LOUISIANA BLUE

Voquezna® (vonoprazan)

Policy # 00878
Original Effective Date: 07/08/2024
Current Effective Date: 12/09/2024

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.

Note: Voquezna®‡ Dual Pak®‡ (vonoprazan fumarate, amoxicillin) and Voquezna®‡ Triple Pak®‡ (vonoprazan fumarate, amoxicillin, clarithromycin) are addressed separately in medical policy 00745 Select Combination Products for the Treatment of H. pylori Infection.

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.*

Erosive Esophagitis

Based on review of available data, the Company may consider Voquezna®‡ (vonoprazan) for the treatment of erosive esophagitis to be **eligible for coverage**** when the patient selection criteria are met:

Patient Selection Criteria

Coverage eligibility will be considered for Voquezna (vonoprazan) for the treatment of erosive esophagitis when the following criteria are met:

- Patient has a diagnosis of erosive esophagitis; AND
- Patient is using for healing or maintenance of healing of erosive esophagitis; AND
- Patient is greater than or equal to 18 years of age; AND
- Patient is *H. pylori* negative; AND
  *(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)*
- Patient has tried and failed (e.g., intolerance or inadequate response) at least TWO of the following generic proton pump inhibitors: esomeprazole, lansoprazole, pantoprazole, or rabeprazole unless there is clinical evidence or patient history that suggests the use of these agents will be ineffective or 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)*

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Non-Erosive Gastroesophageal Reflux Disease

Based on review of available data, the Company may consider Voquezna (vonoprazan) for the treatment of non-erosive gastroesophageal reflux disease to be **eligible for coverage**** when the patient selection criteria are met:

Patient Selection Criteria

Coverage eligibility will be considered for Voquezna (vonoprazan) for the treatment of non-erosive gastroesophageal reflux disease when the following criteria are met:

- Patient has a diagnosis of non-erosive gastroesophageal reflux disease (non-erosive GERD); AND
- Patient is using for relief of heartburn associated with non-erosive GERD; AND
- Patient is greater than or equal to 18 years of age; AND
- Patient is *H. pylori* negative; AND
  *(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)*
- Patient has tried and failed (e.g., intolerance or inadequate response) at least TWO of the following generic proton pump inhibitors: esomeprazole, lansoprazole, pantoprazole, or rabeprazole unless there is clinical evidence or patient history that suggests the use of these agents will be ineffective or cause an adverse reaction to the patient; AND
  *(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)*
- Dose of the requested medication will not exceed 10 mg daily.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Voquezna (vonoprazan) when the patient is not *H. pylori* negative and has not tried and failed at least TWO of the following generic proton pump inhibitors: esomeprazole, lansoprazole, pantoprazole, or rabeprazole 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 Voquezna (vonoprazan) when patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

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Background/Overview

Vonoprazan was first approved by the FDA in May of 2022 in combination with antibiotics for the treatment of *H. pylori* infection in adults and marketed as Voquezna Dual Pak and Voquezna Triple Pak. In November of 2023, Voquezna (vonoprazan) 10 mg and 20 mg tablets were approved by the FDA as the first-in-class potassium-competitive acid blocker (P-CAB) indicated for the treatment of erosive esophagitis (EE), also referred to as erosive GERD. The recommended dose of Voquezna tablets for healing of EE is 20 mg once daily for 8 weeks and 10 mg once daily for up to 6 months for maintenance of healed EE. In July of 2024, Voquezna 10 mg tablets received approval for relief of heartburn associated with non-erosive gastroesophageal reflux disease (non-erosive GERD or NERD) in adult patients. The recommended dose for relief of heartburn associated with non-erosive GERD is 10 mg once daily for 4 weeks.

Gastroesophageal reflux disease (GERD) is a condition that develops when the reflux of gastric contents into the esophagus causes symptoms and/or complications. The diagnosis of GERD is based on a combination of clinical symptoms, endoscopic evaluation of the esophageal mucosa, reflux monitoring, and the patient's response to therapeutic intervention. Typical symptoms of GERD include heartburn and regurgitation. However, atypical symptoms, referred to as extraesophageal symptoms, may occur and can include cough, laryngeal hoarseness, dysphonia, pulmonary fibrosis, asthma, dental erosions/caries, sinus disease, ear disease, post-nasal drip, and throat clearing. Classification of GERD as erosive esophagitis, non-erosive GERD, or Barrett's esophagus (BE) is based upon the appearance of the esophageal mucosa on upper endoscopy. Erosive esophagitis is distinguished by endoscopically visible erosions or ulcerations in the distal esophageal mucosa with or without symptoms of GERD, while non-erosive GERD is characterized by clinical symptoms of GERD without visible esophageal mucosal damage. Approximately 20% of the U.S. adult population has GERD; of those, 60%–70% are diagnosed with non-erosive GERD, 30% with EE, and 6%–12% with Barrett's disease. Inadequately treated EE may progress to more severe disease, including BE and esophageal cancer. The severity of EE is graded A, B, C, or D based on the extent of mucosal abnormalities using the Los Angeles (LA) esophagitis classification system. Treatment options for GERD include lifestyle and dietary modifications, weight management, proton pump inhibitor (PPI) therapy, and adjunctive pharmacotherapy when appropriate. For several decades, first-line pharmacological treatment for EE has been proton pump inhibitors. However, it is estimated that up to 30% of patients with severe EE do not experience complete healing, and 12 months after healing of EE, recurrence occurs in approximately 10%–45% of patients, despite PPI therapy. Long-term maintenance treatment is recommended for patients with severe EE, defined as those with LA Grade C or D disease, because they are likely to relapse and have complications once therapy is discontinued.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Voquezna was FDA approved in November of 2023 for healing of all grades of erosive esophagitis and relief of heartburn associated with erosive esophagitis in adults and to maintain healing of all grades of erosive esophagitis and relief of heartburn associated with erosive esophagitis in adults. In July of 2024, Voquezna received FDA approval for the relief of heartburn associated with non-erosive gastroesophageal reflux disease in adults.

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 federal regulations, other plan medical policies, and accredited national guidelines.

Erosive Esophagitis

The effectiveness and safety of Voquezna were evaluated in a randomized, active-controlled, double-blind, eight-week study (PHALCON-EE) in 1,024 adult patients in the United States and Europe with endoscopically confirmed EE. Patients were randomized to receive treatment with Voquezna 20 mg once daily or lansoprazole 30 mg once daily for 2 to 8 weeks. Patients who were positive for *H. pylori* infection, diagnosed with Barrett's esophagus, and/or had definite dysplastic changes in the esophagus at baseline were excluded from the study. Healing of EE was assessed at week 2 and week 8, and resolution of heartburn symptoms was evaluated daily over the 8-week period. If endoscopic healing of EE was confirmed at week 2, the patient entered the maintenance phase of the study. If endoscopic healing was not confirmed at week 2, the patient continued to receive randomized treatment until Week 8, and only patients with confirmed endoscopic healing entered the maintenance phase. The primary endpoint was endoscopically confirmed complete healing of all grades of erosive esophagitis at week 2 or week 8. The percentage of 24-hour heartburn-free days through week 8 was evaluated as a secondary endpoint. Voquezna 20 mg once daily was associated with a healing rate of 93% compared with 85% for lansoprazole ($P < 0.0001$) at week 2 or week 8, demonstrating noninferiority of Voquezna. Secondary endpoint analysis of complete healing of erosive esophagitis at week 2 demonstrated superiority in the subgroup of patients with LA Grade C or D disease with 70% of Voquezna treated patients and 53% of lansoprazole treated patients achieving healing. Complete healing of erosive esophagitis at either week 2 or week 8 in the subgroup of patients with LA Grade C or D disease was 92% in patients treated with Voquezna and 72% in patients treated with lansoprazole; however, this endpoint was not statistically significant under the prespecified multiple testing procedure. Voquezna 20 mg demonstrated non-inferiority to lansoprazole in percentage of 24-hour heartburn-free days during the healing phase (mean heartburn-free days for Voquezna treated group, 66.8% vs. lansoprazole treated patients, 64.1%). Patients who completed the healing phase of the EE study and showed endoscopically confirmed healed erosive esophagitis at week 2 or week 8 were re-randomized in the maintenance phase 1:1:1 to either Voquezna 10 mg once daily, a higher dosage of Voquezna, or

lansoprazole 15 mg once daily. Maintenance of healing and resolution of heartburn symptoms were evaluated over 24 weeks. The primary endpoint was maintenance of healed erosive esophagitis (all grades) through week 24. A secondary endpoint was maintenance of healed erosive esophagitis in the subgroup of patients with LA Grade C or D disease prior to randomization in the healing phase of the study. The higher Voquezna dose group did not demonstrate additional treatment benefit compared to Voquezna 10 mg once daily; therefore, only the 10 mg dose was approved for maintenance of healing of EE. Both doses of Voquezna were found to be noninferior and superior to lansoprazole for maintaining complete healing of EE through 24 weeks. Analyses of secondary end points showed both doses of Voquezna were superior to lansoprazole for maintenance of healing in LA Grade C/D esophagitis. Voquezna 10 mg demonstrated non-inferiority vs. lansoprazole for percentage of 24-hour heartburn-free days through week 24. The rates of adverse events for Voquezna were comparable to lansoprazole in this trial.

Other Healing of Erosive Esophagitis Studies

Two additional randomized, active-controlled, double-blind studies conducted outside of the United States also demonstrated non-inferiority of Voquezna 20 mg once daily compared to lansoprazole 30 mg once daily for the primary endpoint of healing of all grades of erosive esophagitis by Week 8.

Other Maintenance of Healed Erosive Esophagitis Studies

Two additional randomized, active-controlled, double-blind studies conducted outside of the United States also demonstrated non-inferiority of Voquezna 10 mg once daily compared to lansoprazole 15 mg once daily for the primary endpoint of maintenance of healed erosive esophagitis (all grades) through Week 24.

Non-Erosive GERD

Voquezna was evaluated in a randomized, placebo-controlled, double-blind, four-week efficacy trial with a 20-week safety extension conducted in the United States in 772 adult patients with a diagnosis of symptomatic non-erosive GERD. Patients who identified heartburn as their primary symptom, had a history of heartburn for six months or longer, had heartburn on at least four of seven days immediately prior to randomization, were negative for *H. pylori* infection, and had no esophageal erosions as confirmed by endoscopy were enrolled. Patients were randomized 1:1:1 to one of the following treatment groups in the 4-week placebo-controlled phase: Voquezna 10 mg once daily, a higher dosage of Voquezna, or placebo once daily. The higher Voquezna dose group did not demonstrate additional treatment benefit compared to Voquezna 10 mg once daily through Week 4. The primary endpoint was the percentage of 24-hour heartburn-free days, as assessed by daily diary over 4 weeks. The percentage of 24-hour heartburn-free days was 28% for placebo versus 45% for Voquezna 10 mg (least squares mean difference, 17.1%; $P < .0001$) and 44.4% for Voquezna 20 mg (least squares mean difference, 16.7%; $P < .0001$). The difference in the percentage of patients who were heartburn-free during the 24- hour period on Day 2 of treatment was similar to the difference in 24-hour heartburn free days through Week 4 in patients treated with Voquezna 10 mg once daily compared to patients treated with placebo.

References

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2. Katz P. et al, ACG clinical guideline for the diagnosis and management of gastroesophageal reflux disease. *Am J Gastroenterology*. 2022;117(1):27-56.
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Policy History

Original Effective Date: 07/08/2024
Current Effective Date: 12/09/2024

06/06/2024	Medical Policy Committee review
06/12/2024	Medical Policy Implementation Committee approval. New policy.
11/07/2024	Medical Policy Committee review
11/13/2024	Medical Policy Implementation Committee approval. Added new indication, Non-Erosive GERD, to the policy with associated criteria. Updated background and rationale/source to include new indication.

Next Scheduled Review Date: 11/2025

*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.

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.