STEP THERAPY POLICY

POLICY: Diabetes – Dipeptidyl Peptidase-4 Inhibitors Step Therapy Policy

- 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, 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)
- Zituvio™ (sitagliptin tablets – Zydus, authorized generic)

REVIEW DATE: 05/14/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE

CIGNA NATIONAL FORMULARY COVERAGE:

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 (2025) note that therapy for patients with type 2 diabetes depends on comorbidities, patient-centered treatment factors.[12] Metformin is contraindicated in patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m^2) 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. Because type 2 diabetes is often a progressive disease, combination therapy may be needed for many patients over time to achieve glycemic targets.

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.

- 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: 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.

Diabetes – Dipeptidyl Peptidase-4 Inhibitors Step Therapy Policy
product(s) is(are) covered as medically necessary when the following step therapy criteria is(are) met. Any other exception is considered not medically necessary.

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 (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.

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 – 2025. Diabetes Care. 2025;48(Suppl 1):S1-S359.
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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Automation:** The following products were removed from the automation (obsolete): Glucophage, Glucophage XR, repaglinide/metformin, Actoplus Met XR. Glumetza and Fortamet were clarified to be Glumetza ER and Fortamet ER. **Criteria:** For patients requesting a Step 2 product, the note was updated to reflect that Glucophage, Glucophage XR, repaglinide/metformin, and Actoplus Met XR are obsolete (these still count towards a trial of a Step 1 product). Additionally, Glumetza and Fortamet were clarified to be Glumetza ER and Fortamet ER.	05/03/2023
Selected Revision	**Step 2 Products:** Saxagliptin (generic to Onglyza) and saxagliptin/metformin extended-release (generic to Kombiglyze XR) were added to Step 2 products. **Criteria**: For a patient initiating dual (combination) therapy with a single-entity DPP-4 inhibitor AND metformin, saxagliptin was added to the list of single-entity DPP-4 inhibitors to approve.	09/13/2023
Selected Revision	**Step 2 Products:** Zituvio 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, Zituvio was added to the list of single-entity DPP-4 inhibitors to approve.	02/07/2024
Annual Revision	**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. **Step 2 Products:** sitagliptin (authorized generic to Zituvio) was added to Step 2 products. **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	05/22/2024

	(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.	
Selected Revision	**Step 2 Products: S**itagliptin/metformin (authorized generic) was added to Step 2 products.	08/07/2024
Selected Revision	**Step 2 Products:** Zituvimet and Zituvimet XR were added to the list of Step 2 products	11/20/2024
Annual Revision	**Automation:** Riomet ER was removed from the list of metformin-containing product (obsolete > 3 years). **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).	05/14/2025