



Coverage Policy Number NPF049

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 Medical Necessity

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, authorized generic)
- Onglyza® (saxagliptin tablets)
- Oseni™ (alogliptin/pioglitazone tablets, authorized generic)
- Tradjenta® (linagliptin tablets)

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.

Step 1: metformin, metformin extended-release, Glucophage, Glucophage XR, Glumetza, Fortamet, Riomet, metformin oral solution, Riomet ER, Avandamet, Actoplus Met, pioglitazone/metformin, Actoplus Met XR, Glucovance, metformin/glyburide, Prandimet, repaglinide/metformin, metformin/glipizide, Invokamet, Invokamet XR, Synjardy, Synjardy XR, Xigduo XR, Segluromet

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 one Step 1 Product, approve a Step 2 Product.
2. If the individual is already started on a dipeptidyl peptidase-4 (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, approve a single-entity DPP-4 inhibitor.
4. If the individual 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).

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 as adjuncts to diet and exercise.¹⁻¹¹ 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 (2020) recommend metformin as initial therapy for most patients with type 2 diabetes, unless contraindications to metformin are present.¹² 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.¹³

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.¹⁴ 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 as among the risk factors for development of lactic acidosis.

References

1. Janumet® tablets [prescribing information]. Whitehouse Station, NJ: Merck; August 2019.
2. Janumet® XR tablets [prescribing information]. Whitehouse Station, NJ: Merck; August 2019.
3. Januvia® tablets [prescribing information]. Whitehouse Station, NJ: Merck; August 2019.
4. Jentadueto® tablets [prescribing information]. Ridgefield, CT and Indianapolis, IN: Boehringer Ingelheim/Eli Lilly; July 2019.
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6. Kazano™ tablets [prescribing information]. Deerfield, IL: Takeda; July 2019.
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8. Nesina® tablets [prescribing information]. Deerfield, IL: Takeda; June 2019.
9. Onglyza® tablets [prescribing information]. Wilmington, DE: AstraZeneca; June 2019.
10. Oseni™ tablets [prescribing information]. Deerfield, IL: Takeda; June 2019.
11. Tradjenta® tablets [prescribing information]. Ridgefield, CT and Indianapolis, IN: Boehringer Ingelheim/Eli Lilly; July 2019.
12. American Diabetes Association. Standards of medical care in diabetes – 2020. *Diabetes Care*. 2020;43(Suppl 1):S1-S212. Available at: https://care.diabetesjournals.org/content/43/Supplement_1. Accessed on March 18, 2020.
13. Garber AJ, Abrahamson MJ, Barzilay JI, et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 diabetes management algorithm – 2019 executive summary. *Endocr Pract*. 2019;25(1):69-100. Available at: <https://www.aace.com/sites/all/files/diabetes-algorithm-executive-summary.pdf>. Accessed on: March 18, 2020.
14. Glucophage® and Glucophage® XR [prescribing information]. Princeton, NJ: Bristol-Meyers Squibb; May 2018.

Revision History

Type of Revision	Summary of Changes	Review Date
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
Selected Revision	Metformin oral solution added to Step 1. Additionally, the policy statement was clarified to note that all components of automation involve a 130-day look-back period.	02/10/2021

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