SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT:
ESOVIN (Esomeprazole Tablets 40 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each Enteric Coated Tablet Contains:
Esomeprazole Magnesium Trihydrate BP Equivalent to Esomeprazole.....40 mg
Excipients .....Q.S.
Approved Colour Used

3. PHARMACEUTICAL FORM:
Enteric Coated Tablet

Description: Brown coloured, capsule shaped biconvex, enteric coated tablet breakline on one side and plain on other side.

4. CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS
ESOVIN (Esomeprazole Tablets 40 mg) is indicated for
Gastro-esophageal Reflux Disease (GERD):
- Treatment of erosive reflux oesophagitis
- Long-term management of patients with healed oesophagitis to prevent relapse
- Symptomatic treatment of gastro-esophageal reflux disease (GERD)

In combination with an appropriate antibacterial therapeutic regimen for the eradication of Helicobacter pylori:
- Healing of Helicobacter pylori associated duodenal ulcer
- Prevention of relapse of peptic ulcers in patients with Helicobacter pylori associated ulcers.

Patients requiring continued NSAID therapy:
- Healingof gastric ulcers associated with NSAID therapy.
- Prevention of gastric and duodenal ulcers associated with NSAID therapy, in patients at risk.

Prolonged treatment after i.v. induced prevention of rebleeding of peptic ulcers.
Gastro-esophageal Reflux Disease (GERD):
- Treatment of erosive reflux oesophagitis
- Long-term management of patients with healed oesophagitis to prevent relapse
- Symptomatic treatment of gastro-esophageal reflux disease (GERD)

4.2 POSOLOGY AND METHOD OF ADMINISTRATION
Route: Oral
Adults
Gastro-esophageal Reflux Disease (GERD):
- Treatment of erosive reflux oesophagitis
40 mg once daily for 4 weeks.
Patients requiring continued NSAID therapy:

Healing of gastric ulcers associated with NSAID therapy. The recommended dose is 20 mg once daily. The treatment duration is 4-8 weeks.
Prevention of gastric and duodenal ulcers associated with NSAID therapy in patients at risk 20 mg once daily.

Prolonged treatment after i.v. induced prevention of reblceding of peptic ulcers:

40 mg once daily for 4 weeks after i.v. induced prevention of rebleeding of peptic ulcers.

Treatment of Zollinger Ellison Syndrome:

The recommended initial dosage is Esomeprazole 40 mg twice daily. The dosage should then be individually adjusted and treatment continued as long as clinically indicated. Based on the clinical data available, the majority of patients can be controlled on doses between 80 and 160 mg Esomeprazole daily. With doses above 80 mg daily, the dose should be divided and given twice daily

Special populations

Impaired renal function:

Dose adjustment is not required in patients with impaired renal function. Due to limited experience in patients with severe renal insufficiency, such patients should be treated with caution.

Impaired hepatic function:

Dose adjustment is not required in patients with mild to moderate liver impairment. For patients with severe liver impairment, a maximum dose of 20 mg Esomeprazole should not be exceeded.

Elderly

Dose adjustment is not required in the elderly.

Paediatric population

Not recommended.

4.3 CONTRAINDICATIONS

Esomeprazole Tablets 40 mg are contraindicated in patients with hypersensitivity to esomeprazole, substituted benzimidazoles or to any of the excipients from formulation. Esomeprazole should not be used concomitantly with nelfinavir.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

In the presence of any alarm symptom (e.g. significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis or melaena) and when gastric ulcer is suspected or present, malignancy should be excluded, as treatment with Esomeprazole may alleviate symptoms and delay diagnosis.

Helicobacter pylori eradication:

When prescribing esomeprazole for eradication of Helicobacter pylori possible drug interactions for all components in the triple therapy should be considered. Clarithromycin is a potent inhibitor of CYP3A4 and hence contraindications and interactions for clarithromycin should be considered when the triple therapy is used in patients concurrently taking other drugs metabolised via CYP3A4 such as cisapride.

Gastrointestinal infections:

Treatment with proton pump inhibitors may lead to slightly increased risk of gastrointestinal infections such as Salmonella and Campylobacter.

Absorption of vitamin B12:

Esomeprazole, as all acid-blocking medicines, may reduce the absorption of vitamin B12 (cyanocobalamin) due to hypo- or achlorhydria. This should be considered in patients with reduced body stores or risk factors for reduced vitamin B12 absorption on long-term therapy.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Co-administration of esomeprazole with atazanavir is not recommended. If the combination of atazanavir with a proton pump inhibitor is judged unavoidable, close clinical monitoring is recommended in combination with an increase in the dose of atazanavir to 400 mg with 100 mg of ritonavir; esomeprazole 20 mg should not be exceeded.

Esomeprazole is a CYP2C19 inhibitor. When starting or ending treatment with esomeprazole, the potential for interactions with drugs metabolised through CYP2C19 should be considered. An interaction is observed between clopidogrel and omeprazole. The clinical relevance of this interaction is uncertain. As a precaution, concomitant use of esomeprazole and clopidogrel should be discouraged.

When given together with PPIs, methotrexate levels have been reported to increase in some patients.

In high-dose methotrexate administration a temporary withdrawal of esomeprazole may need to be considered. Concomitant administration of esomeprazole has been reported to increase the serum levels of tacrolimus. A reinforced monitoring of tacrolimus concentrations as well as renal function (creatinine clearance) should be performed, and dosage of tacrolimus adjusted if needed.

Concomitant administration of 30 mg esomeprazole resulted in a 45% decrease in clearance of the CYP2C19 substrate diazepam.

4.6 PREGNANCY AND LACTATION

<u>Pregnancy</u>

For esomeprazole, clinical data on exposed pregnancies are insufficient.

Animal studies with esomeprazole do not indicate direct or indirect harmful effects with respect to embryonal/foetal development.

A moderate amount of data on pregnant women (between 300-1000 pregnancy outcomes) indicates no malformative or foeto/neonatal toxicity of esomeprazole. As a precautionary measure, it is preferable to avoid the use of Pantoprazole during pregnancy.

<u>Lactation</u>

It is not known whether esomeprazole is excreted in human breast milk.

There is insufficient information on the effects of esomeprazole in newborns/infants. Therefore Esomeprazole should be used with caution during breast-feeding.

<u>Fertility</u>

There is no evidence to suggest that taking esomeprazole will reduce fertility in either men or women

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Esomeprazole has minor influence on the ability to drive and use machines.
Adverse reactions such as dizziness (uncommon) and blurred vision (rare) have been reported. If affected, patients should not drive or use machines.

4.8 UNDESIRABLE EFFECTS

Headache, abdominal pain, diarrhoea and nausea are among those adverse reactions that have been most commonly reported in clinical trials (and also from postmarketing use). In addition, the safety profile is similar for different formulations, treatment indications, age groups and patient populations. No dose-related adverse reactions have been identified.

Reporting of Suspected Adverse Reaction: None adverse reactions were reported to National Regulatory Agencies.

4.9 OVERDOSE

Esomeprazole is extensively plasma protein bound and is therefore not readily dialyzable. As in any case of overdose, treatment should be symptomatic and general supportive measures should be utilised.
No specific antidote is known.

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Proton Pump Inhibitor. ATC code: A02BC05
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

Absorption: Esomeprazole is acid labile and is administered orally as enteric coated granules. Absorption of esomeprazole is rapid, with peak plasma levels occurring approximately 1-2 hours after dose. The absolute bioavailability is 64% after a single dose of 40 mg and increases to 89% after repeated once daily administration. For 20 mg esomeprazole the corresponding values are 50% and 68%, respectively.
Distribution: The apparent volume of distribution at steady state in healthy subjects is approximately 0.22 L/kg body weight. Esomeprazole is 97% plasma protein bound.
Metabolisms: Esomeprazole is completely metabolised by the cytochrome P450 system (CYP). The major part of the metabolism of esomeprazole is dependent on the polymorphic CYP2C19, responsible for the formation of the hydroxyl- and desmethyl metabolites of esomeprazole. The remaining part is dependent on

another specific isoform, CYP3A4, responsible for the formation of esomeprazole sulphone, the main metabolite in plasma.
Elimination: The plasma elimination half-life is about 1.3 hours after repeated once-daily dosing. Esomeprazole is completely eliminated from plasma between doses with no tendency for accumulation during once-daily administration.
The major metabolites of esomeprazole have no effect on gastric acid secretion. Almost 80% of an oral dose of esomeprazole is excreted as metabolites in the urine, the remainder in the faeces. Less than 1% of the parent drug is found in urine.

5.3 PRECLINICAL SAFETY DATA
Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development. Adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use were as follows: Carcinogenicity studies in the rat with the racemic mixture (omeprazole) have shown gastric ECL-cell hyperplasia and carcinoids. These gastric effects in the rat are the result of sustained, pronounced hypergastrinaemia secondary to reduced production of gastric acid and are observed after long-term treatment in the rat with inhibitors of gastric acid secretion.

6. PHARMACEUTICAL PARTICULARS
6.1 LIST OF EXCIPIENTS
Lactose monohydrate, Maize starch, Croscarmellose sodium, Meglumine, Calcium Carbonate, Povidone K-30, Magnesium Stearate, Crospovidone, Colloidal anhydrous silica, Cellacefate, Titanium Dioxide, Red Oxide of Iron, Diethyl Phthalate and Macrogol 6000.

Excipient with known effect: Lactose monohydrate

6.2 INCOMPATIBILITIES
Not applicable

6.3 SHELF LIFE
36 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE
Store below 30°C in dry and dark place.
Keep all medicines out of reach of children

6.5 NATURE AND CONTENTS OF CONTAINER
Primary packing: 7 Tablets in an ALU-ALU blister.
Secondary packing: 2 Blisters are packed in an inner carton along with leaflet.
Tertiary packing: Such 10 inner cartons are packed in an outer carton. Shrink individual outer carton. Such 50 Shrinks are packed in a 5 Ply shipper sealed with BOPP tape & strap with strapping roll.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL <AND OTHER HANDLING>
None

7. MARKETING AUTHORIZATION HOLDER AND MANUFACTURING SITE ADDRESS
Marketing Authorisation Holder
M/s. VINCARE CONSULTING LIMITED
P. O. box 7343-00200 Nairobi, Kenya

Manufacturing Site Address
M/s. IMPULSE PHARMA PVT. LTD.
J-201, J-202/1, MIDC Tarapur, Boisar,
Dist. Palghar - 401506, Maharashtra State, India.
Contact Person's Phone No.: +91 7350864803
Contact Person's email: pravin.patil@kamlagroup.co.in

8. MARKETING AUTHORISATION NUMBER
CTD11970

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION
27/06/2026

10. DATE OF REVISION OF THE TEXT
27/06/2026