Vonokit™

Vonoprazan + Amoxicillin + Clarithromycin

Composition: Vonokit™ is a co-packaged product containing Vonoprazan, a potassium -competitive acid blocker (PCAB), Amoxicillin, a penicillin class antibacterial, and Clarithromycin, a macrolide antimicrobial, indicated for the treatment of *Helicobacter pylori* (*H. pylori*) infection in adults.

Each blister strip contains-

- One **Vonoprazan** 20 mg tablet (as Vonoprazan Fumarate INN)
- One **Clarithromycin** 500 mg tablet (as Clarithromycin USP)
- Two **Amoxicillin** 500 mg capsules (as Amoxicillin Trihydrate BP)

Pharmacology: 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 proton pumps in a noncovalent and reversible manner. Amoxicillin is an antibacterial drug. 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.

Pharmacokinetics: Vonoprazan exhibits time independent pharmacokinetics and steady state concentrations are achieved by Day 3 to 4. After multiple doses of Vonoprazan ranging from 10 mg (0.5 times the lowest approved recommended single dosage) to 40 mg (2 times the highest approved recommended single dosage) once daily for 7 days in healthy subjects, C_{max} and AUC values for Vonoprazan increased in an approximately dose-proportional manner.

Amoxicillin is stable in the presence of gastric acid and is rapidly absorbed after oral administration. Orally administered doses of 500-mg Amoxicillin capsules result in average peak blood levels 1 to 2 hours after administration in the range of 5.5 mcg/mL to 7.5 mcg/mL, respectively.

For a single 500 mg dose of Clarithromycin, food slightly delays the onset of Clarithromycin absorption, increasing the peak time from approximately 2 to 2.5 hours. Food also increases the Clarithromycin peak plasma concentration by about 24%, but does not affect the extent of Clarithromycin bioavailability. Food does not affect the onset of formation of the active metabolite, 14-OH Clarithromycin or its peak plasma concentration but does slightly decrease the extent of metabolite formation, indicated by an 11% decrease in AUC. Therefore, Clarithromycin may be given without regard to food. In non-fasting healthy human subjects (males and females), peak plasma concentrations were attained within 2 to 3 hours after oral dosing.

Indication and Usage: It is indicated for the treatment of *Helicobacter pylori* (*H. pylori*) infection in adults. The recommended dosage regimen is Vonoprazan 20 mg plus Amoxicillin 1,000 mg plus Clarithromycin 500 mg, each given twice daily (morning and evening, 12 hours apart), with or without food, for 14 days.

Side Effects: Most common adverse reactions (≥ 2%) were dysgeusia, diarrhea, vulvovaginal candidiasis, headache, abdominal pain, and hypertension.

Over dosage: In case of an overdose, patients should contact a physician, poison control center, or emergency section of hospital.

Contraindications: Known hypersensitivity to Vonoprazan, Amoxicillin or any other beta-lactams, Clarithromycin or any other macrolide antimicrobial or any component of Vonoprazan Triple therapy. Known hypersensitivity to Vonoprazan, Amoxicillin or any other beta-lactams or any component of Vonoprazan Triple therapy. Rilpivirine-containing products. Vonoprazan Triple therapy Due to the Clarithromycin Component: • Pimozide, • Lomitapide, • lovastatin & simvastatin. • Ergot alkaloids (ergotamine or dihydroergotamine). • Colchicine in renal or hepatic impairment. • History of cholestatic jaundice/hepatic dysfunction with use of Clarithromycin inconveniences

Precautions:

• Hypersensitivity Reactions: Serious and occasionally fatal reactions (e.g., anaphylaxis) have been reported with components of Vonoprazan Triple therapy. If hypersensitivity reactions occur, discontinue Vonoprazan Triple therapy and institute immediate therapy (e.g., anaphylaxis management).

• Severe Cutaneous Adverse Reactions (SCAR): Discontinue Vonoprazan Triple therapy at the first signs or symptoms of SCAR or other signs of hypersensitivity and consider further evaluation.

• Clostridioides difficile-associated diarrhea (CDAD): Evaluate if diarrhea occurs with Vonoprazan Triple therapy.

• QT Prolongation: Avoid Vonoprazan Triple therapy in patients with known QT prolongation or receiving drugs known to prolong the QT interval, ventricular arrhythmia (torsades de pointes), hypokalemia/ hypomagnesemia, significant bradycardia, or taking Class IA or III antiarrhythmics.

• Hepatotoxicity: Discontinue if signs and symptoms of hepatitis occur with Vonoprazan Triple therapy.

• Serious adverse reactions due to concomitant use with other drugs: Serious adverse reactions can occur with Vonoprazan Triple therapy due to drug interactions of Clarithromycin with colchicine, some lipid lowering agents, some calcium channel blockers, and other drugs.

• Embryo-Fetal Toxicity: Based on the findings from animal studies and human observational studies in pregnant women treated with Clarithromycin, Vonoprazan Triple therapy is not recommended for use in pregnant women except in clinical circumstances where no alternative therapy is appropriate.

• Myasthenia Gravis: Exacerbation of myasthenia gravis can occur with Vonoprazan Triple therapy since it has been reported in patients receiving Clarithromycin tablets.

Use in Pregnancy & Lactation: Breastfeeding not recommended during treatment, but a lactating woman can pump & discard breast milk during treatment and for 2 days after **Vono**kit™ administration.

Storage: Store below 30° C. Keep all medicines out of reach of children.

How Supplied: Each box contains 14 blister strips.

Manufactured by

SQUARE
PHARMACEUTICALS LTD.
BANGLADESH