

Dipeptidyl Peptidase-4 (DPP-4) Inhibitors, DPP-4 Inhibitor/Metformin Combination Drugs

Policy # 00306

Original Effective Date: 05/22/2013

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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider Onglyza^{®‡} (saxagliptin), Kombiglyze^{®‡} XR (saxagliptin/metformin extended release), branded Alogliptin, Nesina (alogliptin), branded Alogliptin/Metformin, Kazano^{®‡} (alogliptin/metformin), generic saxagliptin tablets, generic saxagliptin/metformin extended release tablets, Zituvio^{®‡} (sitagliptin), branded Sitagliptin tablets, branded Sitagliptin/Metformin tablets, branded Sitagliptin/Metformin extended release tablets, Zituvimet^{®‡} (sitagliptin/metformin), Zituvimet^{®‡} XR (sitagliptin/metformin extended release), or Brynovin^{™‡} (sitagliptin solution) to be **eligible for coverage**** when the patient selection criteria for the selected drug are met:

Patient Selection Criteria

Coverage eligibility will be considered for Onglyza (saxagliptin), Kombiglyze XR (saxagliptin/metformin extended release), branded Alogliptin, Nesina (alogliptin), branded Alogliptin/Metformin, Kazano (alogliptin/metformin), generic saxagliptin tablets, generic saxagliptin/metformin extended release tablets, Zituvio (sitagliptin), branded Sitagliptin tablets, branded Sitagliptin/Metformin tablets, branded Sitagliptin/Metformin extended release tablets, Zituvimet (sitagliptin/metformin), Zituvimet XR (sitagliptin/metformin extended release), and Brynovin (sitagliptin solution) when their respective criteria are met:

- For Onglyza, Kombiglyze XR, branded Alogliptin, Nesina, branded Alogliptin/Metformin, Kazano, generic saxagliptin tablets, generic saxagliptin/metformin extended release tablets, Zituvio, branded Sitagliptin tablets, branded Sitagliptin/Metformin tablets, branded Sitagliptin/Metformin extended release tablets, Zituvimet (sitagliptin/metformin), and Zituvimet XR requests:
 - There is clinical evidence or patient history that suggests the use of Januvia^{®‡} (sitagliptin), Janumet^{®‡} (sitagliptin/metformin), Janumet^{®‡} XR (sitagliptin/metformin extended release), Tradjenta^{®‡} (linagliptin), Jentadueto^{®‡}

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(linagliptin/metformin), or Jentadueto^{®†} XR (linagliptin/metformin extended release) will be/was ineffective or will/did cause an adverse reaction to the patient.

*Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

- For Bynovin requests:
 - Patient has a diagnosis of type 2 diabetes mellitus; AND
 - Patient is 18 years of age or older; AND
 - Patient meets BOTH of the following:
 - Patient is unable to swallow tablets and/or capsules (e.g., has dysphagia or has a gastrostomy tube [G-tube]); AND
 - Patient is not currently taking any medication in tablet or capsule form.

*Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Onglyza (saxagliptin), Kombiglyze XR (saxagliptin/metformin extended release), branded Alogliptin, Nesina (alogliptin), branded Alogliptin/Metformin, Kazano (alogliptin/metformin), generic saxagliptin tablets, generic saxagliptin/metformin extended release tablets, Zituvio (sitagliptin), branded Sitagliptin tablets, branded Sitagliptin/Metformin tablets, branded Sitagliptin/Metformin extended release tablets, Zituvimet (sitagliptin/metformin), or Zituvimet XR (sitagliptin/metformin extended release) WITHOUT clinical evidence or patient history that suggests the use of Januvia (sitagliptin), Janumet (sitagliptin/metformin), Janumet XR (sitagliptin/metformin extended release), Tradjenta (linagliptin), Jentadueto (linagliptin/metformin), or Jentadueto XR (linagliptin/metformin extended release) will be/was ineffective or will/did cause an adverse reaction to the patient to be **not medically necessary.****

Based on review of available data, the Company considers the use of Brynovin (sitagliptin solution) when the patient is able to swallow tablets and/or capsules AND is currently taking any medication in tablet or capsule form to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Brynovin (sitagliptin solution) when patient selection criteria are not met to be **investigational*** (with the exception of the criterion denoted above as **not medically necessary****).

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Schematic

Class	Preferred	Non-Preferred
DPP-4 Inhibitors, DPP-4 Inhibitor/Metformin Combination Products	Januvia Janumet Janumet XR Tadjenta Jentadueto Jentadueto XR	Onglyza Kombiglyze XR Branded Alogliptin Nesina Branded Alogliptin/Metformin Kazano Generic saxagliptin Generic saxagliptin/metformin ER Zituvio Branded Sitagliptin Branded Sitagliptin/Metformin Branded Sitagliptin/Metformin ER Zituvimet Zituvimet XR Brynovin

Background/Overview

Dipeptidyl peptidase-4 inhibitors and DPP-4 inhibitor combination drugs are indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.

The active ingredients in the non-preferred products have not been studied head to head versus the preferred products, and therefore no superiority claims can be made between preferred and non-preferred products.

Brynovin is a branded oral solution formulation of sitagliptin, indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Brynovin was approved by the Food & Drug Administration (FDA) via the 505(b)(2) pathway relying on safety and efficacy information with sitagliptin tablets to support approval. It is supplied at a concentration of 25 mg/mL with a recommended dosage of 100 mg (4 mL) taken orally once daily. Renal dosing adjustments for Brynovin are described in the FDA-approved prescribing information and should be followed as indicated.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

All of these products are indicated for the treatment of type 2 diabetes mellitus.

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Based on a review of the available data and in the absence of any of the caveats mentioned, there is no advantage of using Onglyza (saxagliptin), Kombiglyze XR (saxagliptin/metformin extended release), branded Alogliptin, Nesina (alogliptin), branded Alogliptin/Metformin, Kazano (alogliptin/metformin), generic saxagliptin tablets, generic saxagliptin/metformin extended release tablets, Zituvio (sitagliptin), Zituvimet (sitagliptin/metformin), Zituvimet XR (sitagliptin/metformin extended release), branded Sitagliptin tablets, branded Sitagliptin/Metformin tablets, or branded Sitagliptin/Metformin extended release tablets over Januvia (sitagliptin), Janumet (sitagliptin/metformin), Janumet XR (sitagliptin/metformin extended release), Tradjenta (linagliptin), Jentadueto (linagliptin/metformin), or Jentadueto XR (linagliptin/metformin extended release).

The patient selection criteria for Brynovin (sitagliptin solution) are intended to ensure FDA-approved label usage and to take into consideration whether the patient is able to take medications in tablet or capsule form. Based on a review of the available data, if the above mentioned criteria are not met, there is no advantage to the use of this product over the traditional dosage forms.

References

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5. Janumet tablets [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; February 2013.
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9. Kazano tablets [package insert]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; January 2013.
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Policy History

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05/02/2013	Medical Policy Committee review
05/22/2013	Medical Policy Implementation Committee approval. New policy.
05/01/2014	Medical Policy Committee review
05/21/2014	Medical Policy Implementation Committee approval. No change to coverage.
10/02/2014	Medical Policy Committee review
10/15/2014	Medical Policy Implementation Committee approval. Implemented a PA for non-preferred products to use preferred products, which are Januvia, Janumet, Janumet XR, Onglyza, and Kombiglyze XR.
10/08/2015	Medical Policy Committee review.
10/21/2015	Medical Policy Implementation Committee approval. Considering other preferred products within next few months based on more updated modeling discussions. Will update policy in February 2016 with decisions. Will halt posting until that point.
02/04/2016	Medical Policy Committee review
02/17/2016	Medical Policy Implementation Committee approval. No change to coverage. Will not change preferred products.
06/30/2016	Medical Policy Committee review
07/20/2016	Medical Policy Implementation Committee approval. Added branded Alogliptin, branded Alogliptin/Metformin, Alogliptin/Pioglitazone and Jentadueto XR to the policy.
10/06/2016	Medical Policy Committee review
10/19/2016	Medical Policy Implementation Committee approval. Moving Onglyza and Kombiglyze ER to non-preferred. Moving Tradjenta and Jentadueto/XR to preferred.
10/05/2017	Medical Policy Committee review
10/18/2017	Medical Policy Implementation Committee approval. No change to coverage.
10/04/2018	Medical Policy Committee review
10/17/2018	Medical Policy Implementation Committee approval. Added "metformin" to the title. Removed the step therapy only and step therapy/prior authorization sections. Updated schematic. Updated background info/rationale.
10/03/2019	Medical Policy Committee review
10/09/2019	Medical Policy Implementation Committee approval. No change to coverage.
10/01/2020	Medical Policy Committee review
10/07/2020	Medical Policy Implementation Committee approval. No change to coverage.
10/07/2021	Medical Policy Committee review
10/13/2021	Medical Policy Implementation Committee approval. No change to coverage.
10/06/2022	Medical Policy Committee review
10/11/2022	Medical Policy Implementation Committee approval. No change to coverage.
10/05/2023	Medical Policy Committee review
10/11/2023	Medical Policy Implementation Committee approval. Added generic saxagliptin tablets and generic saxagliptin/metformin ER tablets to the policy.

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03/07/2024	Medical Policy Committee review
03/13/2024	Medical Policy Implementation Committee approval. Added Zituvio to the policy.
09/05/2024	Medical Policy Committee review
09/11/2024	Medical Policy Implementation Committee approval. Added brand Sitagliptin tablets and brand Sitagliptin/Metformin tablets to the policy.
02/06/2025	Medical Policy Committee review
02/12/2025	Medical Policy Implementation Committee approval. Added Zituvimet and Zituvimet XR to the policy.
11/06/2025	Medical Policy Committee review
11/12/2025	Medical Policy Implementation Committee approval. Added the new product, Sitagliptin/Metformin ER to the policy.
03/05/2026	Medical Policy Committee review
03/11/2026	Medical Policy Implementation Committee approval. Added the new product, Brynovin to the policy with relevant criteria. Background section updated.

Next Scheduled Review Date: 03/2027

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

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For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan’s authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan’s pharmacy benefit.