Tanavul Tablets

تناوُل ٹیبلٹس

COMPOSITION:

Each film coated tablet contains:

Vonoprazan fumarate equivalent to Vonoprazan…..10mg , 20mg

DESCRIPTION:

Tanavul contains Vonoprazan which is a potassium competitive acid blocker (PCAB). Chemically, Vonoprazan is 1-[5-(2-fluorophenyl)-1-(pyridin-3-ylsulfonyl)-1H-pyrrol-3-yl]- N-methylmethanamine monofumarate. Its molecular formula is C17H16FN3O2SC4H4O4.

CLINICAL PHARMACOLOGY

Mechanism of Action: Vonoprazan is a potassium competitive acid blocker (P-CAB) and does not require activation by acid. It inhibits H+, K+-ATPase in a reversible and potassium-competitive manner. Vonoprazan has a strong basicity and resides on the acid production site of gastric parietal cells for a long time, thereby inhibiting gastric acid production. Vonoprazan exerts a strong inhibitory effect on formation of mucosal damage in upper part of the gastrointestinal tract. Vonoprazan does not exhibit anti-Helicobacter pylori activity nor inhibitory activity against Helicobacter pylori urease.

Adjunctive effect on eradication of Helicobacter pylori: The role of Vonoprazan in the Helicobacter pylori eradication is considered to increase intragastric pH leading to the enhancement of antibacterial activity of amoxicillin hydrate, clarithromycin and metronidazole which are concomitantly administered.

PHARMACOKINETICS: At consecutive administration of a daily dose of 10mg or 20mg of Vonoprazan in healthy adult male subjects once daily for 7 days, AUC (0-tau) and Cmax increase as the dose increases. The degree of these increases is slightly higher than the dose ratio. It is considered that the 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.

Absorption: 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, Cmax and AUC values for vonoprazan increased in an approximately dose-proportional manner.

Distribution: Plasma protein binding of vonoprazan ranged from 85 to 88% in healthy subjects and was independent of concentration from 0.1 to 10 mcg/mL.

Metabolism: 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. CYP2C19 polymorphisms have been evaluated in clinical studies and there were no considerable differences in the pharmacokinetics of vonoprazan based on CYP2C19 metabolizer status.

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.

Special population

Patients with renal impairment: The effect of renal disorders on pharmacokinetics of Vonoprazan in subjects with normal renal function, patients with mild, moderate, and severe renal disorder and patients with end-stage renal disease (ESRD) when administered the drug as a single dose of Vonoprazan 20mg shows that AUC∞ and Cmax were higher by 1.3 to 2.4 times and 1.2 to 1.8 times, respectively, in patients with mild, moderate, and severe renal disorder compared to subjects with normal renal function, showing an increase with a reduction in renal function. AUC∞ and Cmax were higher by 1.3 times and 1.2 times, respectively, in ESRD patients compared to those in subjects with normal renal function.

Patients with hepatic impairment: The effect of hepatic disorders on pharmacokinetics in subjects with normal hepatic function and patients with mild, moderate and severe hepatic disorder when administered the drug as a single dose of Vonoprazan 20mg shows that AUC∞ and Cmax were higher by 1.2 to 2.6 times and 1.2 to 1.8 times, respectively, in patients with mild, moderate and severe hepatic disorder, compared to subjects with normal hepatic function.

THERAPEUTIC INDICATIONS (Vonoprazan) is indicated for:

. Gastric ulcer, duodenal ulcer, reflux esophagitis, prevention of recurrence of gastric or duodenal ulcer during low-dose aspirin administration, prevention of recurrence of gastric or duodenal ulcer during non-steroidal anti-inflammatory drug (NSAID) administration.

. Adjunct to Helicobacter pylori eradication in the following settings: Gastric ulcer, duodenal ulcer, gastric mucosa-associated lymphatic tissue (MALT) lymphoma, idiopathic thrombocytopenic purpura, the stomach after endoscopic resection of early-stage gastric cancer or Helicobacter pylori gastritis.

DOSAGE AND ADMINISTRATION

Gastric ulcer and duodenal ulcer The usual adult dosage for oral use is 20mg of Tanavul (Vonoprazan) administered orally once daily an 8 week treatment for gastric ulcer and a 6 week treatment for duodenal ulcer.

· The usual dose for prevention of recurrence of gastric or duodenal ulcer during low-dose aspirin administration is one tablet of 10mg of Tanavul (Vonoprazan) once daily.

· The usual dose for prevention of recurrence of gastric or duodenal ulcer during non-steroidal anti-inflammatory drug (NSAID) is one tablet of 10mg of Tanavul (Vonoprazan) once daily.

Reflux esophagitis: The usual adult dose for oral use is 20mg of Tanavul (Vonoprazan) administered once daily for a total of 4 weeks of treatment. If that dosing proves insufficient, the administration should be extended, but for no longer than 8 weeks of treatment. For the maintenance therapy of reflux esophagitis showing recurrence and recrudescence, the dose for oral use is 10mg of Tanavul (Vonoprazan) once daily. However, when the efficacy is inadequate, the dosage may be increase up to 20mg of Tanavul (Vonoprazan) once daily.

CONTRAINDICATIONS

Vonoprazan is contraindicated in:

. Patients with hypersensitivity to Vonoprazan or to any excipient of the product.

. Patients receiving atazanavir sulphate, nelfinavir or rilpivirine hydrochloride.

ADVERSE REACTIONS: Following adverse reactions have been reported with the use of Vonoprazan: Diarrhea, constipation, drug hypersensitivity (including anaphylactic shock), drug eruption, urticaria, hepatotoxicity, jaundice, rash, nausea, abdominal distension, gamma-glutamyl transferase increased, AST increased, Liver function test abnormal, ALT increased, ALP increased, LDH increased, γ - GPT increased, edema and eosinophilia.

PRECAUTIONS

General: At the treatment, the course of the disease should closely be observed and the minimum therapeutic necessity should be used according to the disease condition. In the long-term, treatment with Vonoprazan, close observation by such means as endoscopy should be made. In the maintenance of healing of reflux esophagitis, Vonoprazan should be administered only to the patients who repeat recurrence and recrudescence of the condition. Administration to the patients who do not necessitate maintenance of healing should be avoided. When the healing is maintained over a long period and when there is no risk of recurrence, the dose reduction to a dose of 10mg from a dose 20mg, or suspension of administration should be considered.

Impaired Renal Function: 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.

Impaired Hepatic Function: 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. Hepatic function abnormalities including liver injury have been reported. 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. Symptomatic response to Vonoprazan does not preclude the presence of gastric malignancy. It is therefore, necessary to ascertain the ulcer is not of a malignant nature before initiating the administration of this drug.

Clostridium difficile, serious colitis, including pseudomembranous colitis, there is an increased risk of gastrointestinal infection caused by Clostridium difficile. Serious colitis accompanied with bloody stools, such as pseudomembranous colitis, may occur due to amoxicillin hydrate or clarithromycin being used for Helicobacter pylori eradication, in combination with Vonoprazan. If abdominal pain and frequent diarrhea occur, appropriate measures, such as immediate discontinuation of the treatment, should be taken.

Benign gastric polyps: Benign gastric polyp has been observed in patient on long-term administration of PPIs.

Fractures: An increased risk for osteoporosis-related fractures of the hip, wrist or spine have been reported in patients under treatment with proton pump inhibitors. The risk of fracture was especially increased in the patients receiving high dose or long term (a year or longer) treatment.

Hypomagnesemia: Severe hypomagnesemia has been reported in patients on prolonged treatment with PPIs for at least three months and in most cases for a year.

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

Pregnancy: Vonoprazan should be used in pregnant women or women having possibilities of being pregnant only if the expected therapeutic benefit is thought to outweigh any possible risk.

Nursing Mothers: It is advisable to avoid the administration of Vonoprazan to nursing mothers. However, when the administration is indispensable, nursing should be discontinued.

INTERACTIONS: Advise patients that vanaprazon may interact with some drugs like Floconazole, Clochicine, Ritonavir, Omeprozole and Theophylline therefore, advise patients to report to their healthcare provider the use of any other medications including natural substitutes and nutritional supplements.

OVERDOSAGE: There is no experience of overdose with Vonoprazan. In clinical studies, a single dose of 120 mg resulted in no serious adverse reaction, while Vonoprazan is not removed from the circulation by hemodialysis. If overdose occurs, treatment should be symptomatic and supportive.

STORAGE/ PRECAUTIONS: Avoid direct sunlight and protect from moisture and heat. Store below 25. Keep all medicines out of the reach of children.

PRESENTATION: Tanavul Tablets 10mg and 20mg are available in Alu-Alu packing containing 14 film coated tablets.

خوراک: ڈاکٹر کی ہدایت کے مطابق۔ احتیاط: دھوپ، نمی اور گرمی سے بچائیں۔ 25 ڈگری سینٹی گریڈ سے کم درجہ حرارت پر محفوظ کریں۔ تمام ادویات بچوں کی پہنچ سے دور رکھیں۔ مستند ڈاکٹر کے نسخہ پر استعمال کریں۔

Complete Medical Information available only for doctors on request.

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Manufactured by: **SCOTMANN PHARMACEUTICALS**
5-D, I-10/3 Industrial Area, Islamabad-Pakistan.
www.scotmann.com

Reference: FDA Label