 - End-stage renal disease or dialysis (*Glyxambi only*)
 - 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

- 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 American Association of Clinical Endocrinologists and 2017 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, DPP-4 inhibitor, sodium-glucose co-transporter 2 [SGLT2] inhibitor, glucagon-like peptide 1 [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).

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- Starting with combination injectable therapy (i.e., with GLP-1 receptor agonist or insulin) may be considered for patients with baseline HbA1c $\geq 10\%$ per the ADA ($\geq 9\%$ 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
Glyxambi (linagliptin/empagliflozin)	5/10 mg PO QD	5/25 mg/day
Janumet (sitagliptin/metformin)	Individualized dose PO BID	100/2000 mg/day
Janumet XR (sitagliptin/metformin)	Individualized dose PO QD	100/2000 mg/day
Januvia (sitagliptin)	100 mg PO QD	100 mg/day
Jentadueto (linagliptin/metformin)	Individualized dose PO BID	5/2000 mg/day
Jentadueto XR (linagliptin/metformin)	Individualized dose PO QD	5/2000 mg/day
Kazano (alogliptin/metformin)	Individualized dose PO BID	25/2000 mg/day
Kombiglyze XR (saxagliptin/metformin)	Individualized dose PO QD	5/2000 mg/day
Nesina (alogliptin)	25 mg PO QD	25 mg/day
Onglyza (saxagliptin)	2.5 or 5 mg PO QD	5 mg/day
Oseni (alogliptin/pioglitazone)	Individualized dose PO QD	25/45 mg/day
Tradjenta (linagliptin)	5 mg PO QD	5 mg/day

VI. Product Availability

Drug Name	Availability
Glyxambi (linagliptin /empagliflozin)	Tablets: 5/10 mg, 5/25 mg
Janumet (sitagliptin/metformin)	Tablets: 50/500 mg, 50/1000 mg
Janumet XR (sitagliptin/metformin)	Tablets: 100/1000 mg, 50/500 mg, 50/1000 mg
Januvia (sitagliptin)	Tablets: 25 mg, 50 mg, 100 mg
Jentadueto (linagliptin/metformin)	Tablets: 2.5/500 mg, 2.5/850 mg, 2.5/1000 mg
Jentadueto XR (linagliptin/metformin)	Tablets: 5/1000 mg, 2.5/1000 mg
Kazano (alogliptin/metformin)	Tablets: 12.5/500 mg, 12.5/1000 mg
Kombiglyze XR (saxagliptin/metformin)	Tablets: 5/500 mg, 5/1000 mg, 2.5/1000 mg
Nesina (alogliptin)	Tablets: 6.25 mg, 12.5 mg, 25 mg
Onglyza (saxagliptin)	Tablets: 2.5 mg, 5 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
Tradjenta (linagliptin)	Tablets: 5 mg

VII. References

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created: adapted from previously corporate approved policy CP.PST.18	09.11.18	11.18

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

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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.

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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.

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