PHARMACY COVERAGE GUIDELINE

VOQUEZNA® (vonoprazan)
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Voquezna (vonoprazan) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Gastroenterologist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Healing of all grades of **erosive esophagitis** and relief of heartburn associated with erosive esophagitis

b. Maintain healing of all grades of **erosive esophagitis** and relief of heartburn associated with erosive esophagitis

c. ***Helicobacter pylori* (*H. pylori*) infection** in combination with two antibiotics (based on macrolide resistance and penicillin allergy)

4. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
   a. **For erosive esophagitis** and **ALL** of the following**:**
      i. Endoscopic confirmation of erosive esophagitis
      ii. Los Angeles classification grade C or D (see Definitions section)
      iii. Heartburn symptoms two or more times per week
   b. **For H. pylori**: a positive ^{13}C urea breath test (UBT) for *H. pylori* and **ONE** of the following:
      i. Dyspepsia for at least 2 weeks
      ii. Functional dyspepsia (i.e., dyspepsia from no known cause)
      iii. Recent or new diagnosis of non-bleeding peptic ulcer
      iv. History of peptic ulcer not previously treated for *H. pylori* infection
      v. Requires long-term non-steroidal anti-inflammatory drug treatment using a stable dose

5. **If available:** Individual has failure after adequate trial, contraindication per FDA label or intolerance to a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **ONE** the following:
   a. **For erosive esophagitis/heartburn:**
      i. Two of the following proton pump inhibitors used at two times the standard dosing (see Definitions section):
         1. Dexlansoprazole: 30 mg twice daily
         2. Esomeprazole: 20 mg twice daily
         3. Lansoprazole: 30 mg twice daily
         4. Omeprazole: 20 mg twice daily
         5. Pantoprazole: 40 mg twice daily
         6. Rabeprazole: 20 mg twice daily
   b. **For H. pylori infection:**
      i. Patients **without** risk factors for macrolide resistance **ONE** of the following: (see Definitions section)
         1. A proton pump inhibitor (PPI), amoxicillin, and clarithromycin
         2. A proton pump inhibitor (PPI), metronidazole, and clarithromycin
      ii. Patients **with** risk factors for macrolide resistance (see Definitions section)
         1. A proton pump inhibitor (PPI), metronidazole, tetracycline and bismuth subsalicylate

7. Individual is not currently taking any other drugs which may result in a significant drug interaction requiring discontinuation such as:
   a. Concurrent use with atazanavir or nelfinavir
   b. Moderate or strong CYP3A4 inducers (see Definitions section)

8. Individual does **NOT** have the FDA-label contraindication of concurrent use with Rilpivirine-containing products

9. **For H. pylori infection only**: Requested agent **will not** be used if estimated GFR is less than 30 mL/min

10. **For H. pylori infection only**: Requested agent **will not** be used in moderate to severe hepatic impairment (Child-Pugh Class B and C)

Initial approval duration:
6 months for erosive esophagitis or Barrett's esophagitis
14 days for *H. pylori* infection

- **Criteria for continuation of coverage (renewal request):** Voquezna (vonoprazan) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Gastroenterologist

2. Individual's condition has responded while on therapy with response defined as:
    a. **For erosive esophagitis healing:**
        i. Endoscopic evidence of complete healing
        ii. Increased number of days without heartburn
        iii. Maintains healing and resolution of heartburn symptoms
    b. **For H. pylori:** Renewal requests will be evaluated using criteria from Initial Therapy. Multiple requests for renewal treatment will not be approved and these requests will be forwarded to Utilization Management for review

3. Individual has been adherent with the medication

4. **If available:** Individual has failure after adequate trial, contraindication per FDA label or intolerance, or not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as:
    a. Acute tubulointerstitial nephritis
    b. Severe cutaneous reactions such as Stevens-Johnson syndrome, toxic epidermal necrolysis

6. Individual is not currently taking any other drugs which may result in a significant drug interaction requiring discontinuation, such as:
    a. Concurrent use with atazanavir or nelfinavir
    b. Moderate or strong CYP3A4 inducers (see Definitions section)

Renewal duration:
12 months for erosive esophagitis or Barrett's esophagitis

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- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-Cancer Medications**

  2. **Off-Label Use of Cancer Medications**

Description:

Voquezna (vonoprazan) is a potassium-competitive acid blocker indicated for both healing and to maintain healing of all grades of erosive esophagitis and relief of heartburn associated with erosive esophagitis in adults. Voquezna (vonoprazan) is also indicated for the treatment of *Helicobacter pylori* (*H. pylori*) infection in adults in combination with amoxicillin and clarithromycin or in combination with amoxicillin alone.

Vonoprazan suppresses basal and stimulated gastric acid secretion at the secretory surface of the gastric parietal cell through inhibition of the H+, K+-ATPase enzyme system in a potassium competitive manner. Because this enzyme is regarded as the acid (proton) pump within the parietal cell, vonoprazan has been characterized as a type of gastric proton-pump inhibitor, in that it blocks the final step of acid production. Vonoprazan does not require activation by acid. Vonoprazan may selectively concentrate in the parietal cells in both the resting and stimulated states. Vonoprazan binds to the active pumps in a noncovalent and reversible manner.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Los Angeles Classification of Esophagitis Grading Scale:

LA Grade Classification	
Grade A	One or more mucosal breaks with a length of **no longer** than 5 mm that does not extend between the tops of 2 mucosal folds
Grade B	One or more mucosal breaks with a length of **longer** than 5 mm that does not extend between the tops of 2 mucosal folds
Grade C	One or more mucosal breaks that are continuous between the tops of 2 or more mucosal folds, which involves less than 75% of the circumference
Grade D	One or more mucosal breaks, which involves at least 75% of the circumference
A mucosal break is defined as “an area of slough or erythema with a sharp line of demarcation from adjacent normal mucosa”	

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Definitions of Heartburn Severity (Daytime/Nighttime):

Definitions of Daytime Heartburn Severity (Daytime=Awake Time)	
None	No heartburn
Mild	Occasional heartburn, can be ignored, does not influence daily routine
Moderate	Heartburn cannot be ignored and/or occasionally influences daily routine
Severe	Heartburn present most of day and/or regularly influences daily routine
Very severe	Constant heartburn and/or markedly influences daily routine
Definitions of Nighttime Heartburn Severity (Nighttime=Sleep Time)	
None	No heartburn
Mild	Occasional heartburn, can be ignored, does not influence sleep
Moderate	Heartburn cannot be ignored and/or occasionally influences sleep
Severe	Heartburn present most of night and/or regularly influences sleep
Very severe	Constant heartburn and/or markedly influences sleep

Treatment of Gastroesophageal Reflux Disease in Adults:

Histamine 2 receptor antagonists*	**Low dose (oral)**	**Standard dose (oral)**
Famotidine	10 mg twice daily¶	20 mg twice daily$^{\Delta}$
Nizatidine	75 mg twice daily◊	150 mg twice daily
Cimetidine§	200 mg twice daily¶	400 mg twice daily$^{\Delta}$
Proton pump inhibitors: (H-K) ATPase Pump	**Low dose (oral)**	**Standard dose (oral)**
Dexlansoprazole	Not available	30 mg daily$^{\Delta}$
Esomeprazole	10 mg daily¥	20 mg daily¶
Lansoprazole	15 mg daily¶	30 mg daily
Omeprazole	10 mg daily	20 mg daily¶
Pantoprazole	20 mg daily¶	40 mg daily
Rabeprazole	10 mg daily¥	20 mg daily

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* Histamine 2 receptor antagonists require dose adjustment in the setting of renal insufficiency.

¶ Available without a prescription (over the counter) in the US.

Δ The **daily dose for erosive esophagitis with symptoms of GERD** in the US prescribing information **is up to twice the standard dose shown in this table**.

◇ Strength not available in US. Available elsewhere.

§ Significant drug interactions can occur. When initiating or altering drug therapy, use of a drug interactions database, such as the drug interactions program, is advised. Other histamine 2 receptor antagonists with more favorable adverse effect profiles and fewer drug interactions (e.g., famotidine) are generally preferred.

¥ Dose strength limited to certain dosage forms (e.g., granules for oral suspension or sprinkle capsule). Consult local product availability.

Risk factors for Barrett's esophagus: (**must** have a duration of GERD of at least 5-10 years)

- Age 50 years or older
- Male sex
- White individuals
- Hiatal hernia
- Obesity
- Nocturnal reflux
- Tobacco use (past or current)
- First-degree relative with Barrett's esophagus and/or adenocarcinoma

Alarm features suggestive of a gastrointestinal malignancy:

- New onset of dyspepsia in patient ≥60 years
- Evidence of gastrointestinal bleeding (hematemesis, melena, hematochezia, occult blood in stool)
- Iron deficiency anemia
- Anorexia
- Unexplained weight loss
- Dysphagia
- Odynophagia
- Persistent vomiting
- Gastrointestinal cancer in a first-degree relative

Some examples of Cytochrome P450 Interactions: (Not a complete list)

CYP2C19			
Strong Inducer	Moderate Inducer	Strong Inhibitor	Moderate Inhibitor
rifampin	carbamazepine, dabrafenib, enzalutamide, letermovir, phenytoin derivatives, Saint John's wort, tipranavir/ritonavir	delavirdine, fluconazole, fluvoxamine, ticlopidine	armodafinil, cimetidine, eslicarbazepine, esomeprazole, felbamate, fluoxetine, isoniazid, modafinil, omeprazole, oxcarbazepine, voriconazole
CYP3A4			
Strong Inducer	Moderate Inducer	Strong Inhibitor	Moderate Inhibitor

carbamazepine, phenobarbital, phenytoin derivatives, primidone, rifabutin, rifampin, rifapentine, rufinamide, Saint John's wort	armodafinil, bexarotene, bosentan, dabrafenib, deferasirox, dexamethasone, efavirenz, modafinil, nafcillin, nevirapine, oxcarbazepine	clarithromycin, isoniazid, itraconazole, ketoconazole, nefazodone, nelfinavir, posaconazole, ritonavir, telaprevir, telithromycin, tipranavir/ritonavir, voriconazole	amiodarone, aprepitant, cyclosporine, diltiazem, dronedarone, erythromycin, fluconazole, fluvoxamine, grapefruit juice, isavuconazonium, netupitant, verapamil, zafirlukast

Resources:

Voquezna (vonoprazan) product information, revised by Phathom Pharmaceuticals, Inc. 11-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 22, 2024.

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Laine L, DeVault K, Katz P, et al.: Vonoprazan Versus Lansoprazole for Healing and Maintenance of Healing of Erosive Esophagitis: A Randomized Trial. Gastroenterology 2023;164(1) :61–71. Accessed February 23, 2024.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT04124926: A Phase 3, Randomized, Double-Blind, Two Phase, Multicenter Study to Evaluate the Efficacy and Safety of Vonoprazan 20 mg Compared to Lansoprazole 30 mg for Healing in Patients With Erosive Esophagitis and to Evaluate the Efficacy and Safety of Vonoprazan (10 mg and 20 mg) Compared to Lansoprazole 15 mg for the Maintenance of Healing in Patients With Healed Erosive Esophagitis. Available from: http://clinicaltrials.gov. Last update posted July 29, 2022. Last verified July 2022. Accessed February 23, 2024.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT04124926: Protocol Number: EE-301. A Phase 3, Randomized, Double-Blind, Two Phase, Multicenter Study to Evaluate the Efficacy and Safety of Vonoprazan 20 mg Compared to Lansoprazole 30 mg for Healing in Patients With Erosive Esophagitis and to Evaluate the Efficacy and Safety of Vonoprazan (10 mg and 20 mg) Compared to Lansoprazole 15 mg for the Maintenance of Healing in Patients With Healed Erosive Esophagitis. Available from: http://clinicaltrials.gov. October 01, 2019. Accessed February 23, 2024.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT04167670: A Phase 3 Randomized Multicenter Study to Evaluate the Efficacy and Safety of Open-Label Dual Therapy With Oral Vonoprazan 20 mg or Double-Blind Triple Therapy With Oral Vonoprazan 20 mg Compared to Double-Blind Triple Therapy With Oral Lansoprazole 30 mg Daily in Patients With Helicobacter Pylori Infection. Available from: http://clinicaltrials.gov. Last update posted April 05, 2022. Last verified March 2022. Accessed February 23, 2024.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT04167670: Protocol Number: HP-301. A Phase 3 Randomized Multicenter Study to Evaluate the Efficacy and Safety of Open-Label Dual Therapy With Oral Vonoprazan 20 mg or Double-Blind Triple Therapy With Oral Vonoprazan 20 mg Compared to Double-Blind Triple Therapy With Oral Lansoprazole 30 mg Daily in Patients With Helicobacter Pylori Infection. Available from: http://clinicaltrials.gov. Last update posted April 05, 2022. Last verified March 2022. Accessed February 23, 2024.

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