

## 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)
  - Nesina<sup>®</sup> (alogliptin tablets – Takeda, authorized generic)
  - Onglyza<sup>®</sup> (saxagliptin tablets – AstraZeneca)
  - Oseni<sup>™</sup> (alogliptin/pioglitazone tablets – Takeda, authorized generic)
  - Tradjenta<sup>®</sup> (linagliptin tablets – Boehringer Ingelheim)

**REVIEW DATE:** 05/11/2022

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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</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 (2022) recommend metformin as initial therapy for most patients with type 2 diabetes, unless contraindications to metformin are present.<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> Any of several classes of medications, including DPP-4 inhibitors, SGLT-2 inhibitors, and TZDs, may be used 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</sup>

### 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.

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**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: Fortamet, Glucophage, Glucophage XR, Glumetza, Riomet, metformin oral solution, Riomet ER, metformin extended-release (generics to Fortamet and Glumetza), glyburide/metformin, glipizide/metformin, Actoplus Met, pioglitazone/metformin, Actoplus Met XR, repaglinide/metformin, Invokamet, Invokamet XR, Synjardy, Synjardy XR, 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, Onglyza, Kombiglyze XR, Tradjenta, Jentadueto, Jentadueto XR, Nesina, alogliptin, Kazano, alogliptin/metformin, Oseni, alogliptin/pioglitazone

## 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, Glucophage, Glucophage XR, Glumetza, Riomet, metformin oral solution, Riomet ER, metformin extended-release (generics to Fortamet and Glumetza), glyburide/metformin, glipizide/metformin, Actoplus Met, pioglitazone/metformin, Actoplus Met XR, repaglinide/metformin, Invokamet, Invokamet XR, Synjardy, Synjardy XR, 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, Onglyza, Tradjenta, Nesina or alogliptin) 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; November 2021.
2. Janumet® XR tablets [prescribing information]. Whitehouse Station, NJ: Merck; November 2021.
3. Januvia® tablets [prescribing information]. Whitehouse Station, NJ: Merck; December 2020.
4. Jentadueto® tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; April 2022.
5. Jentadueto® XR tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; October 2021.
6. Kazano™ tablets [prescribing information]. Lexington, MA: Takeda; March 2022.
7. Kombiglyze® XR tablets [prescribing information]. Wilmington, DE: AstraZeneca; July 2019.
8. Nesina® tablets [prescribing information]. Lexington, MA: Takeda; March 2022.
9. Onglyza® tablets [prescribing information]. Wilmington, DE: AstraZeneca; June 2019.
10. Oseni™ tablets [prescribing information]. Lexington, MA: Takeda; March 2022.
11. Tradjenta® tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; April 2022.
12. American Diabetes Association. Standards of medical care in diabetes – 2022. *Diabetes Care*. 2022;45(Suppl 1):S1-S258.

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13. Garber AJ, Handelsman Y, Grunberger G, et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 diabetes management algorithm – 2020 executive summary. *Endocr Pract.* 2020 Jan;26(1):107-139.
14. Metformin tablets [prescribing information]. Raleigh, NC: Indicus Pharma; June 2020.

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