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IN THIS ISSUE

Vonoprazan *(Voquezna)* for Nonerosive GERD .....p 164

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Vonoprazan *(Voquezna)* for Nonerosive GERD

The potassium-competitive acid blocker vonoprazan (*Voquezna* – Phathom), which was approved earlier for treatment of erosive esophagitis, has now been approved by the FDA for relief of heartburn associated with nonerosive gastroesophageal reflux disease (GERD) in adults.[1] Vonoprazan is also available copackaged with amoxicillin *(Voquezna Dual Pak)* and with amoxicillin and clarithromycin *(Voquezna Triple Pak)* for treatment of *Helicobacter pylori* infection.[2]

Pronunciation Key

Vonoprazan: von oh' pra zan *Voquezna*: voe kwez' nah

GERD — Heartburn and regurgitation are the classic symptoms of GERD. Other symptoms may include chest pain and chronic cough. Drugs that suppress gastric acid are the standard treatment for GERD. Proton pump inhibitors (PPIs) are more effective than H_2-receptor antagonists (H2RAs) in relieving heartburn. Most patients will have a relapse of symptoms after stopping treatment; long-term maintenance treatment is often necessary.[3,4]

PHARMACOLOGY — Vonoprazan blocks the final step of acid secretion in the gastric parietal cell by competitively blocking potassium binding to hydrogen-potassium ATPase (the "proton pump"). Unlike PPIs, vonoprazan does not require activation by acid. Vonoprazan is more rapidly absorbed, has a longer half-life (~7 hours vs ~1-2 hours), and achieves a higher intragastric pH than PPIs.[5]

CLINICAL STUDIES — FDA approval of vonoprazan for the new indication was based on the results of a double-blind trial in 772 patients with nonerosive GERD who had heartburn on at least 4 of 7 days prior to randomization. Patients were randomized to receive vonoprazan 10 or 20 mg or placebo once daily for 4 weeks. After 4 weeks, patients taking placebo were rerandomized to receive vonoprazan 10 or 20 mg for an additional 20 weeks; those already taking vonoprazan continued taking their original dose. The percentage of heartburn-free days through week 4, the primary endpoint, was statistically significantly greater with both doses of vonoprazan than with placebo (44.8% with 10 mg and 44.4% with 20 mg vs 27.7%). The mean percentage of heartburn-free days during the 20-week extension period with vonoprazan was 61-63%.[6]

Key Points: Vonoprazan *(Voquezna)*

- **Description:** Oral potassium-competitive acid blocker.
- **Indication:** Relief of heartburn associated with nonerosive GERD in adults.
- **Efficacy:** Vonoprazan was associated with more heartburn-free days compared to placebo in one 4-week trial.
- **Adverse Effects:** GI adverse effects and urinary tract infection were most common.
- **Drug Interactions:** Vonoprazan may interact with drugs that induce CYP3A4, are substrates of CYP2C19, or require gastric acid for absorption.
- **Dosage:** 10 mg orally once daily.
- **Cost:** A 28-day supply costs $606.
- **Conclusion:** Until more long-term safety data become available, other acid-suppressing drugs are preferred.

In a trial in 483 patients in Japan with nonerosive GERD who were randomized to receive vonoprazan 10 mg or placebo once daily for 4 weeks, the percentage of heartburn-free days, the primary endpoint, was not significantly greater with vonoprazan compared to placebo (72.6% vs 61.5%).[7]

No trials directly comparing vonoprazan to PPIs or H2RAs for treatment of nonerosive GERD are available.

ADVERSE EFFECTS — In the pivotal clinical trial, the most common adverse effects (frequency ≥2%) of vonoprazan were abdominal pain, constipation, diarrhea, nausea, and urinary tract infection. As with PPIs, *Clostridioides difficile* infection, acute tubulointerstitial nephritis, bone fractures, and severe cutaneous adverse reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis can occur with use of vonoprazan. Vitamin B12 deficiency and hypomagnesemia have also been reported. Hyperplasia of the gastric mucosa and gastric hyperplastic polyps with

chronic bleeding have been reported with long-term use of vonoprazan in patients with erosive esophagitis.[8]

DRUG INTERACTIONS — Vonoprazan can decrease serum concentrations of drugs that require gastric acidity for absorption, such as the antiretroviral drugs rilpivirine and atazanavir. Vonoprazan is a CYP3A4 substrate; use with strong or moderate CYP3A4 inducers can decrease serum concentrations of vonoprazan and should be avoided. Vonoprazan is an inhibitor of CYP2C19; it may increase serum concentrations of CYP2C19 substrates and can reduce the antiplatelet effect of clopidogrel, which is converted to its active form by CYP2C19.[9]

PREGNANCY AND LACTATION — No adequate data are available on vonoprazan use in pregnant women. In animal studies, liver lesions and increased stomach weight were reported in rats that had gestational or lactational exposure to vonoprazan. Vonoprazan and its metabolites are present in rat milk. No data are available on the presence of vonoprazan in breast milk or its effects on the breastfed infant or milk production. Breastfeeding is not recommended during treatment with the drug.

DOSAGE, ADMINISTRATION, AND COST — *Voquezna* is supplied in 10- and 20-mg tablets. The recommended dosage for relief of heartburn associated with nonerosive GERD is 10 mg once daily for 4 weeks. The tablets should be swallowed whole; they should not be chewed or crushed. The wholesale acquisition cost (WAC) for a 28-day supply of *Voquezna* is $606.[10]

CONCLUSION — The potassium-competitive acid blocker vonoprazan *(Voquezna)* reduced heartburn significantly in patients with nonerosive GERD in one 4-week placebo-controlled trial, but not in a second trial. Data on its long-term safety are lacking. Older, less expensive acid-suppressing drugs should be tried first. ■

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10. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. September 5, 2024. Reprinted with permission by First Databank, Inc. All rights reserved. ©2024. www.fdbhealth.com/policies/drug-pricing-policy.