PDL DRUG REVIEW

Proprietary Name: Voquezna® Triple Pak and Voquezna® Dual Pak
Common Name: vonoprazan/amoxicillin/clarithromycin and vonoprazan/amoxicillin
PDL Category: GI-Ulcer-Anti-Infective

Comparable Products	Preferred Drug List Status
Amox-Clarith-Lansoprazole	Non-Preferred
Pylera (bismuth-metronidazole-tetracycline)	Preferred

Pharmacology/Usage: Voquezna® Triple Pak contains vonoprazan tablets, amoxicillin capsules, and clarithromycin tablets. Voquezna® Dual Pak contains vonoprazan tablets and amoxicillin capsules. Vonoprazan is a potassium-competitive acid blocker. It 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 (PPI), in that it blocks the final step of acid production. Vonoprazan does not require activation by acid. It may selectively concentrate in the parietal cells in both the resting and stimulated states. Vonoprazan binds to the active proton pumps in a non-covalent and reversible manner. Amoxicillin is an antibacterial drug, while clarithromycin is a macrolide antimicrobial drug.

Acid suppression enhances the replication of *H. pylori* bacteria and the stability and effectiveness of antimicrobials in the treatment of *H. pylori* infection.

Indication: For the treatment of *Helicobacter pylori* (*H. pylori*) infection in adults.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Voquezna® Triple Pak, Voquezna® Dual Pak, and other antibacterial drugs, Voquezna® Triple Pak and Voquezna® Dual Pak should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

There is no pregnancy category for this medication; however, the risk summary indicates that based on findings from animal studies and observational studies in pregnant women with use of clarithromycin, use of Voquezna® Triple Pak is not recommended in pregnant women except in clinical circumstances where no alternative therapy is appropriate. There are no adequate and well-controlled studies of Voquezna® Triple Pak in pregnant women to assess for drug-associated risks of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. If Voquezna® Triple Pak is used during pregnancy, advise the pregnant women of the potential risk to a fetus. There are no adequate and well-controlled studies of Voquezna® Dual Pak in pregnant women to assess for drug-associated risks of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. The safety and efficacy of use in the pediatric population have not been established.

Dosage Form: Triple Pak, co-package consisting of 14 administration packs for morning and evening dosing. Each administration pack contains the following 3 drug products:

- Vonoprazan tablets, 20mg.
- Amoxicillin capsules, 500mg.
- Clarithromycin tablets, 500mg.

Dual Pak, co-package consisting of 14 administration packs for morning, mid-day, and evening dosing. Each administration pack contains the following two drug products:

- Vonoprazan tablets, 20mg.
- Amoxicillin capsules, 500mg.

Recommended Dosage: The recommended adult dosage of Voquezna® Triple Pak is vonoprazan 20mg plus amoxicillin 1,000mg plus clarithromycin 500mg, each given BID (in the morning and evening, 12 hours apart), with or without food, for 14 days.

The recommended adult dosage of Voquezna® Dual Pak is vonoprazan 20mg given BID (in morning and evening) plus amoxicillin 1,000mg TID (in the morning, mid-day, and evening), with or without food, for 14 days.

If a dose is missed, administer the Triple Pak or Dual Pak as soon as possible, within 4 hours after the missed dose. If more than 4 hours have passed, skip the missed dose and administer the next dose on the regularly scheduled time. Patients should continue the normal dosing schedule until the medication is completed.

Dosage adjustments of Voquezna® Triple Pak or Voquezna® Dual Pak are not recommended in patients with mild to moderate renal impairment; however, avoid the use of Voquezna® Triple Pak or Voquezna® Dual Pak in patients with severe renal impairment. Dosage adjustments are not recommended in patients with mild hepatic impairment; however, avoid the use of Voquezna® Triple Pak or Voquezna® Dual Pak in patients with moderate to severe hepatic impairment.

Drug Interactions: Drug interaction studies with Voquezna® Triple Pak and Voquezna® Dual Pak have not been conducted. Clarithromycin, a component of Voquezna® Triple Pak, is a strong CYP3A inhibitor. Concomitant use of Voquezna® Triple Pak with a drug(s) primarily metabolized by CYP3A may cause elevations in CYP3A substrate drug's concentrations that could increase or prolong both therapeutic and adverse effects of the concomitant drug. Avoid concomitant use of Voquezna® Triple Pak and Voquezna® Dual Pak with strong or moderate CYP3A inducers.

There is a substantial list of drug interactions listed. Please refer to the prescribing information for additional information.

Box Warning: There is no box warning with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Voquezna® Dual Pak) minus reported incidence for lansoprazole/amoxicillin/clarithromycin (LAC).* The most frequently reported adverse events included diarrhea (0%), dysgeusia (0%), vulvovaginal candidiasis (0.6%), abdominal pain (0%), headache (0%), hypertension (0.2%), and nasopharyngitis (1.1%).

Listed % incidence for adverse drug reactions= reported % incidence for drug (Voquezna® Triple Pak) minus reported incidence for lansoprazole/amoxicillin/clarithromycin (LAC). The most frequently reported adverse events included diarrhea (0%), dysgeusia (0%), vulvovaginal candidiasis (1.8%), abdominal pain (0%), headache (1.2%), hypertension (1.1%), and nasopharyngitis (0%).

Serious and occasionally fatal hypersensitivity reactions have been reported with components of Voquezna® Triple Pak and Voquezna® Dual Pak. Discontinue treatment immediately and start appropriate treatment if hypersensitivity occurs.

Severe cutaneous adverse reactions (SCARS), including Steven-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with the components of Voquezna® Triple Pak and Voquezna® Dual Pak. In addition, drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalized exanthematous pustulosis (AGEP) have been reported with amoxicillin and clarithromycin. Discontinue treatment at the first signs or symptoms of SCAR or other signs of hypersensitivity and consider further evaluation.

Drug-induced enterocolitis syndrome (DIES) has been reported with the use of amoxicillin, a component of Voquezna® Triple Pak and Voquezna® Dual Pak. Discontinue treatment if DIES occurs.

Clostridioides difficile-associated diarrhea (CDAD) has been reported with the use of acid suppressing therapies and nearly all antibacterial agents and may range in severity from mild diarrhea to fatal colitis. Consider CDAD in all patients who present with diarrhea following antibacterial use. Careful medical history is necessary since CDAD has been reported to occur over 2 months after the administration of antibacterial agents. If CDAD is confirmed, Voquezna® Triple and Voquezna® Dual Pak should be discontinued.

A high percentage of patients with mononucleosis who receive amoxicillin develop an erythematous skin rash. Avoid Voquezna® Triple Pak and Voquezna® Dual Pak in patients with mononucleosis.

Prescribing Voquezna® Triple Pak or Voquezna® Dual Pak in the absence of a proven or strongly suspected bacterial infection or prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Refer to the prescribing information regarding additional warnings and precautions for Voquezna® Triple Pak due to the clarithromycin component.

Contraindications:

- In patients with a known hypersensitivity to any component of the product.
- With rilpivirine-containing products.
- Additional contraindications to Voquezna® Triple Pak due to the clarithromycin component. Concomitant use of:
    - Pimozide: There have been post marketing reports of drug interactions when clarithromycin is co-administered with pimozide, resulting in cardiac arrhythmias. Fatalities have been reported.
    - Lipid-Lowering Agents: lomitapide, simvastatin, and lovastatin.
    - Ergot Alkaloids: ergotamine or dihydroergotamine.
    - Colchicine in patients with renal or hepatic impairment.
    - Lurasidone: Coadministration of clarithromycin and lurasidone may lead to an increase in lurasidone exposure and the potential for serious adverse reactions.
- Voquezna® Triple Pak is contraindicated in patients with a history of cholestatic jaundice or hepatic dysfunction associated with prior use of clarithromycin.

Manufacturer: Phathom Pharmaceuticals

Analysis: The safety and efficacy of Voquezna® Triple Pal and Voquezna® Dual Pak were assessed in a randomized, controlled, double-blind (triple therapy)/open-label (dual therapy) study conducted in the US and Europe in treatment-naïve *H. pylori*-positive adults with at least one clinical condition, including dyspepsia lasting at least 2 weeks, functional dyspepsia, recent/new diagnosis of peptic ulcer, peptic ulcer not treated for *H. pylori* infection, or a stable dose of long-term NSAID treatment. Patients were randomized to one of the following regimens administered for 14 consecutive days, including:

- Vonoprazan 20mg BID, plus amoxicillin 1,000mg BID, and clarithromycin 500mg BID (Voquezna® Triple Pak).
- Vonoprazan 20mg BID plus amoxicillin 1,000mg TID (Voquezna® Dual Pak).
- Lansoprazole 30mg BID plus amoxicillin 1,000mg BID, and clarithromycin 500mg BID (LAC).

H. pylori infection at baseline was defined as positive by ^{13}C urea breath test (UBT) and follow-up upper endoscopy (culture or histology). *H. pylori* eradication was confirmed with a negative ^{13}C UBT test-of-cure at ≥27 days post-therapy. Patients with negative test results were considered treatment successes. Patients who tested positive for *H. pylori* infection and patients with missing results from the test-of-cure visit were considered treatment failures.

Voquezna® Triple Pak and Voquezna® Dual Pak were shown to be non-inferior to LAC in patients who did not have a clarithromycin or amoxicillin resistant strain of *H. pylori* at baseline. Voquezna® Triple Pak and Voquezna® Dual Pak were shown to be superior to LAC in patients who had a clarithromycin resistant strain of *H. pylori* at baseline and in the overall population. *H. pylori* eradication rates are presented in the table below, which was adapted from the prescribing information.

	Voquezna® Triple Pak % (n)	Voquezna® Dual Pak % (n)	Lansoprazole, amoxicillin & clarithromycin (LAC) % (n)
Patients with *H. pylori* infection who did not have a clarithromycin or amoxicillin resistant strain at baseline	84.7% (222)	78.5% (208)	78.8% (201)
Treatment difference from LAC	5.9%[1]	-0.3%[2]	
All randomized patients with *H. pylori* infection at baseline	80.8% (273)	77.2% (250)	68.5% (226)
Treatment difference from LAC	12.3%[3]	8.7%[4]	
Patients with *H. pylori* infection who had a clarithromycin resistant strain of *H. pylori* at baseline	65.8% (48)	69.6% (39)	31.9% (23)
Treatment difference from LAC	33.8%[5]	37.7%[5]	

[1] p<0.0001 for test of non-inferiority vs LAC [2]p<0.01 for test of non-inferiority vs LAC [3]p=0.0003 for test of superiority vs LAC
[4] p=0.01 for test of superiority vs LAC [5]p<0.0001 for test of superiority vs LAC

Place in Therapy: Voquezna® Triple Pak and Voquezna® Dual Pak are indicated for the treatment of *Helicobacter pylori* (*H. pylori*) infection in adults. When evaluated in patients with *H. pylori*, Voquezna® Triple Pak and Voquezna® Dual Pak were superior to lansoprazole, amoxicillin, and clarithromycin (LAC) in the overall population and in patients who had a clarithromycin resistant strain of *H. pylori* at baseline. Voquezna® Triple Pak and Voquezna® Dual Pak are a first-in-class treatment that offers providers another treatment option.

Summary

There is some evidence at this time from a phase 3 study to suggest that Voquezna® Triple Pak and Voquezna® Dual Pak may be more effective than lansoprazole/amoxicillin/clarithromycin for treatment of *H. pylori* infection. However, there is no evidence at this time to support that Voquezna® Triple Pak or Voquezna® Dual Pak are safer or more effective than the other currently preferred, more cost-effective medications. It is therefore recommended that Voquezna® Triple Pak and Voquezna® Dual Pak remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred**

References

[1] Voquezna® Triple Pak and Voquezna® Dual Pak [package insert]. Buffalo Grove, IL: Phathom Pharmaceuticals, Inc; 2024.