26-07-2023
3rd Copy

(NEW LAUNCHING)

210mm

VONOLIA™ Tablet

(Vonoprazan Fumarate)

QUALITATIVE AND QUANTITATIVE COMPOSITION

VONOLIA™ 10mg Tablet
Each film coated tablet contains:
Vonoprazan as Fumarate MS….10mg

VONOLIA™ 20mg Tablet
Each film coated tablet contains:
Vonoprazan as Fumarate MS….20mg

PHARMACEUTICAL FORM

Tablet.

CLINICAL PARTICULARS

THERAPEUTIC INDICATIONS:

- Treatment of gastric ulcer (GU) and duodenal ulcer (DU).
- Treatment of reflux oesophagitis (RE) and erosive oesophagitis (EE).
- Prevention of recurrence of gastric ulcer or duodenal ulcer during low-dose aspirin administration. 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.

POSOLOGY AND METHOD OF ADMINISTRATION:
Dosage:
Adults:
Gastric ulcer: 20mg of vonoprazan once a day. Administration should be limited to 8 weeks.
Duodenal ulcer: 20mg of vonoprazan once a day. Administration should be limited to 6 weeks.
Reflux oesophagitis (erosive oesophagitis): The usual dose is 20mg 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.
Prevention of recurrence of gastric ulcer or duodenal ulcer during low-dose aspirin & NSAID administration: The usual dose is 10mg of vonoprazan once a day.
Adjunct to Helicobacter pylori eradication: Usually, the following 3 drugs are orally administered at the same time twice daily for 7 days: 20mg vonoprazan, 750mg amoxicillin hydrate, and 200mg clarithromycin. The dose of clarithromycin may be appropriately increased as required; however, the upper limit is 400mg twice daily or physician judgement.
When *Helicobacter pylori* eradication treatment with 3 drugs consisting of a proton pump inhibitor, amoxicillin hydrate, and clarithromycin fails, alternative treatment with the following 3 drugs is recommended; 20mg vonoprazan, 750mg amoxicillin hydrate, and 250mg 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.

CONTRAINDICATIONS:
Hypersensitivity to the active substances.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE:
Hepatotoxicity:
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:
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 diarrhoea, 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 diarrhoea 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.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION:
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.
Coadministration 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 low-dose aspirin or NSAIDs on the pharmacokinetics of vonoprazan, and no clinically significant effects of vonoprazan on the pharmacokinetics of low-dose aspirin or NSAIDs.

PREGNANCY AND LACTATION:
Pregnancy:
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.
Breast-feeding:
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.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
The influence of vonoprazan on the ability to drive or use machines is unknown.

UNDESIRABLE EFFECTS:
Following adverse reactions have been reported with the use of vonoprazan:

- **Gastrointestinal disorders:** ***Common:*** Diarrhoea, constipation. ***Uncommon:*** Nausea, abdominal distention.
- **Investigation:** ***Uncommon:*** Gamma-glutamyl transferase increased, AST increased, Liver function test abnormal, ALT increased, ALP increased, LDH increased, γ - GPT increased, oedema and oeosinophilia.

Post-marketing:
Following is a list of ADRs which have been observed in post-marketing (Frequency unknown):

- ***Immune system disorders:*** Drug hypersensitivity (including anaphylactic shock), drug eruption, urticaria.
- ***Hepatobiliary disorders:*** Hepatotoxicity, jaundice.
- ***Skin and Subcutaneous tissue disorders:*** Rash, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis.

OVERDOSE:
There is no experience of overdose with vonoprazan. Vonoprazan is not removed from the circulation by haemodialysis. If overdose occurs, treatment should be symptomatic and supportive.

120mm

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PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMIC PROPERTIES:

Pharmacotherapeutic group: Alimentary tract and metabolism, Drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD), PPIs, **ATC code:** A02B C04

Mechanism of Action:

Vonoprazan is a potassium competitive acid blocker (PCAB) and inhibits H+, K+-ATPase in a reversible and potassium-competitive manner. 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.

Serum Gastrin and Serum Pepsinogen Effects:

Increased serum gastrin and serum pepsinogen concentrations are physiological responses to treatment with acid suppression therapy, including vonoprazan.

PHARMACOKINETIC PROPERTIES:

Vonoprazan does not exhibit time-dependent pharmacokinetics.

Absorption:

Absolute bioavailability has not been determined.

Distribution:

The mean binding rate is 85.2 to 88.0% when vonoprazan in the range of 0.1 to 10μg/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 SULT2A.

Excretion and Elimination:

Excretion and elimination are through urine and faeces.

Age, Gender, Race:

Vonoprazan has not been studied in patients under 18 years of age. There are no clinically relevant gender effects of vonoprazan.

SHELF LIFE

See expiry on the pack.

AVAILABILITY

VONOLIA™ 10mg tablet in a pack of 14's.
VONOLIA™ 20mg tablet in a pack of 14's.

INSTRUCTIONS

Dosage: As directed by the physician.
To be sold on prescription of a registered medical practitioner only.
Keep out of the reach of children.
Do not store over 30°C, and protect from heat, light and moisture.
Improper storage may deteriorate the medicine.

وُنولیا™ ٹیبلٹ

(وُنوپرازان فیومیریٹ)

ہدایات:

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

بچوں کی پہنچ سے دور رکھیں۔

دوا کو ۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں،
گرمی، روشنی اور نمی سے محفوظ رکھیں ورنہ دوا خراب ہو جائیگی۔

Manufactured by:
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