Front

Vonma

(vonoprazan)

Tablet

وونما

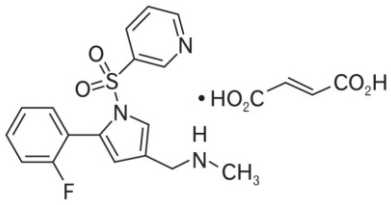
COMPOSITION:
VonmaTablet 10 mg:
Each film coated tablet contains:
Vonoprazan as fumarate ..... 10 mg.

Product Specs.: Innovator

Vonma Tablet 20 mg:
Each film coated tablet contains:
Vonoprazan as fumarate ..... 20 mg.

Product Specs.: Innovator

DESCRIPTION: Vonoprazan is a novel, orally active P-CAB (Potassium-competitive acid blockers) that binds and inhibits H+, K+-ATPase at the final step in the acid secretory pathway in gastric parietal cells.



$C_{17}H_{16}FN_3O_2S \cdot C_4H_4O_4$

Mechanism of Action:
Vonoprazan inhibits the proton pump in a potassium ion-competitive manner to reduce gastric acid secretion in the stomach. It is usually used to treat gastric/duodenal ulcer, reflux esophagitis and for suppression of recurrence of gastric/duodenal ulcer associated with low-dose aspirin or nonsteroidal anti-inflammatory drug medication. It does not require activation by acid. Vonoprazan is a strong base with a high affinity for the acid pump of gastric cells inhibiting gastric acid production.

CLINICAL PHARMACOLOGY:
Pharmacokinetics:
Serum gastrin and serum pepsinogen effects: Increased serum gastrin and serum pepsinogen concentrations are physiological responses to treatment with acid suppression therapy, including vonoprazan. Increased serum gastrin and serum pepsinogen concentrations were reported with a higher incidence in the vonoprazan treatment groups compared with lansoprazole treatment groups. Serum gastrin and serum pepsinogen concentrations returned to baseline over time upon discontinuation of vonoprazan. The increase in serum gastrin concentration occurred early in treatment with vonoprazan and remained stable for the remainder of treatment.
The efficacy of vonoprazan has been demonstrated in a number of clinical studies across several indications including Gastric Ulcer (GU), Duodenal Ulcer (DU), Reflux Esophagitis (RE), prevention of GU/DU during NSAID administration and as an adjunct to H. pylori eradication. These data are divided into the categories based upon the specific indication, including GU, DU, RE, prevention of recurrence of gastric or duodenal ulcer during NSAID administration, and H. pylori eradication. Following administration of vonoprazan at a dose of 10 mg or 20 mg in healthy adult male subjects for 7 days, pH 4 HTR (pH 4 holding time ratio) (percentage of time pH is maintained at a level ⩾4 in 24 hours) was 63±9% and 83±17% respectively.
A phase 1 open-label pharmacodynamics study to investigate the acid-inhibitory effect of vonoprazan 20 mg compared with esomeprazole 20 mg or rabeprazole sodium 10 mg in healthy adult male Japanese subjects showed that the acid-inhibitory effect of vonoprazan was greater than that of esomeprazole or rabeprazole. After all treatments, the mean 24-hour pH 4 HTRs increased from Baseline to Day 1 and from Day 1 to Day 7. The mean pH 4 HTRs were higher after administration of vonoprazan on Day 1 than after administration of esomeprazole or rabeprazole on Day 7. The mean 24-hour pH 4 HTRs for vonoprazan and rabeprazole at Baseline were both 8.9%, and on Day 1 and on Day 7 were 84.16% vs 26.29%, and 93.79% vs 65.09%, respectively.
Following 7 day repeat once daily doses of vonoprazan at doses of 10-40 mg, in healthy adult male subjects, AUCτ,ss and Cmax,ss increase in a slightly greater than dose proportional manner. Steady state has been reached by day 3 of administration, since the trough level of the blood concentration of vonoprazan is constant between day 3 and day 7 of administration.
Distribution: The mean binding rate is 85.2 to 88.0% when [14C] vonoprazan in the range of 0.1 to 10 μg/mL is added to human plasma *(in vitro)*.
Metabolism: Vonoprazan is metabolized mainly by hepatic drug-metabolizing enzyme CYP3A4 and partially by CYP2B6, CYP2C19 and CYP2D6. Vonoprazan is also metabolized by sulfotransferase SULT2A1 (in vitro).
Vonoprazan exhibits time-dependent inhibitory effect on CYP2B6, CYP2C19 and CYP3A4/5 (in vitro). In addition, vonoprazan shows a slight concentration-dependent inductive effect on CYP1A2, but it shows little inductive effect on CYP2B6 and CYP3A4/5 (in vitro).
Excretion and elimination: When radioactive-labeled drug (15 mg as vonoprazan) is orally administered to healthy adult male subjects, 98.5% of the radioactivity administered is excreted into urine and feces by 168 hours after administration: 67.4% into urine and 31.1% into feces.

INDICATIONS:
Treatment of Gastric Ulcer (GU).
Treatment of Duodenal Ulcer (DU).
Treatment of Reflux Esophagitis (RE) (Erosive Esophagitis EE).
Maintenance treatment of Reflux Esophagitis (Erosive Esophagitis) in patients with repeat recurrence and relapse of the condition. The duration of administration in the long-term efficacy clinical Study OCT-001 is up to 52 weeks.
Prevention of recurrence of gastric ulcer or duodenal ulcer during NSAIDs administration.
Adjunct to Helicobacter pylori eradication associated with: Gastric ulcer, duodenal ulcer, gastric MALT lymphoma, idiopathic thrombocytopenic purpura, the stomach after endoscopic resection of early-stage cancer, or Helicobacter pylori gastritis.

DOSAGE AND ADMINISTRATION:
Adults:
Gastric ulcer: The usual dose is 20 mg of vonoprazan once a day. Administration should be limited to 8 weeks.
Duodenal ulcer: The usual dose is 20 mg of vonoprazan once a day. Administration should be limited to 6 weeks.
Reflux esophagitis (Erosive Esophagitis): The usual dose is 20 mg of vonoprazan once a day. Administration should be limited to 4 weeks. However, when the effect is insufficient, treatment may be continued for up to 8 weeks. In addition, for the maintenance of healing of reflux esophagitis in patients with repeat recurrence and relapse of the condition, a dose of 10 mg is administered once a day; however, when the efficacy is inadequate, a dose of 20 mg may be administered once a day. The duration of administration in the long-term efficacy clinical Study OCT-001 is up to 52 weeks.
Prevention of recurrence of gastric ulcer or duodenal ulcer during NSAIDs administration: The usual dose is 10 mg of vonoprazan once a day.

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*****Adjunct to Helicobacter pylori eradication*****

Usually, the following 3 drugs are orally administered at the same time twice daily for 7 days: 20 mg vonoprazan, 750 mg amoxicillin, and 200 mg clarithromycin. The dose of clarithromycin may be appropriately increased as required; however, the upper limit is 400 mg twice daily. When Helicobacter pylori eradication treatment with 3 drugs consisting of a proton pump inhibitor, amoxicillin, and clarithromycin fails, alternative treatment with the following 3 drugs is recommended; 20 mg vonoprazan, 750 mg amoxicillin, and 250 mg metronidazole, orally administered at the same time twice daily for 7 days. The doses of antibiotic should follow the respective label recommendations for H. pylori eradication.

Method of administration: Vonoprazan can be taken without regard to food or timing of food.

WARNINGS & PRECAUTIONS:

Hepatotoxicity: Hepatic function abnormalities including liver injury have been reported in clinical studies (see Adverse Reactions). Post marketing reports have also been received in patients treated with vonoprazan, many of which occurred shortly after initiation of treatment. Discontinuation of vonoprazan is recommended in patients who have evidence of liver function abnormalities or if they develop signs or symptoms suggestive of liver dysfunction.

Elevation of intragastric pH: Administration of vonoprazan results in elevation of intragastric pH and is therefore not recommended to be taken with drugs for which absorption is dependent on acidic intragastric pH.

Masking of symptoms associated with gastric malignancy: Gastric malignancy may present with symptoms associated with acid-related disorders which initially respond to drugs that elevate intragastric pH. A symptomatic response to vonoprazan does not exclude the presence of gastric malignancy.

Clostridium difficile associated diarrhea, including pseudomembranous colitis: Drugs that elevate intragastric pH may be associated with an increased risk of Clostridium difficile gastrointestinal infection. Pseudomembranous colitis may be due to antibiotics used for Helicobacter pylori eradication in combination with vonoprazan. If abdominal pain and frequent diarrhea occur, appropriate measures, including discontinuation of the treatment, should be taken.

Bone fracture: An increased risk for osteoporosis-related fractures of the hip, wrist, or spine, predominantly in the elderly or in presence of other recognized risk factors, has been reported with the use of proton pump inhibitors, especially with use of high doses over a long-term period (>1 year). The mechanism is not clear and is likely to be multifactorial.

Renal impairment: Vonoprazan should be administered with care in patients with renal disorders as a delay in the excretion of vonoprazan may occur, which may result in an increase in the concentration of vonoprazan in the blood.

Hepatic impairment: Vonoprazan should be administered with care in patients with hepatic disorders as a delay in the metabolism and excretion of vonoprazan may occur, which may result in an increase in the concentration of vonoprazan in the blood.

ADVERSE REACTIONS:

The following convention is used for the classification of the frequency of an adverse drug reaction (ADR) and is based on the Council for International Organizations of Medical Sciences (CIOMS) guidelines: very common (⩾1/10); common (⩾1/100 to < 1/10); uncommon (⩾1/1,000 to < 1/100); rare (⩾1/10,000 to < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data).

Clinical trials: Clinical trial data for expected adverse events is based on pooled safety analysis from the following studies: EE healing (CCT-001 and CCT-002), EE maintenance therapy (CCT-003 and OCT-001), GU healing (CCT-101), DU healing (CCT-102), prevention of recurrence of peptic ulcer associated with NSAID use (CCT-301, OCT-301 and OCT-303) and treatment of non-erosive reflux disease (NERD; CCT-201). Although the study in patients with NERD has the placebo arm and is considered as the best data, the number of patients (N=449 and 278 for TAK-438 and placebo, respectively) is relatively small compared to the number of patients of all other active-comparator studies combined (N=3162 and 1392 for TAK-438 and AG-1749 [Lansoprazole], respectively). Therefore, the pooled safety data of active-comparator studies are used for the primary analysis. The safety data of CCT-201 study are analyzed separately. (Note: AG-1749 (Lansoprazole) is the only comparator used in the comparator studies.)

SPECIAL POPULATIONS:

Use in children: Vonoprazan has not been studied in patients under 18 years of age.

Use in the elderly: Since the physiological functions such as hepatic or renal function are decreased in elderly patients in general, vonoprazan should be carefully administered.

Use In Pregnancy & Lactation:

Pregnancy: No clinical studies have been conducted to date to evaluate vonoprazan in subjects who are pregnant. In a rat toxicology study, embryo-foetal toxicity was observed following exposure of more than approximately 28 times of the exposure (AUC) at the maximum clinical dose (40 mg/day) of vonoprazan. As a precaution, vonoprazan should not be administered to women who are or may be pregnant, unless the expected therapeutic benefit is thought to outweigh any possible risk.

Lactation: No clinical studies have been conducted to date to evaluate vonoprazan in subjects who are lactating. It is unknown whether vonoprazan is excreted in human milk. In animal studies it has been shown that vonoprazan was excreted in milk. During treatment with vonoprazan, nursing should be avoided if the administration of this drug is necessary for the mother.

CONTRAINDICATIONS:

Hypersensitivity to the active ingredients or to any of the excipients.

DRUG INTERACTIONS:

Administration of vonoprazan results in elevation of intragastric pH, suggesting that it may interfere with the absorption of drugs where gastric pH is an important determinant of oral bioavailability. Use of vonoprazan is therefore not recommended with some of these drugs for which absorption is dependent on acidic intragastric pH such as atazanavir and nelfinavir, due to significant reduction in their bioavailability.

Vonoprazan is metabolized mainly by hepatic drug-metabolizing enzyme CYP3A4 and partially by CYP2B6, CYP2C19 and CYP2D6.

With strong CYP3A4 inhibitors, e.g., clarithromycin, blood concentration of vonoprazan may increase. It has been reported that blood concentration of vonoprazan increased in concomitant use with clarithromycin by 1.5-fold, but no dose adjustment of vonoprazan is considered necessary.

Co-administration of vonoprazan with the antibiotic regimen clarithromycin and amoxicillin increased concentrations of vonoprazan by up to 1.9-fold. No increase was observed with the antibiotic regimen of metronidazole and amoxicillin. No dose adjustment of vonoprazan is considered necessary.

There were no clinically significant effects of NSAIDs on the pharmacokinetics of vonoprazan, and no clinically significant effects of vonoprazan on the pharmacokinetics of NSAIDs.

Co-administration of midazolam (a sensitive CYP3A4 substrate) with multiple doses of vonoprazan increased concentration of midazolam by 1.9-fold in healthy subjects. Caution is advised when vonoprazan is co-administered with other sensitive CYP3A4 substrates, notably those having a narrow therapeutic index.

INSTRUCTIONS:

- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

Vonma Tablet 10 mg	:	Pack of 2 x 7 tablets.
Vonma Tablet 20 mg	:	Pack of 2 x 7 tablets.

ہدایات:

۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

گرمی، دھوپ اور نمی سے بچائیں۔

بچوں کی پہنچ سے دور رکھیں۔

صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

Manufactured by:
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Plot No. 69/1, Block B, Phase-I-II, Industrial Estate Hattar, Pakistan.

FOR FURTHER INFORMATION PLEASE CONTACT:

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