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

VELOZ L

1. Generic Name

Enteric Coated Rabeprazole Sodium and Levosulpiride Sustained Release Capsules.

2. Qualitative and quantitative Composition:

Each hard gelatin capsule contains:

Rabeprazole Sodium I.P……20mg (as enteric coated pellets)

Levosulpiride……... 75mg (as sustained release tablet)

Colors: Titanium Dioxide I.P., Ferric Oxide (Red) USP-NF and Ferric Oxide (Black) USP-NF. Approved colors used in capsule shell.

The excipients used are Microcrystalline Cellulose, Lactose Monohydrate, HPMC K I 00 M, Citric Acid Monohydrate, P.V.P.K-30, Purified Water, Magnesium Stearate, Ready to use pellets and Talcum Powder.

3. Dosage form and strength

Dosage form: Hard gelatin capsules

Strength: Rabeprazole (20 mg) and Levosulpiride (75 mg)

4. Clinical particulars

4.1. Therapeutic indication

It is indicated for the treatment of Gastro-easophageal reflux disease (GERD).

4.2. Posology and method of administration

One capsule per day with empty stomach or as directed by physician.

4.3. Contraindications

- Hypersensitivity to the active substance or to any of the excipients.
- Pregnancy and during breast feeding.
- Parkinson disease
- History of epilepsy

4.4. Special warnings and precautions for use

Symptomatic response to therapy with rabeprazole sodium does not preclude the presence of gastric or oesophageal malignancy, therefore the possibility of malignancy should be excluded prior to commencing treatment with VELOZ L.

Patients on long-term treatment (particularly those treated for more than a year) should be kept under regular surveillance.

A risk of cross-hypersensitivity reactions with other proton pump inhibitor (PPI) or substituted benzimidazoles cannot be excluded.

Patients should be cautioned that VELOZ L capsule should not be chewed or crushed, but should be swallowed whole.

VELOZ L is not recommended for use in children, as there is no experience of its use in this group.

There have been post marketing reports of blood dyscrasias (thrombocytopenia and neutropenia). In the majority of cases where an alternative etiology cannot be identified, the events were uncomplicated and resolved on discontinuation of rabeprazole.

Hepatic enzyme abnormalities have been seen in clinical trials and have also been reported since market authorization. In the majority of cases where an alternative etiology cannot be identified, the events were uncomplicated and resolved on discontinuation of rabeprazole.

No evidence of significant drug related safety problems was seen in a study of patients with mild to moderate hepatic impairment versus normal age and sex matched controls. However because there are no clinical data on the use of VELOZ L in the treatment of patients with severe hepatic dysfunction the prescriber is advised to exercise caution when treatment with VELOZ L is first initiated in such patients.

Co-administration of atazanavir with VELOZ L is not recommended.

Treatment with PPIs, including VELOZ L, may possibly increase the risk of gastrointestinal infections such as Salmonella, Campylobacter and Clostridium difficile.

PPIs, especially if used in high doses and over long durations (>1 year), may modestly increase the risk of hip, wrist and spine fracture, predominantly in older people or in presence of other recognized risk factors. Observational studies suggest that PPIs may increase the overall risk of fracture by 10–40%. Some of this increase may be due to other risk factors.

Patients at risk of osteoporosis should receive care according to current clinical guidelines and they should have an adequate intake of vitamin D and calcium.

Severe hypomagnesaemia has been reported in patients treated with PPIs like VELOZ L for at least three months, and in most cases for a year. Serious manifestations of hypomagnesaemia such as fatigue, tetany, delirium, convulsions, dizziness and ventricular arrhythmia can occur but they may begin insidiously and be overlooked. In most affected patients, hypomagnesaemia improved after magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPIs with digoxin or drugs that may cause hypomagnesaemia (e.g., diuretics), health care professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.

Concomitant use of rabeprazole with methotrexate

Literature suggests that concomitant use of PPIs with methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration, a temporary withdrawal of the PPI may be considered in some patients.

Influence on vitamin B12 absorption.

Rabeprazole sodium, as all acid-blocking medicines, may reduce the absorption of vitamin B12 (cyanocobalamin) due to hypo- or a- chlorhydria. This should be considered in patients with reduced body stores or risk factors for reduced vitamin B12 absorption on long-term therapy or if respective clinical symptoms are observed.Subacute cutaneous lupus erythematosus (SCLE)

PPIs are associated with very infrequent cases of SCLE. If lesions occur, especially in sun-exposed areas of the skin, and if accompanied by arthralgia, the patient should seek medical help promptly and the health care professional should consider stopping VELOZ L. SCLE after previous treatment with a PPI may increase the risk of SCLE with other PPIs.

Interference with laboratory tests

Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, VELOZ L treatment should be stopped for at least 5 days before CgA measurements. If CgA and gastrin levels have not returned to reference range after initial measurement, measurements should be repeated 14 days after cessation of PPI treatment.

4.5. Drugs interactions

Rabeprazole

Rabeprazole sodium produces a profound and long lasting inhibition of gastric acid secretion. An interaction with compounds whose absorption is pH dependent may occur. Co-administration of rabeprazole sodium with ketoconazole or itraconazole may result in a significant decrease in antifungal plasma levels. Therefore individual patients may need to be monitored to determine if a dosage adjustment is necessary when ketoconazole or itraconazole are taken concomitantly with VELOZ L.

In clinical trials, antacids were used concomitantly with the administration of VELOZ L and, in a specific drug-drug interaction study, no interaction with liquid antacids was observed.

Co-administration of atazanavir 300 mg/ritonavir 100 mg with omeprazole (40 mg once daily) or atazanavir 400 mg with lansoprazole (60 mg once daily) to healthy volunteers resulted in a substantial reduction in atazanavir exposure. The absorption of atazanavir is pH dependent. Although not studied, similar results are expected with other PPIs. Therefore

PPIs, including rabeprazole, should not be co-administered with atazanavir. Methotrexate

Case reports, published population pharmacokinetic studies, and retrospective analyses suggest that concomitant administration of PPIs and methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite hydroxymethotrexate. However, no formal drug interaction studies of methotrexate with PPIs have been conducted.

Levosulpiride

Antacids and Sucralfate: They can decrease the absorption of the drug from the intestine. So, these medicines should not be taken along with levosulpiride. There should be a minimum 2 hour time lag between the two medicines.

Alcohol: there is increased chance of sedation.

Smoking: increased metabolism of the drug may require higher dose.

Antihypertensive medications: concomitant use may enhance the hypotensive effect seen with the drug.

Anticholinergics: increased incidence of anticholinergic side effects.

Levodopa: It may oppose the antipsychotic action of the drug, conversely levosulpiride can cause decrease the efficacy of levo-dopa in the management of Parkinsonism.

Arrhythmia especially prolonged QT interval with the concurrent use of

Atomoxetine

Antiarrhythmics

Terfenadine

Chloroquine, quinine

Cisapride

Drugs causing hypokalemia (corticosteroids, laxatives, diuretics like furosemide)

4.6. Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

There are no data on the safety of rabeprazole in human pregnancy.

Reproduction studies performed in rats and rabbits have revealed no evidence of impaired fertility or harm to the fetus due to rabeprazole sodium, although low foeto-placental transfer occurs in rats. VELOZ L is contraindicated during pregnancy.

Breast feeding

It is not known whether rabeprazole sodium is excreted in human breast milk. No studies in breast- feeding women have been performed. Rabeprazole sodium is however excreted in rat mammary secretions. Therefore VELOZ L should not be used during breast feeding.

4.7. Effects on ability to drive and use machines

Based on the pharmacodynamic properties and the adverse events profile, it is unlikely that VELOZ L would cause an impairment of driving performance or compromise the ability to use machinery. If however, alertness is impaired due to somnolence, it is recommended that driving and operating complex machinery be avoided.

4.8. Undesirable effects

Rabeprazole

The most commonly reported adverse drug reactions, during controlled clinical trials with rabeprazole were headache, diarrhoea, abdominal pain, asthenia, flatulence, rash and dry mouth. The majority of adverse events experienced during clinical studies were mild or moderate in severity, and transient in nature.

The following adverse events have been reported from clinical trial and post-marketing experience.

Frequencies are defined as: common (> 1/100, < 1/10), uncommon (> 1/1,000, < 1/100), rare (>1/10,000, <1/1000) very rare (<1/10,000), not known (cannot be estimated from the available data).

System Organ Class	Common	Uncommon	Rare	Very Rare	Not Known
Infections and infestations	Infection				
Blood and the			Neutropenia		
lymphatic system disorders			Leucopenia Thrombocytopenia Leucocytosis		
Immune system disorders			Hypersensitivity 1,2		

System Organ Class	Common	Uncommon	Rare	Very Rare	Not Known
Metabolism and nutrition disorders			Anorexia		Hyponatremia Hypomagnesaemia
Psychiatric disorders	Insomnia	Nervousness	Depression		Confusion
Nervous system Disorders	Headache Dizziness	Somnolence			
Eye disorders			Visual disturbance		
Vascular disorders					Peripheral Oedema
Respiratory, thoracic and mediastinal disorders	Cough Pharyngitis Rhinitis	Bronchitis Sinusitis			
Gastrointestinal Disorders	Diarrhoea Vomiting Nausea Abdominal pain Constipation Flatulence Fundic Gland Polyps (Benign)	Dyspepsia Dry mouth Eructation	Gastritis Stomatitis Taste disturbance		Microscopic colitis
Hepato-biliary Disorders			Hepatitis Jaundice Hepatic		
			Encephalopathy 3		
Skin and subcutaneous tissue disorders		Rash Erythema	Pruritus Sweating Bullous reactions	Erythema multiforme, toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS)	Subacute cutaneous lupus erythematosus
Musculoskeletal connective	Non-specific pain Back pain	Myalgia Leg cramps Arthralgia			

System Organ Class	Common	Uncommon	Rare	Very Rare	Not Known
tissue and bone disorders					
Renal and urinary Disorders		Urinary tract Infection	Interstitial nephritis		Acute Kidney Injury
Reproductive system and breast disorders					Gynaecomastia
General disorders and administration site conditions	Asthenia Influenza like Illness	Chest pain Chills Pyrexia			
Investigations		Increased hepatic Enzymes	Weight increased		

1: Includes facial swelling, hypotension and dyspnoea

2: Erythema, bullous reactions and hypersensitivity reactions have usually resolved after discontinuation of therapy.

3: Rare reports of hepatic encephalopathy have been received in patients with underlying cirrhosis.

In treatment of patients with severe hepatic dysfunction, the prescriber is advised to exercise caution when treatment with VELOZ L is first initiated in such patients

Levosulpiride

The following side effects can occur with the use of this drug;

Acute muscular dystonia characterized by abnormal movements (twitching, tremor etc.) of hands, leg, tongue and facial muscles.

Sedation or drowsiness (because of decrease in sensory inputs to reticular activating system)

Increase in plasma prolactin levels manifested by breast enlargement, production of milk and stopping of menstrual periods. This can be taken care of with the use of lower dose of this drug.

Neuroleptic malignant syndrome (characterized by hyperpyrexia, muscle rigidity, increased myoglobin and creatine kinase; the last two suggestive of muscle damage.

Akathisia (uncontrollable desire to move about without any anxiety).

Tardive dyskinesia, it occurs late in the therapy and its features include involuntary rhythmical movements of face, mouth and jaw. The reason for tardive dyskinesia is synthesis of newer DA receptors which are supersensitive to even a small amount of DA. This causes a decrease in cholinergic activity in the striatum followed by decrease in GABA release. This decreased in inhibitory GABA is responsible for increased involuntary motor activity.

Postural hypotension (because of autonomic blockade), tolerance develops to this effect after some time.

Elevated liver transaminases.

Reporting of adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Report suspected adverse reactions via any point of contact available at www.torrentpharma.com.

4.9. Overdose

Experience to date with deliberate or accidental overdose is limited. The maximum established exposure has not exceeded 60 mg twice daily, or 160 mg once daily. Effects are generally minimal, representative of the known adverse event profile and reversible without further medical intervention. No specific antidote is known. Rabeprazole sodium is extensivelyprotein bound and is, therefore, not dialysable. As in any case of overdose, treatment should be symptomatic and general supportive measures should be utilised.

5. Pharmacological properties

5.1. Mechanism of Action

Rabeprazole

Rabeprazole sodium belongs to the class of anti-secretory compounds, the substituted benzimidazoles, that do not exhibit anticholinergic or H2 histamine antagonist properties, but suppress gastric acid secretion by the specific inhibition of the H+/K+-ATPase enzyme (the acid or proton pump) The effect is dose-related and leads to inhibition of both basal and stimulated acid secretion irrespective of the stimulus. Animal studies indicate that after administration, rabeprazole sodium rapidly disappears from both the plasma and gastric mucosa. As a weak base, rabeprazole is rapidly absorbed following all doses and is concentrated in the acid environment of the parietalcells. Rabeprazole is converted to the active sulphenamide form through protonation and it subsequently reacts with the available cysteines on the proton pump.

Levosulpiride

Levosulpiride is selective blocks D2 receptors at the submucosal and myenteric plexus peripheral level, the selective antagonistic action of levosulpiride on the D2 receptors also makes it useful as a prokinetic drug.

5.2. Pharmacodynamic properties

Rabeprazole

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

Anti-secretory activity

After oral administration of a 20 mg dose of rabeprazole sodium the onset of the anti-secretory effect occurs within one hour, with the maximum effect occurring within two to four hours. Inhibition of basal and food stimulated acid secretion 23 hours after the first dose of rabeprazole sodium are 69% and 82% respectively and the duration of inhibition lasts up to 48 hours. The inhibitory effect of rabeprazole sodium on acid secretion increases slightly with repeated once- daily dosing, achieving steady state inhibition after three days. When the drug is discontinued, secretory activity normalises over 2 to 3 days. Decreased gastric acidity due to any means, including PPIs such as rabeprazole, increases counts of bacteria normally present in the gastrointestinal tract. Treatment with PPIs may possibly increase the risk of gastrointestinal infections such as Salmonella, Campylobacter and Clostridium difficile.

Serum gastrin effects

In clinical studies patients were treated once daily with 10 or 20 mg rabeprazole sodium, for up to 43 months duration. Serum gastrin levels increased during the first 2 to 8 weeks reflecting the inhibitory effects on acid secretion and remained stable while treatment was continued. Gastrin values returned to pre-treatment levels, usually within 1 to 2 weeks after discontinuation of therapy.

Human gastric biopsy specimens from the antrum and the fundus from over 500 patients receiving rabeprazole or comparator treatment for up to 8 weeks have not detected changes in ECL cell histology, degree of gastritis, incidence of atrophic gastritis, intestinal metaplasia or distribution of

H. pylori infection. In over 250 patients followed for 36 months of continuous therapy, no significant change in findings present at baseline was observed.

Other effects

Systemic effects of rabeprazole sodium in the CNS, cardiovascular and respiratory systems have not been found to date. Rabeprazole sodium, given in oral doses of 20 mg for 2 weeks, had no effect on thyroid function, carbohydrate metabolism, or circulating levels of parathyroid hormone, cortisol, oestrogen, testosterone, prolactin, cholecystokinin, secretin, glucagon, follicle stimulating hormone (FSH), luteinising hormone (LH), renin, aldosterone or somatotrophic hormone.

Studies in healthy subjects have shown that rabeprazole sodium does not have clinically significant interactions with amoxicillin. Rabeprazole does not adversely influence plasma concentrations of amoxicillin or clarithromycin when coadministered for the purpose of eradicating upper gastrointestinal H. pylori infection. During treatment with antisecretory medicinal products, serum gastrin increases in response to the decreased acid secretion. Also CgA increases due to decreased gastric acidity. The increased CgA level may interfere with investigations for neuroendocrine tumours.

Available published evidence suggests that PPIs should be discontinued between 5 days and 2 weeks prior to CgA measurements. This is to allow CgA levels that might be spuriously elevated following PPI treatment to return to reference range.

Levosulpiride

Levosulpiride is selective blocks D2 receptors, significant amounts of dopamine are present in the gastrointestinal tract, where it causes a marked inhibitory effect on motility. Dopamine acting at inhibitory dopamine D2 receptors located on excitatory neuronal structures and smooth muscle was found to cause reduction in lower oesophageal sphincter tone, gastric tone and intragastric pressure, as well as inhibition of gastro duodenal co-ordination. Blockade of peripheral D2 receptors is considered the main mechanism by which antidopaminergic prokinetic drugs, such as levosulpiride, exert their gastrointestinal stimulatory effect. Antidopaminergic properties of levosulpiride at D2 receptors of the chemoreceptor trigger zone in the area postrema of the fourth ventricle floor is responsible for anti-emetic property.

5.3. Pharmacokinetic properties

Rabeprazole

Absorption

VELOZ L contains enteric-coated (gastro-resistant) pellets of rabeprazole sodium. This presentation is necessary because rabeprazole is acid-labile.

Absorption of rabeprazole therefore begins only after capsule leaves the stomach. Absorption is rapid, with peak plasma levels of rabeprazole occurring approximately 3.5 hours after a 20 mg dose. Peak plasma concentrations (C) of rabeprazole and AUC are linear over the dose range of 10 mg to 40 mg. Absolute bioavailability of an oral 20 mg dose (compared to intravenous administration) is about 52% due in large part to pre-systemic metabolism. Additionally the bioavailability does not appear to increase with repeat administration. In healthy subjects the plasma half-life is approximately one hour (range 0.7 to 1.5 hours), and the total body clearance is estimated to be 283 ± 98 ml/min. There was no clinically relevant interaction with food. Neither food nor the time of day of administration of the treatment affect the absorption of rabeprazole sodium.

Distribution

Rabeprazole is approximately 97% bound to human plasma proteins.

Metabolism and excretion

Rabeprazole sodium, as is the case with other members of the PPI class of compounds, is metabolised through the cytochrome P450 (CYP450) hepatic drug metabolising system. In vitro studies with human liver microsomes indicated that rabeprazole sodium is metabolised by isoenzymes of CYP450 (CYP2C19 and CYP3A4). In these studies, at expected human plasma concentrations rabeprazole neither induces nor inhibits CYP3A4; and although in vitro studies may not always be predictive of in vivo status these findings indicate that no interaction is expected between rabeprazole and cyclosporin. In humans the thioether (M1) and carboxylic acid (M6) are the main plasma metabolites with the sulphone (M2), desmethyl-thioether (M4) and mercapturic acid conjugate (M5) minor metabolites observed at lower levels. Only the desmethyl metabolite (M3) has a small amount of anti-secretory activity, but it is not present in plasma.

Following a single 20 mg 14C labelled oral dose of rabeprazole sodium, no unchanged drug was excreted in the urine.Approximately 90% of the dose was eliminated in urine mainly as the two metabolites: a mercapturic acid conjugate (M5) and a carboxylic acid (M6), plus two unknown metabolites. The remainder of the dose was recovered in faeces.

Gender

Adjusted for body mass and height, there are no significant gender differences in pharmacokinetic parameters following a single 20 mg dose of rabeprazole.

Renal dysfunction

In patients with stable, end-stage, renal failure requiring maintenance haemodialysis (creatinine clearance ≤5ml/min/1.73 m2), the disposition of rabeprazole was very similar to that in healthy volunteers. The AUC and the Cmax in these patients was about 35% lower than the corresponding parameters in healthy volunteers. The mean half-life of rabeprazole was 0.82 hours in healthy volunteers, 0.95 hours in patients during haemodialysis and 3.6 hours post dialysis. The clearance of the drug in patients with renal disease requiring maintenance haemodialysis was approximately twice that in healthy volunteers.

Hepatic dysfunction

Following a single 20 mg dose of rabeprazole to patients with chronic mild to moderate hepatic impairment the AUC doubled and there was a 2-3 fold increase in half-life of rabeprazole compared to the healthy volunteers. However, following a 20 mg dose daily for 7 days the AUC had increased to only 1.5-fold and the Cmax to only 1.2-fold. The half-life of rabeprazole in patients with hepatic impairment was 12.3 hours compared to 2.1 hours in healthy

volunteers. The pharmacodynamic response (gastric pH control) in the two groups was clinically comparable.

Older people

Elimination of rabeprazole was somewhat decreased in older people. Following 7 days of daily dosing with 20 mg of rabeprazole sodium, the AUC approximately doubled, the Cmax increased by 60% and

t½ increased by approximately 30% as compared to young healthy volunteers. However there was no evidence of rabeprazole accumulation.

CYP2C19 polymorphism

Following a 20 mg daily dose of rabeprazole for 7 days, CYP2C19 slow metabolisers, had AUC and t½ which were approximately 1.9 and 1.6 times the corresponding parameters in extensive metabolisers whilst Cmax had increased by only 40%.

Levosulpiride

Absorption

The bioavailability of levosulpiride, when given orally is low (about 27% to 34%) with incomplete absorption as opposed to presystemic metabolism. Food reduces absorption by 30%. The time to peak concentration is 3 to 9 hours with median tmax 5.5 hours. The oral AUC values for levosulpiride extended release for a dose of 200 mg is 6050 ng.hr/ml.

Distribution

Levosulpiride displays a protein binding of about 14% and a volume of distribution of 1 to 2.7 L/kg which is similar in elderly and younger subjects.

Metabolism

Metabolism does not occur and the drug is excreted unchanged into the urine. The renal clearance is 15 to 30%. The drug is substantially excreted in the feces due to poor absorption. The lack of hepatic metabolism makes metabolic interactions with cytochrome P-450 related substrates very unlikely.

Excretion

The elimination half-life ranges from 4.7 to 14.6 hours for oral 200mg dose of levosulpiride ER formulation. The elimination half-life is prolonged in patients with renal impairment. The peak concentrations, time to peak levels and the elimination half-life is similar in younger and elderly patients.

6. Nonclinical properties

6.1. Animal Toxicology or Pharmacology

Non-clinical effects were observed only at exposures sufficiently in excess of the maximum human exposure that make concerns for human safety negligible in respect of animal data.

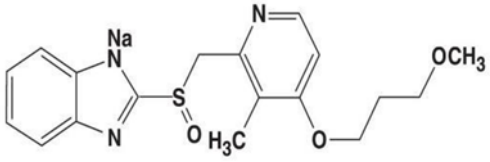
Studies on mutagenicity gave equivocal results. Tests in mouse lymphoma cell line were positive, but in vivo micronucleus and in vivo and in vitro DNA repair tests were negative. Carcinogenicity studies revealed no special hazard for humans.

7. Description

Rabeprazole Sodium:

Rabeprazole Sodium is a substituted benzimidazole known chemically as 2-[[[4-(3-•methoxypropoxy)-3-methyl-2-pyridinyl]-methyl]sulfinyl]-1H–benzimidazole sodium salt. It

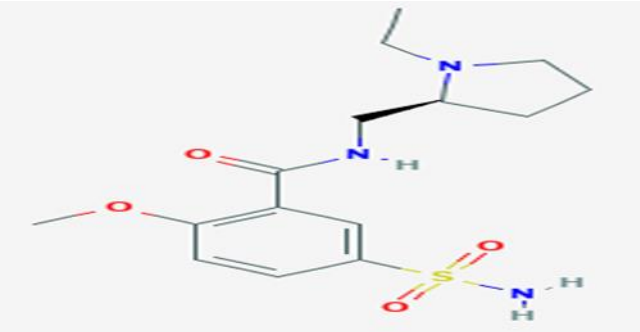
has an empirical formula of $C_{18}H_{20}N_3NaO_3S$ and a molecular weight of 381.42. The chemical structural figure is:



Rabeprazole sodium is white to light yellow, crystalline powder, hygroscopic which is soluble in water.

Levosulpiride:

Levosulpiride is N-[[(2S)-1-ethylpyrrolidin-2-yl]methyl]-2-methoxy-5-sulfamoylbenzamide. It has an empirical formula of $C_{15}H_{23}N_3O_4S$ and a molecular weight of 341.4. The chemical structural figure is:



Enteric Coated Rabeprazole Sodium And Levosulpiride Sustained Release Capsules are Orange color "0" size, hard gelatin capsules, containing white coloured round biconvex uncoated plain on both side Levosulpiride tablet and brownish coloured spherical pellets of Rabeprazole sodium. The excipients used are Microcrystalline Cellulose, Lactose Monohydrate, HPMC K 100M, Citric Acid Monohydrate, P.V.P.K-30, Purified Water, Magnesium Stearate, Ready to use pellets and Talcum Powder.

8. Pharmaceutical particulars

8.1. Incompatibilities

Not applicable

8.2. Shelf-life

Do not use later than the expiry.

8.3. Packaging information

VELOZ L is packed in strips of 10 capsules.

8.4. Storage and handing instructions

Store below 30°C, protected from light and moisture. Keep out of reach of children.

9. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant

- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

10. Details of manufacturer

M/s. Acme Generics Private Limited
Plot No. 115, HPSIDC,
Industrial Area, Vill. Davni,
P.O. Gurumajra, Tehsil Nalagarh,
Distt. Solan, H.P.-174101

11. Details of permission or licence number with date

Mfg Lic No. MNB/15/880 issued on 28.09.2015

12. Date of revision

Feb 2026

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/VELOZ L/20,75mg/FEB-2026/07/PI