For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory xxxxxxxx-8883

VELOZ

(Rabeprazole Sodium Enteric Coated Tablets, 10 mg/20 mg)

COMPOSITION

Each enteric coated tablet of Veloz 10mg contains Rabeprazole sodium 10 mg.
Each enteric coated tablet of Veloz 20mg contains Rabeprazole sodium 20 mg.

PROPERTIES

Rabeprazole sodium is a proton pump inhibitor, which inhibits gastric acid secretion, raising gastric pH.

CLINICAL PHARMACOLOGY

MECHANISM OF ACTION

Rabeprazole belongs to a class of antisecretory compounds (substituted benzimidazole proton-pump inhibitors) that do not exhibit anticholinergic or histamine H_2-receptor antagonist properties, but suppress gastric acid secretion by inhibiting the gastric H^+ K^+ATPase at the secretory surface of the gastric parietal cell. Because this enzyme is regarded as the acid (proton) pump within the parietal cell, Rabeprazole has been characterized as a gastric proton-pump inhibitor. Rabeprazole blocks the final step of gastric acid secretion. In gastric parietal cells, Rabeprazole is protonated, accumulates and is transformed to an active sulfenamide.

PHARMACOKINETICS

Veloz delayed-release tablets are enteric-coated to allow Rabeprazole sodium, which is acid labile, to pass through the stomach relatively intact. After oral administration of 20 mg Veloz, peak plasma concentrations (C_{max}) of Rabeprazole occur over a range of 2.0 to 5.0 hours (T_{max}). The Rabeprazole C_{max} and AUC are linear over an oral dose range of 10 mg to 40 mg. There is no appreciable accumulation when doses of 10 mg to 40 mg are administered every 24 hours; the pharmacokinetics of Rabeprazole is not altered by multiple dosing. The plasma half-life ranges from 1 to 2 hours.

Absorption

Following oral administration of 20 mg, Rabeprazole is absorbed and can be detected in plasma by 1 hour. Absolute bioavailability for a 20 mg oral tablet of Rabeprazole (compared to intravenous administration) is approximately 52%. The effects of food on the absorption of Rabeprazole have not been evaluated.

Distribution

Rabeprazole is 96.3% bound to human plasma proteins.

Metabolism

Rabeprazole is extensively metabolized. The thioether and sulphone are the primary metabolites measured in human plasma. These metabolites were not observed to have significant antisecretory activity. *In vitro* studies have demonstrated that rabeprazole is primarily metabolized in the liver by cytochromes P450 3A (sulphone metabolite) and 2C19 (desmethyl rabeprazole). The thioether metabolite is formed by reduction of Rabeprazole.

Elimination

Following a single 20 mg oral dose of ^{14}C-labeled Rabeprazole, approximately 90% of the drug was eliminated in the urine, primarily as thioether carboxylic acid; its glucuronide, and mercapturic acid metabolites. The remainder of the dose was recovered in the feces. Total recovery of radioactivity was 99.8%. No unchanged Rabeprazole was recovered in the urine or feces.

INDICATIONS

Veloz is used to treat the following conditions :
Gastroesophageal reflux disease, duodenal ulcer and Zollinger Ellison syndrome

CONTRAINDICATIONS

Veloz is contraindicated in patients with known hypersensitivity to Rabeprazole, substituted benzimidazoles or to any component of the formulation.

PRECAUTIONS

General

Symptomatic response to therapy with Veloz does not preclude the presence of gastric malignancy. Safety and efficacy of Rabeprazole sodium in pregnant women, lactating mothers and pediatric population has not been established.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Rabeprazole did not produce any tumor occurrence in carcinogenecity studies at dose of 100mg/kg, greater than that of the recommended dose for GERD (20mg/kg). Rabeprazole at intravenous doses of up to 30mg/kg/day was found to have no effect on fertility and reproductive performance of male and female rats.

Pregnancy

Teratogenic studies were performed in rats at intravenous doses up to 50mg/kg/day and in rabbits at intravenous doses up to 30mg/kg/day and have revealed no evidence of impaired fertility or harm to the fetus due to Rabeprazole. There are however no adequate studies in pregnant women. This drug should be used during pregnancy only if clearly needed.

Nursing Mothers

Animal studies have revealed that Rabeprazole is excreted in the milk and it is not well understood whether unmetabolised Rabeprazole is excreted in the milk. Since many drugs are excreted in the milk and because of the potential for adverse reactions to nursing infants from Rabeprazole, a decision should be made to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Geriatric Use

No overall differences in safety, effectiveness and adverse reactions were observed between young and old subjects, but greater sensitivity of some older individuals cannot be ruled out.

ADVERSE REACTIONS

The most common adverse events reported with Veloz are :
Asthenia, fever, allergic reaction, chills, malaise, chest pain substernal, neck rigidity, photosensitivity reaction, diarrhea, nausea, abdominal pain, vomiting, dyspepsia, flatulence, constipation, dry mouth, eructation, gastroenteritis, rectal hemorrhage, melena, anorexia, cholelithiasis, mouth ulceration, stomatitis, dysphagia, gingivitis, cholecystitis, increased appetite, abnormal stools, colitis, esophagitis, glossitis, pancreatitis and proctitis.

DRUG INTERACTIONS

The cytochrome P450 (CYP450) drug metabolizing enzyme system metabolizes Rabeprazole. Studies in healthy subjects have shown

that Rabeprazole does not have clinically significant interactions with other drugs metabolized by the CYP450 system, such as warfarin, theophylline, diazepam (IV), and phenytoin (IV). Rabeprazole produces sustained inhibition of gastric acid secretion. An interaction with compounds, which are dependent on gastric pH for absorption, may occur due to the magnitude of acid suppression observed with Rabeprazole. Co-administration of Rabeprazole and antacids produced no clinically relevant changes in plasma Rabeprazole concentrations.

DOSAGE AND METHOD OF ADMINISTRATION

Healing of Erosive or Ulcerative Gastroesophageal Reflux Disease (GERD)

The recommended adult oral dose is one Veloz 20mg delayed-release tablet to be taken once daily for four to eight weeks. For those patients who have not healed after 8 weeks of treatment, an additional 8-week course of Veloz may be considered.

Healing of Duodenal Ulcers

The recommended adult oral dose is one Veloz 20 mg delayed-release tablet to be taken once daily after the morning meal for a period up to four weeks. Most patients with duodenal ulcer heal within four weeks. A few patients may require additional therapy to achieve healing.

Treatment of Zollinger-Ellison Syndrome

Zollinger Ellison Syndrome is a pathological hypersecretory condition. The dosage of Veloz in patients with pathologic hypersecretory conditions varies with the individual patient. The recommended adult oral starting dose is 60 mg once a day. Doses should be adjusted to individual patient needs and should continue for as long as clinically indicated. Some patients may require divided doses. Doses up to 100 mg QD and 60 mg BID have been administered. Some patients with Zollinger-Ellison syndrome have been treated continuously with Rabeprazole for up to one year.

No dosage adjustment is necessary in elderly patients, in patients with renal disease or in patients with mild to moderate hepatic impairment. Administration of Rabeprazole to patients with mild to moderate liver impairment resulted in increased exposure and decreased elimination. Due to the lack of clinical data on Rabeprazole in patients with severe hepatic impairment, caution should be exercised in those patients. **Veloz tablets should be swallowed whole. The tablets should not be chewed or crushed.**

OVERDOSAGE

There has been no experience with large overdoses with Rabeprazole. Rabeprazole is extensively protein bound and is not readily dialyzable. In the event of overdosage, treatment should be symptomatic and supportive.

EXPIRY DATE

Do not use later than the date of expiry

STORAGE

STORE BELOW 25^{o}C, PROTECTED FROM LIGHT & MOISTURE
Keep all tablets out of the reach of children

PRESENTATION AND AVAILABILITY

Veloz 10 : It is available as yellow coloured, round biconvex, enteric coated tablet, in strip of 10 tablets and blister strip of 7 tablets.
Veloz 20 : It is available as yellow coloured, round biconvex, enteric coated tablet, in strip of 10 tablets and blister strip of 7 tablets.

torrent PHARMA

Manufactured by :
TORRENT PHARMACEUTICALS LTD.
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