Journal Academy Formulary (JACF)

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Drug Review: Vonoprazan

Registrations: It had been registered in the following countries**:** United States of America (USA), United Kingdom (UK), Canada, and Saudi Arabia (SA.) USA, and Japan.
Trade name (USA); VOQUEZNA
Registration number (SA); Not available.
Insurance Drug Formulary (SA); Not available.
General Information:
Registered Company: Pathom Pharmaceutics.
Regulatory Status: RX.
Mechanism of Action:

Vonoprazan
Potassium-competitive acid blocker (PCAB); inhibition in a potassium-competitive manner the H+, K+-ATPase enzyme system.
Ampicillin derivative
penicillin-binding proteins and cell wall inhibitor.
Clarithromycin
reversibly binds to the P site of 50S ribosomal subunit as macrolide antimicrobial; and inhibits RNA-dependent protein synthesis by stimulating the peptidyl t-RNA dissociation from ribosomes.

Indication
Approved (Labeled) indication: Helicobacter pylori gastrointestinal tract infection.
Route of Administration: oral.
Dosage Forms: Oral *tablet.*

Dosing/Administration:
- Administer with or without food.
- If missed dose, administer the next dose as soon as possible, within 4 hr after the missed dose.
- If >4 hr have passed, skip the missed dose and administer the next dose at the regularly scheduled time. Then continue the regular dosing schedule until the medication is completed.

Dose: orally twice daily in the morning and evening, 12 hr for 14 days.
Dose in Renal/Hepatic failure:
- Avoid the use if the estimated GFR is less than 30 mL/min.
Geriatric dose: consider monitoring renal function in this population as amoxicillin is renally excreted; this population may also be more susceptible to the development of clarithromycin-associated torsades de pointes arrhythmias than younger patients.

Adjustment required in Specific population
Avoid use in patients who have moderate to severe hepatic failure, Child-Pugh B or C.
Indicated for pediatrics: Safety and effectiveness not established in pediatric patients.

Pharmacokinetic:
Absorption
steady-state concentrations are achieved within 3 – 4 Days.

Distribution
vonoprazan is metabolized to inactive metabolites via multiple pathways by a combination of cytochrome P450 (CYP) isoforms (CYP3A4/5, CYP2B6, CYP2C19, CYP2C9, and CYP2D6) along with sulfo- and glucuronosyl-transferases.
Excretion:
Following oral administration of radiolabeled vonoprazan, approximately 67% of the radiolabeled dose (8% as unchanged vonoprazan) was recovered in urine, and 31% (1.4% as unchanged vonoprazan) was recovered in feces.
Safety:
Common Adverse Reactions (%):
Abdominal pain, Diarrhea, Taste sense altered, headache, and Candida vaginitis.
Severe/rare adverse Reactions (%):
Cardiovascular: Prolonged Q.T. interval, Torsades de pointes.
Dermatologic: G, acute, Stevens-Johnson syndrome, Toxic epidermal necrolysis.
Gastrointestinal: Clostridioides difficile infection.
Hepatic: Cholestatic hepatitis, Hepatocellular liver damage, Increased liver enzymes, Liver failure.
Immunologic: Anaphylaxis, Drug reaction with eosinophilia and systemic symptoms, Hypersensitivity reaction.
Neurologic: Myasthenia gravis.

Drug Interactions
With CYP3A4 substrate, include colchicine, verapamil, and amlodipine.
Rhabdomyolysis with simvastatin, lovastatin, and atorvastatin.
Hypoglycemia and cardiac arrhythmias (e.g., torsades de pointes) with disopyramide.

Contraindications / Precautions
Hypersensitivity to vonoprazan, amoxicillin (or other beta-lactam antibacterials, e.g.. penicillins, and cephalosporins), or clarithromycin (or other macrolide antibacterial drugs, e.g., erythromycin).
Concomitant use with rilpivirine-containing products.
Concomitant use with the following lipid-lowering agents: Lomitapide, simvastatin, and lovastatin.
Concomitant use with colchicine in patients with renal or hepatic impairment.
History of hepatic dysfunction associated with prior use of clarithromycin.
Cardiovascular: Avoid use in patients with known prolongation of QT interval, ventricular cardiac arrhythmia (including torsades de pointes).

Monitoring Requirements:
• Renal function: In elderly patients.
• Signs and symptoms of myasthenia gravis.

Sound-Alikes/ Look-Alikes: Not available.
High Alert: Not available.
Toxicity if antidote required: Not available.
Storage if there is a special condition: Store in a controlled room temperature between 20- 25°C and Protect from light.

Patient counseling

Side effects may include dysgeusia, vulvovaginal candidiasis, diarrhea, headache, and hypertension.
Avoid omeprazole during therapy.
Report any bloody diarrhea according after treatment.

Cost Analysis

Drugs	Drug classes	Approval Indication	Dose	Cost (American Dollar)	Insurance drug formulary(SCHI)
Voquezna	Antibiotic Anti-infective.	Helicobacter pylori Gastrointestinal tract infection.	Vonoprazan 20 mg plus amoxicillin 1000 mg plus clarithromycin 500 mg, each given orally twice daily (in the morning and evening, 12 hr apart), with or without food.	Around $865.	Not covered (28.2.2023).
Omeclamox-Pak	Antibiotic	Helicobacter pylori Duodenal ulcer disease.	Omeprazole 20mg + clarithromycin 500mg + amoxicillin 1g, all twice daily (AM + PM) for ten days.	$775 for a supply of 80 oral kits.	Not covered (28.2.2023).

REFERENCES

1. VOQUEZNA. Vonoprazan oral tablets. [package insert]. Phathom Pharmaceuticals (per FDA). Buffalo Grove, IL; 2022.
2. Murakami K, Sakurai Y, Shiino M, Funao N, Nishimura A, Asaka M. Vonoprazan, a novel potassium-competitive acid blocker, as a component of first-line and second-line triple therapy for Helicobacter pylori eradication: a phase III, randomized, doubleblind study. Gut. 2016;65(9):1439-46. doi: 10.1136/gutjnl-2015-311304, PMID 26935876.

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Received: 14-10-2022;

Accepted: 25-12-2022;

Access this article online

www.ptbreports.org

DOI: 10.5530/PTB.2023.9.12