BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 11/17/16**
SECTION: DRUGS	**LAST REVIEW DATE: 11/16/17**
	LAST CRITERIA REVISION DATE: 11/16/17
	ARCHIVE DATE:

NESINA™ (alogliptin benzoate) oral tablet and ALOGLIPTIN BENZOATE oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

NESINA™ (alogliptin benzoate) oral tablet and ALOGLIPTIN BENZOATE oral tablet (cont.)

Description:

Nesina (alogliptin benzoate) tabs and generic alogliptin benzoate tabs are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. They are not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis. Alogliptin is a selective dipeptidyl peptidase-4 (DPP-4) inhibitor.

Several recent guidelines on treatment of type 2 diabetes mellitus have been published. Each guideline analyzes the current literature and makes recommendations on treatment based on the strength of the clinical evidence and incorporates expert opinion. Each guideline suggests that a patient centered approach should be implemented in the treatment of type 2 diabetes mellitus that takes into account multiple factors such as medication effectiveness and safety, patient preferences, patient co-morbidities, and cost of medication to name a few.

The guidelines suggest Metformin as the generally accepted first line single agent for treatment. When monotherapy does not achieve or maintain target hemoglobin (Hbg)-A1C, the guidelines recommend adding another agent. However, due to limited comparative studies and limited long-term information, uniform agreement on the best agent to combine with Metformin was not stated by the guidelines. Potential second line therapy includes selection of an agent from one of the following categories; a sulfonylurea, a meglitinide, a thiazolidindione, a dipeptidyl peptidase-4 inhibitor, a glucagon-like peptide-1 agonist, or an alpha glucosidase inhibitor. The guidelines state selection of one of these agents should take into account other patient variables to implement a patient centered approach to therapy. Insulin may be added at any point, especially when serum glucose levels are substantially elevated and/or the individual has significant hyperglycemic symptoms.

In response to meal, incretin hormones such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) are released into the bloodstream from the small intestine. These hormones cause insulin release from the pancreatic beta cells in a glucose-dependent manner but are inactivated by the dipeptidyl peptidase-4 (DPP-4) enzyme within minutes. GLP-1 also lowers glucagon secretion from pancreatic alpha cells, reducing hepatic glucose production. In patients with type 2 diabetes, concentrations of GLP-1 are reduced but the insulin response to GLP-1 is preserved.

Alogliptin is a DPP-4 inhibitor that slows the inactivation of the incretin hormones, thereby increasing their bloodstream concentrations and reducing fasting and postprandial glucose concentrations in a glucose-dependent manner in patients with type 2 diabetes mellitus. Alogliptin selectively binds to and inhibits DPP-4 but not DPP-8 or DPP-9 activity *in vitro* at concentrations approximating therapeutic exposures. There are no clinical trials that have demonstrated a superior benefit of a DPP-4 inhibitor over Metformin and there is no evidence that one DPP-4 inhibitors is more effective than another.

Nesina (alogliptin benzoate)
Alogliptin benzoate

Medication class:
Antidiabetic agent, dipeptidyl peptidase 4 (DPP-4) inhibitor

NESINA™ (alogliptin benzoate) oral tablet and ALOGLIPTIN BENZOATE oral tablet (cont.)

FDA-approved indication(s):
- An adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus as monotherapy or combination therapy.

Recommended Dose:
- 25 mg once daily

Maximum dosage
- 25 mg once daily

Available Dosage Forms:
- 6.25 mg, 12.5 mg, and 25 mg tablets

Limitations of use:
- It is not indicated for the treatment of type 1 diabetes or diabetic ketoacidosis

Warnings and Precautions:
- With moderate renal impairment (CrCl 30- 59 mL/min) the dose is 12.5 mg once daily
- With severe renal impairment (CrCl < 30 mL/min) or ESRD (CrCl < 15 mL/min or HD) the dose is 6.25 mg once daily
- If have confirmed liver injury from use of alogliptin, stop alogliptin
- Should not be used if there are confirmed liver abnormalities and no etiology can be found
- Discontinue if pancreatitis is suspected
- If heart failure develops, treat according to standard of care and consider stopping alogliptin
- If serious hypersensitivity develops, stop alogliptin and initiate alternative treatment for diabetes
- If bullous pemphigoid is suspected stop alogliptin
- Alogliptin has not been shown to be safe and effective in treatment of pre-diabetes, prevention of diabetes, weight loss, metabolic syndrome, or polycystic ovary syndrome

Criteria:

- **Criteria for initial therapy:** Nesina (alogliptin benzoate) and alogliptin benzoate is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual is 18 years of age or older
  2. A confirmed diagnosis of type 2 diabetes mellitus
  3. Failed to obtain adequate glycemic control on diabetes diet and exercise program
  4. Individual has failure, contraindication or intolerance to **metformin PLUS either Onglyza or Januvia**:
  5. There are **NO** contraindications:
     - History of a serious hypersensitivity reaction to alogliptin-containing products, such as anaphylaxis, angioedema or severe cutaneous adverse reactions

NESINA™ (alogliptin benzoate) oral tablet and ALOGLIPTIN BENZOATE oral tablet (cont.)

Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** Nesina (alogliptin benzoate) and alogliptin benzoate is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual's condition has not worsened while on therapy
    - Worsening is defined as:
        - Hemoglobin A1C is > 7%, fasting plasma glucoses are > 130 mg/dL, 2-hour postprandial glucose are > 180, has gained weight

2. Individual has been adherent with the medication **and** diabetes diet and exercise

3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
    - Contraindications or adverse effect:
        - Acute Pancreatitis
            - Signs & symptoms may include: persistent, severe abdominal pain sometimes radiating to the back, may have vomiting
        - Liver injury
            - Signs & symptoms may include: fatigue, anorexia, right upper quadrant pain or discomfort, dark urine or jaundice
        - Heart failure
            - Signs & symptoms may include: shortness of breath, weight gain, swelling of feet, ankles, or legs
        - Hypersensitivity
            - Signs & symptoms may include: swelling of face, lips, throat, difficulty swallowing or breathing, rash, hives, itching,
        - Bullous pemphigoid
            - Signs & symptom may include: blisters or erosions

4. There are no significant interacting drugs

Renewal duration: 12 months

Resources:

Nesina. Package Insert. Revised by manufacturer 5/2016. Accessed 9/16/16.

2009 National Institute for Health and Clinical Excellence: Type 2 diabetes: newer agents for blood glucose control in type 2 diabetes. Available from www.nice.org.uk/CG87ShortGuideline

2010 National Institute for Health and Care Excellence: The management of Type 2 diabetes. NICE clinical guideline 87

2012 Diabetes Care: Management of hyperglycemia in Type 2 diabetes: A patient-centered approach. Position Statement of the American Diabetes Association and the European Association for the Study of Diabetes

Canadian Diabetes Association Clinical Practice Guidelines Expert Committee: Canadian Diabetes Association 2013 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. Can J Diabetes 2013; 37 (Suppl 1): S1-S212

2016 American Diabetes Association. Approaches to glycemic treatment. Section 7. In Standards of Medical Care in Diabetes. Diabetes Care 2016; 39 (Suppl 1):S52-S59

Chamberlain JJ, Rhinehart AS, Shaefer CF, and Neuman A. Diagnosis and Management of Diabetes: Synopsis of the 2016 American Diabetes Association Standard of Medical care in Diabetes. Ann Intern Med doi:10.7326/M15-3016 www.annals.org

UpToDate: Dipeptidyl peptidase-4 (DPP-4) inhibitors for the treatment of type 2 diabetes mellitus. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/dipeptidyl-peptidase-4-dpp-4-inhibitors-for-the-treatment-of-type-2-diabetes-mellitus?source=search_result&search=diabetes%20mellitus%20type%202&selectedTitle=1~150#H1205101

UpToDate: Initial management of blood glucose in adults with type 2 diabetes mellitus. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/initial-management-of-blood-glucose-in-adults-with-type-2-diabetes-mellitus?source=search_result&search=diabetes%20mellitus%20type%202&selectedTitle=2~150#H22

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:		Dosage Form:
Directions for Use:	Quantity:	Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.