

## STEP THERAPY POLICY

- POLICY:** Diabetes – Dipeptidyl Peptidase-4 Inhibitors Step Therapy Policy
- Janumet<sup>®</sup> (sitagliptin/metformin tablets – Merck)
  - Janumet<sup>®</sup> XR (sitagliptin/metformin extended-release tablets – Merck)
  - Januvia<sup>®</sup> (sitagliptin tablets – Merck)
  - Jentadueto<sup>®</sup> (linagliptin/metformin tablets – Boehringer Ingelheim)
  - Jentadueto<sup>®</sup> XR (linagliptin/metformin extended-release tablets – Boehringer Ingelheim)
  - Kazano<sup>™</sup> (alogliptin/metformin tablets – Takeda, authorized generic)
  - Kombiglyze<sup>®</sup> XR (saxagliptin/metformin extended-release tablets – AstraZeneca, generic)
  - Nesina<sup>®</sup> (alogliptin tablets – Takeda, authorized generic)
  - Onglyza<sup>®</sup> (saxagliptin tablets – AstraZeneca, generic)
  - Oseni<sup>™</sup> (alogliptin/pioglitazone tablets – Takeda, authorized generic)
  - Sitagliptin/metformin tablets (authorized generic to Zituvimet<sup>™</sup> [not available])
  - Tradjenta<sup>®</sup> (linagliptin tablets – Boehringer Ingelheim)
  - Zituvio<sup>™</sup> (sitagliptin tablets – Zydus, authorized generic)

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### 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.<sup>1-11,15</sup>

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 (2024) note that therapy for patients with type 2 diabetes depends on comorbidities, patient-centered treatment factors, and management needs and generally includes metformin and comprehensive lifestyle modification.<sup>12</sup> Very high circulating levels of metformin have been associated with lactic acidosis. However, the occurrence of this complication is now known to be very rare. In patients with contraindications or intolerance to metformin, initial therapy should be based on patient factors. Metformin is contraindicated in patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m<sup>2</sup>) and in patients with acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma.<sup>14</sup> DPP-4 inhibitors are among the classes of medications recommended as add-on therapy after metformin (or as initial therapy if metformin cannot be used). Because type 2 diabetes is often a progressive disease, combination therapy may be needed for many patients over time to achieve glycemic targets. Other guidelines have similar recommendations.<sup>13,16</sup>

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## 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 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, Riomet ER, 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 (authorized generic to Xigduo XR), 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, saxagliptin (Onglyza, generic), saxagliptin/metformin extended-release (Kombiglyze XR, generic), Tradjenta, Jentadueto, Jentadueto XR, alogliptin (Nesina, authorized generic), alogliptin/metformin (Kazano, authorized generic), alogliptin/pioglitazone (Oseni, authorized generic), sitagliptin (Zituvio, authorized generic), sitagliptin/metformin (authorized generic)

## 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, 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 (authorized generic to Xigduo XR), 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, saxagliptin [Onglyza, generic], Tradjenta, alogliptin [Nesina, authorized generic], or sitagliptin [Zituvio, authorized generic]) 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

## Diabetes – Dipeptidyl Peptidase-4 Inhibitors Step Therapy Policy

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