

STEP THERAPY POLICY

- POLICY:** Diabetes – Dipeptidyl Peptidase-4 Inhibitors Step Therapy Policy
- Brynovin™ (sitagliptin oral solution – Azurity)
 - Janumet® (sitagliptin/metformin tablets – Merck)
 - Janumet® XR (sitagliptin/metformin extended-release tablets – Merck)
 - Januvia® (sitagliptin tablets – Merck)
 - Jentadueto® (linagliptin/metformin tablets – Boehringer Ingelheim)
 - Jentadueto® XR (linagliptin/metformin extended-release tablets – Boehringer Ingelheim)
 - Kazano™ (alogliptin/metformin tablets – Takeda, authorized generic)
 - alogliptin/metformin tablets – A-S Medication
 - Kombiglyze® XR (saxagliptin/metformin extended-release tablets – AstraZeneca, generic)
 - Nesina® (alogliptin tablets – Takeda, authorized generic)
 - alogliptin tablets – multiple manufacturers
 - Onglyza® (saxagliptin tablets – AstraZeneca [*brand obsolete 02/29/2024*], generic)
 - Oseni™ (alogliptin/pioglitazone tablets – Takeda, authorized generic)
 - Tradjenta® (linagliptin tablets – Boehringer Ingelheim)
 - Zituvimet™ (sitagliptin/metformin tablets – Zydus, authorized generic)
 - Zituvimet™ XR (sitagliptin/metformin extended-release tablets – Zydus, authorized generic)
 - Zituvio™ (sitagliptin tablets – Zydus, authorized generic)

REVIEW DATE: 05/06/2026

OVERVIEW

The dipeptidyl peptidase-4 (DPP-4) inhibitors and combination products are indicated to improve glycemic control in adults with **type 2 diabetes mellitus** (as monotherapy and as combination therapy) when used as adjuncts to diet and exercise.^{1-11,15-17}

Various combination products are available which combine DPP-4 inhibitors with metformin, sodium glucose co-transporter-2 (SGLT-2) inhibitors, and/or thiazolidinediones (TZDs). Of note, the SGLT-2/DPP-4 combination products are not addressed in this policy; refer to the *Diabetes – Sodium Glucose Co-Transporter-2 and Dipeptidyl Peptidase-4 Inhibitors Step Therapy Policy*.

GUIDELINES

The American Diabetes Association Standards of Care in Diabetes (2026) note that therapy for patients with type 2 diabetes depends on comorbidities and patient-centered treatment factors.¹² Metformin is contraindicated in patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m²) and in patients with acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma.¹³ DPP-4 inhibitors are among the classes of medications recommended as add-on therapy after metformin; however, they have lower glycemic efficacy than other classes and lack cardiorenal indications. Metformin is more effective than DPP-4 inhibitors in lowering hemoglobin A_{1c} and weight when used as monotherapy. Because type 2 diabetes is often a progressive disease, combination therapy may be needed for many patients over time to achieve glycemic targets.

The American Association of Clinical Endocrinology Consensus Statement: Algorithm for Management of Adults With Type 2 Diabetes (2026) emphasizes individualization of antihyperglycemic therapy based

on glycemic targets and comorbidities/complications.¹⁸ In the glucose-centric approach (used when high-risk comorbidities are not present), metformin should be initiated for most individuals if there is no contraindication. Early combination therapy may be considered, usually with metformin plus another agent that does not cause hypoglycemia (including a DPP-4 inhibitor).

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a history of one of the following within the 130-day look-back period is excluded from Step Therapy:

- One Step 1 Product; OR
- One of the following metformin-containing products: Glumetza ER, Riomet, metformin oral solution, metformin extended-release (generics to Fortamet ER and Glumetza ER), glyburide/metformin, glipizide/metformin, Actoplus Met, pioglitazone/metformin, Invokamet, Invokamet XR, Synjardy, Synjardy XR, Xigduo XR, dapagliflozin/metformin extended-release, Segluromet; OR
- One Step 2 Product.

Step 1: generic metformin, generic metformin extended-release (generic to Glucophage XR only)

Step 2: Brynovin, Januvia, Janumet, Janumet XR, Kombiglyze XR, saxagliptin/metformin extended-release, Onglyza, saxagliptin, Tradjenta, Jentadueto, Jentadueto XR, Nesina, alogliptin, Kazano, alogliptin/metformin, Oseni, alogliptin/pioglitazone, Zituvio, sitagliptin (authorized generic to Zituvio), Zituvimet, sitagliptin/metformin (authorized generic to Zituvimet), Zituvimet XR, sitagliptin/metformin extended-release (authorized generic to Zituvimet XR).

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

Note: A trial of one of the following metformin-containing products also satisfies the requirement: Fortamet ER (obsolete), Glucophage (obsolete), Glucophage XR (obsolete), Glumetza ER, Riomet, metformin oral solution, Riomet ER (obsolete), metformin extended-release (generics to Fortamet ER and Glumetza ER), glyburide/metformin, glipizide/metformin, Actoplus Met, pioglitazone/metformin, Actoplus Met XR (obsolete), repaglinide/metformin (obsolete), Invokamet, Invokamet XR, Synjardy, Synjardy XR, Xigduo XR, dapagliflozin/metformin extended-release, Segluromet.

2. If the patient has tried one Step 2 Product, approve the requested Step 2 Product.

3. If the patient is initiating dual (combination) therapy with a single-entity DPP-4 inhibitor (Brynovin, Januvia, Onglyza, saxagliptin, Tradjenta, Nesina, alogliptin, Zituvio, or sitagliptin [authorized generic to Zituvio]) AND metformin, approve a single-entity DPP-4 inhibitor.

4. If the patient has a contraindication to metformin, according to the prescriber, approve a single-entity DPP-4 inhibitor.

Note: Examples of contraindications to metformin include acute or chronic metabolic acidosis, including diabetic ketoacidosis.

5. No other exceptions are recommended.

REFERENCES

1. Janumet® tablets [prescribing information]. Whitehouse Station, NJ: Merck; June 2022.
2. Janumet® XR tablets [prescribing information]. Whitehouse Station, NJ: Merck; June 2022.
3. Januvia® tablets [prescribing information]. Rahway, NJ: Merck; December 2023.
4. Jentadueto® tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; June 2023.
5. Jentadueto® XR tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; June 2023.
6. Kazano™ tablets [prescribing information]. Lexington, MA: Takeda; July 2023.
7. Kombiglyze® XR tablets [prescribing information]. Wilmington, DE: AstraZeneca; October 2024.
8. Nesina® tablets [prescribing information]. Lexington, MA: Takeda; July 2023.
9. Onglyza® tablets [prescribing information]. Wilmington, DE: AstraZeneca; October 2024.
10. Oseni™ tablets [prescribing information]. Lexington, MA: Takeda; June 2024.
11. Tradjenta® tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; June 2023.
12. American Diabetes Association. Standards of care in diabetes – 2026. *Diabetes Care*. 2026;49(Suppl 1):S1-S371..
13. Metformin tablets [prescribing information]. Raleigh, NC: Indicus Pharma; June 2020.
14. Zituvio™ tablets [prescribing information]. Pennington, NJ: Zydus; October 2023.
15. Zituvimet™ tablets [prescribing information]. Pennington, NJ: Zydus; November 2023.
16. Zituvimet™ XR tablets [prescribing information]. Pennington, NJ: Zydus; July 2024.
17. Brynovin™ oral solution [prescribing information]. Woburn, MN: Azurity; January 2025.
18. Samson SL, Vellanki P, Blonde L, et al. American Association of Clinical Endocrinology consensus statement: algorithm for management of adults with type 2 diabetes – 2026 update. *Endocr Pract*. 2026;32:473-518.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	<p>Automation: Fortamet ER was removed from the list of metformin-containing products (obsolete). Dapagliflozin/metformin extended-release (authorized generic to Xigduo XR) was added to the list of metformin-containing products.</p> <p>Step 2 Products: sitagliptin (authorized generic to Zituvio) was added to Step 2 products.</p> <p>Criteria: For a patient requesting a Step 2 product, the note was updated to reflect that Fortamet ER is obsolete (this still counts towards a trial of a Step 1 product). The note was also updated to add dapagliflozin/metformin extended-release (authorized generic to Xigduo XR). For a patient initiating dual (combination) therapy with a single-entity DPP-4 inhibitor AND metformin, sitagliptin (authorized generic to Zituvio) was added to the list of single-entity DPP-4 inhibitors to approve.</p>	05/22/2024
Selected Revision	<p>Step 2 Products: Sitagliptin/metformin (authorized generic) was added to Step 2 products.</p>	08/07/2024
Selected Revision	<p>Step 2 Products: Zituvimet and Zituvimet XR were added to the list of Step 2 products</p>	11/20/2024
Annual Revision	<p>Automation: Riomet ER was removed from the list of metformin-containing product (obsolete > 3 years).</p> <p>Criteria: For a patient requesting a Step 2 product, that has tried a Step 1 product, the note listing metformin-containing products was updated to reflect that Riomet ER is obsolete (this still counts towards a trial of a Step 1 product).</p>	05/14/2025

HISTORY (CONTINUED)

Type of Revision	Summary of Changes	Review Date
Selected Revision	Step 2 Products: Sitagliptin/metformin extended-release (authorized generic to Zituvimet XR) was added to the list of Step 2 products.	08/06/2025
Selected Revision	Step 2 Products: Brynovin was added to the list of Step 2 products. Criteria: For a patient initiating dual (combination) therapy with a single-entity DPP-4 inhibitor AND metformin, Brynovin was added to the list of single-entity DPP-4 inhibitors to approve.	10/22/2025
Annual Revision	No criteria changes.	05/06/2026
