SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Trade name : TORZIAM
Generic name : Esomeprazole magnesium tablets 20 mg and 40 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Torziam 20 : Each film coated tablet contains:
Esomeprazole Magnesium equivalent to
Esomeprazole (as enteric coated pellets)…..... 20 mg.

Torziam 40 : Each film coated tablet contains:
Esomeprazole Magnesium equivalent to
Esomeprazole (as enteric coated pellets)…..... 40 mg.

3. PHARMACEUTICAL FORM

Film coated tablets

4. CLINICAL PARTICULAR

4.1 Therapeutic Indication

Treatment of Gastroesophageal Reflux Disease (GERD) Healing of Erosive Esophagitis Torziam is indicated for the short-term treatment (4 to 8 weeks) in the healing and symptomatic resolution of diagnostically confirmed erosive esophagitis. For those patients who have not healed after 4-8 weeks of treatment, an additional 4-8-week course of Torziam may be considered.

4.2 Posology and Method of Administration

Gastroesophageal Reflux Disease (GERD)

Healing of Erosive Esophagitis	20 mg or 40 mg Once Daily for 4 to 8 Weeks
Maintenance of Healing of Erosive Esophagitis	20 mg Once Daily
Prevention of relapse of esophagitis	20 mg Once Daily

H. Pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence
Triple Therapy:

Torziam	40 mg	Once Daily for 10 Days
Amoxicillin	1000 mg	Twice Daily for 10 Days
Clarithromycin	500 mg	Twice Daily for 10 Days

DIRECTION FOR USE

SWALLOW WHOLE OR DIVIDED HALF OF THE TABLET, DO NOT CHEW OR CRUSH.

4.3 Contraindications

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

4.4 Special Warnings and Precautions for Use

General

Symptomatic response to therapy with Esomeprazole Magnesium does not preclude the presence of gastric malignancy. Atrophic gastritis has been noted occasionally in gastric corpus biopsies from patients treated long-term with omeprazole, of which Esomeprazole Magnesium is an enantiomer.

Information for Patients

Patients should be informed of the following:

- Torziam tablets should be taken at least one hour before meals.
- Antacids may be used while taking Torziam.

4.5 Interaction with Other Medicinal Products and Other Forms of Interactions

Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4.
In vitro and in vivo studies have shown that Esomeprazole is not likely to inhibit CYPs 1A2, 2A6, 2C9, 2D6, 2E1 and 3A4. No clinically relevant interactions with drugs metabolized by these CYP enzymes would be expected. Drug interaction studies have shown that Esomeprazole does not have any clinically significant interactions with phenytoin, warfarin, quinidine, clarithromycin or amoxicillin.

Esomeprazole may potentially interfere with CYP2C19, the major Esomeprazole metabolizing enzyme. Coadministration of Esomeprazole 30mg and diazepam, a CYP2C19 substrate, resulted in a 45% decrease in clearance of diazepam. Increased plasma levels of diazepam were observed 12 hours after dosing and onwards. However, at that time, the plasma levels of diazepam were below the therapeutic interval, and thus this interaction is unlikely to be of clinical relevance. Esomeprazole inhibits gastric acid secretion. Therefore, Esomeprazole may interfere with the absorption of drugs where gastric pH is an important determinant of bioavailability (e.g., ketoconazole, iron salts and digoxin).

Coadministration of oral contraceptives, diazepam, phenytoin, or quinidine did not seem to change the pharmacokinetic profile of Esomeprazole.

4.6 Pregnancy and Lactation

Pregnancy Category B

Teratology studies performed in rats at oral doses up to 280 mg/kg/day (about 57 times the human dose on a body surface area basis) and in rabbits at oral doses up to 86

mg/kg/day (about 35 times the human dose on a body surface area basis) revealed no evidence of impaired fertility or harm to the foetus due to Esomeprazole. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

The excretion of Esomeprazole in milk has not been studied. Since Esomeprazole is likely to be excreted in human milk, because of the potential for serious adverse reactions in nursing infants from Esomeprazole, and because of the potential for tumorigenicity shown for omeprazole in rat carcinogenicity studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Undesirable Effects

Esomeprazole Magnesium was well tolerated in both short and long-term clinical trials. The most frequently occurring adverse events (≥1%) with Esomeprazole 20 mg and 40mg were headache, diarrhoea, nausea, flatulence, abdominal pain, constipation, and dry mouth.

4.8 Overdose

There have been no reports of overdose with Esomeprazole. Reports have been received of over dosage with omeprazole in humans. Doses ranged up to 2,400 mg (120 times the usual recommended clinical dose). Manifestations were variable, but included confusion, drowsiness, blurred vision, tachycardia, nausea, diaphoresis, flushing, headache, dry mouth, and other adverse reactions similar to those seen in normal clinical experience. No specific antidote for Esomeprazole is known. Since Esomeprazole is extensively protein bound, it is not expected to be removed by dialysis. In the event of over dosage, treatment should be symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics Properties

Pharmacotherapeutic group: Proton Pump Inhibitor
ATC code: A02B C05

Mechanism of Action

Esomeprazole is the S-isomer of omeprazole and reduces gastric acid secretion through a specific targeted mechanism of action. Esomeprazole is a weak base and is concentrated and converted to the active form in the highly acidic environment of the secretory canaliculi of the parietal cell, where it inhibits the enzyme H+K+-ATPase – the acid pump and inhibits both basal and stimulated acid secretion.

5.2 Pharmacokinetic Properties

PHARMACOKINETICS
Absorption

After oral administration of Esomeprazole magnesium, peak plasma levels (Cmax) occur at approximately 1.5 hours (Tmax). The Cmax increases proportionally when the dose is increased and there is a three-fold increase in the area under the plasma concentration-time curve (AUC) from 20 to 40 mg. At repeated once daily dosing with 40 mg, the systemic bioavailability is approximately 90% compared to 64% after a single dose of 40 mg. The mean exposure (AUC) to Esomeprazole increases from 4.32 μmol.hr/L on day 1 to 11.2 μmol.hr/L on day 5 after 40mg once daily dosing.

The AUC after administration of a single 40mg dose of Esomeprazole is decreased by 33-53% after food intake compared to fasting conditions. Esomeprazole should be taken at least one hour before meals.

Distribution

Esomeprazole is 97% bound to plasma proteins. Plasma protein binding is constant over the concentration range of 2-20 μmol/L.
The apparent volume of distribution at steady state in healthy volunteers is approximately 16 L.

Metabolism

Esomeprazole is extensively metabolized in the liver by the cytochrome P450 (CYP) enzyme system. Following administration of equimolar doses, the S-and R-isomers are metabolized differently by the liver, resulting in higher plasma levels of the S- than of the R-isomer.

Excretion

The plasma elimination half-life of Esomeprazole is approximately 1-1.5 hours. Less than 1% of parent drug is excreted in the urine. Approximately 80% of an oral dose of Esomeprazole is excreted as inactive metabolites in the urine and the remainder is found as inactive metabolites in the faeces.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Microcrystalline Cellulose (Avicel PH 200), Copovidone (K-28), Crospovidone (Polyplasdone XL-10), Talc, Colloidal Silicon Dioxide (Aerosil 200), Magnesium Stearate, TRC COAT – A, Ferric Oxide Red and Purified water.

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

2 years

6.4 Special Precaution for Storage

Storage below 30°C.

6.5 Name and Content of Container

Torziam tablets are packed in Alu – Alu blisters of 10 tablets, such blisters are packed in a carton along with patient information leaflet.

6.6 Special Precautions for Disposal and other Handling

No special requirement.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. MANUFACTURED BY

TORRENT PHARMACEUTICALS LTD.
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MARKETED BY

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