Cigna National Preferred Formulary Coverage Policy

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Step Therapy
Diabetes – Dipeptidyl Peptidase-4 Inhibitors

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Related Coverage Resources

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. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

NPF Coverage Policy

Drugs Affected
• Janumet® (sitagliptin/metformin tablets)
• Janumet® XR (sitagliptin/metformin extended-release tablets)
• Januvia® (sitagliptin tablets)
• Jentadueto® (linagliptin/metformin tablets)
• Jentadueto® XR (linagliptin/metformin extended-release tablets)
• Kazano™ (alogliptin/metformin tablets generics)
• Kombiglyze™ XR (saxagliptin/metformin extended-release tablets)
• Nesina® (alogliptin tablets, generics)
• Onglyza® (saxagliptin tablets)
• Oseni™ (alogliptin/pioglitazone tablets, authorized generic)
• Tradjenta® (linagliptin tablets)

This step therapy program encourages the use of metformin (brand or generic) or a metformin-containing combination product (brand or generic) prior to the use of Januvia, Janumet, Janumet XR, Onglyza, Kombiglyze XR, Tradjenta, Jentadueto, Jentadueto XR, Nesina, Kazano, or Oseni. If the step therapy rule is not met, coverage will be determined by step therapy criteria below.

Step 2: Januvia, Janumet, Janumet XR, Onglyza, Kombiglyze XR, Tradjenta, Jentadueto, Jentadueto XR, Nesina, alogliptin, Kazano, alogliptin/metformin, Oseni, alogliptin/pioglitazone.

Cigna covers Step 2 agents as medically necessary when the following criteria are met:

1. If the individual has tried metformin or a metformin-containing combination product (brand or generic) in the past, then authorization for a Step 2 product may be given.

2. If the individual is already started on a DPP-4 inhibitor, approve a Step 2 product.

3. If the individual is initiating dual (combination) therapy with Januvia, Onglyza, Tradjenta, Nesina or alogliptin AND metformin, then authorization may be given for Januvia, Onglyza, Tradjenta, Nesina, or alogliptin without a trial of metformin.

4. If the individual has a contraindication to metformin, according to the prescriber, then authorization for Januvia, Onglyza, Tradjenta, Nesina, or alogliptin may be given without a trial of metformin.
   (Note: Examples of contraindications to metformin include acute or chronic metabolic acidosis, including diabetic ketoacidosis).

Conditions Not Covered

Any other exception is considered not medically necessary.

Background

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 in adjunct to diet and exercise. Various combination products are available which combine DPP-4 inhibitors with metformin, sodium glucose co-transporter-2 (SGLT-2) inhibitors, and/or thiazolidinediones (TZDs).

Guidelines
The American Diabetes Association Standards of Care (2020) recommend metformin as initial therapy for most patients with type 2 diabetes, unless contraindications to metformin are present. 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. 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 a progressive disease in many patients, combination therapy may be needed for many patients over time to achieve glycemic targets. Other guidelines have similar recommendations.

Safety
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. There have been post-marketing cases of metformin-associated lactic acidosis, including fatal cases. Metformin decreases liver uptake of lactate, increasing lactate blood levels which may increase the risk of lactic acidosis, especially in patients at risk. Hypoxic states (e.g., acute congestive heart failure, cardiovascular collapse, acute myocardial infarction, sepsis), excessive alcohol intake, and hepatic impairment are noted in the metformin prescribing information among the risk factors for development of lactic acidosis.
References

4. Jentadueto® tablets [prescribing information]. Ridgefield, CT and Indianapolis, IN: Boehringer Ingelheim/Eli Lilly; July 2019.
5. Jentadueto® XR tablets [prescribing information]. Ridgefield, CT and Indianapolis, IN: Boehringer Ingelheim/Eli Lilly; July 2019.
11. Tradjenta® tablets [prescribing information]. Ridgefield, CT and Indianapolis, IN: Boehringer Ingelheim/Eli Lilly; July 2019.

Last Revision Details

| Annual revision | Riomet ER added to Step 1. | “Prescribing physician” changed to “prescriber” throughout criteria. | Note added to provide example of metformin contraindications. | 04/15/2020 |

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