PROFESSIONAL INFORMATION FOR

ESOMEPRAZOLE 10 GRANULES CIPLA

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

ESOMEPRAZOLE 10 GRANULES CIPLA 10 mg, granules for oral suspension.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains esomeprazole magnesium dihydrate equivalent to esomeprazole 10 mg granules for oral suspension.

Contains sugar: dextrose 2955,9 mg and sucrose 7,46 mg per sachet For full list of excipients, see **section 6.1**.

3. PHARMACEUTICAL FORM

Granules for oral suspension.

Powder: fine yellow powder consisting of white to pale brownish esomeprazole granules and pale yellow inactive granules.

After reconstitution: opaque, pale yellow coloured, viscous liquid with suspended particle.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ESOMEPRAZOLE 10 GRANULES CIPLA are indicated for:

Gastro-oesophageal reflux disease (GORD):

- treatment of erosive reflux oesophagitis
- long-term management of patients with healed oesophagitis to prevent relapse
- symptomatic treatment of Gastro-oesophageal Reflux Disease (GORD).

4.2 Posology and method of administration

Posology

Paediatric population

Children 1 to 11 years

Gastro-oesophageal reflux disease (GORD)

Treatment of erosive reflux oesophagitis:

Weight < 20 kg: the recommended dose is 10 mg once daily for 8 weeks.

Weight ≥ 20 kg: the recommended dose is 10 mg or 20 mg once daily for 8 weeks.

Symptomatic treatment of Gastro-oesophageal Reflux Disease (GORD):

The recommended dose is 10 mg once daily for up to 8 weeks.

Long-term management of patients with healed oesophagitis to prevent relapse:

The recommended dose is 10 mg once daily.

Doses over 1 mg/kg have not been studied.

Children under 1 year

ESOMEPRAZOLE 10 GRANULES CIPLA should not be used in children less than a year old since no data is available.

Special populations

Impaired renal function

Dose adjustment is not necessary in patients with renal impairment. ESOMEPRAZOLE 10

GRANULES CIPLA should be used with caution in patients with severe renal insufficiency due to limited experience in these patients.

Impaired hepatic function

Dose adjustment is not necessary in patients with mild to moderate hepatic impairment. A maximum daily dose of 20 mg should be used in patients with severe hepatic impairment.

Elderly (patients ≥ 65 years)

Dose adjustment is not necessary in the elderly.

Method of administration

For oral use.

The contents of the 10 mg sachet should be emptied into a container containing a tablespoon (15 mL) of water. Stir the contents and leave for a few minutes to thicken. Stir again and drink within 30 minutes. If any material remains after drinking, add more water, stir, and drink immediately.

For patients who have a nasogastric or gastric tube in place, the contents of the sachet can be added to a syringe containing 15 mL of water. Immediately shake the syringe and leave for a few minutes to thicken. Shake the syringe and inject through the nasogastric or gastric tube within 30 minutes. Refill the syringe with an equal amount of water and shake and flush any remaining contents from the nasogastric or gastric tube into the stomach.

4.3 Contraindications

ESOMEPRAZOLE 10 GRANULES CIPLA is contraindicated in:

- Patients with known hypersensitivity to esomeprazole, substituted benzimidazoles or to any of the excipients in ESOMEPRAZOLE 10 GRANULES CIPLA (see **section 6.1**).

ESOMEPRAZOLE 10 GRANULES CIPLA should not be used concomitantly with atazanavir and nelfinavir (see **section 4.5**).

4.4 Special warnings and precautions for use

Esomeprazole as in ESOMEPRAZOLE 10 GRANULES CIPLA is not indicated for mild gastrointestinal complaints such as nervous dyspepsia.

Prior to treatment or in the presence of any alarm symptom (e.g. significant unintentional weightloss, recurrent vomiting, dysphagia, haematemesis or melaena) and when gastric ulcer is suspected or present, the possibility of malignancy of gastric ulcer or a malignant disease of the oesophagus should be excluded as the treatment with esomeprazole may alleviate the symptoms of malignant ulcers and can thus delay diagnosis.

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

On demand treatment:

Patients on on-demand treatment should be instructed to contact their medical practitioner if their symptoms change in character. On demand treatment has not been investigated in children and is therefore not recommended in this patient group.

Reported concomitant administration of clopidogrel and esomeprazole resulted in decreased exposure to the active metabolite of clopidogrel by an average of 40 %. The reported maximum inhibition of (ADP induced) platelet aggregation decreased by an average of 14 %. Based on these data, concomitant use of esomeprazole and clopidogrel should be avoided.

During treatment with antisecretory medicines, serum gastrin increases in response to the decreased acid secretion. Also, chromogranin A (CgA) increase due to decreased gastric acidity.

The increased CgA level may interfere with investigations for neuroendocrine tumours. To avoid this interference, the esomeprazole treatment should be temporarily stopped 5 days before CgA measurements.
If CgA and gastrin levels have not returned to the reference range after initial measurement, measurements should be repeated 14 days after cessation of proton pump inhibitor treatment.

Decreased gastric acidity increases gastric contents counts of bacteria normally present in the gastrointestinal tract. Treatment with proton pump inhibitors may lead to increased risk of gastrointestinal infections such as Salmonella and Campylobacter and, in hospitalised patients, possibly also Clostridium difficile.

Clostridium difficile is a bacterium that can cause severe debilitating diarrhoea that does not improve. Symptoms may include watery stools, abdominal pain, fever, and patients may develop more serious intestinal conditions.

Proton pump inhibitors are associated with very infrequent cases of subacute cutaneous lupus erythematosus (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 practitioner should consider stopping ESOMEPRAZOLE 10 GRANULES CIPLA. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

Special Precautions

Patients on long-term treatment (particularly those treated for more than a year) should be kept under regular surveillance.
Decreased gastric acidity due to any means including proton pump inhibitors such as esomeprazole, increases gastric counts of bacteria normally present in the gastrointestinal tract.

Treatment with esomeprazole may lead to increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacter* and also *Clostridium difficile* in hospitalised patients.

Risk of interstitial nephritis

Interstitial nephritis has been reported on patience treated with esomeprazole. Interstitial nephritis may progress to acute kidney injury and/or chronic renal failure even after esomeprazole treatment discontinuation.

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 triple therapy is used in patients concurrently taking other medicines metabolised via CYP3A4, such as cisapride.

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.

Hypomagnesaemia

Severe hypomagnesaemia has been reported in patients treated with proton pump inhibitors (PPIs) like esomeprazole for at least three months, and in most cases for a year. In most affected patients, hypomagnesaemia improved after magnesium replacement and discontinuation of the esomeprazole.

Risk of fractures

Proton pump inhibitors, 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 the elderly or in presence of other recognised risk factors. Observational studies suggest that proton pump inhibitors may increase the overall risk of fracture by 10 to 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.

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

Serious cutaneous adverse reactions (SCARs)

Serious cutaneous adverse reactions (SCARs) such as erythema multiforme (EM), Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening, have been reported very rarely in association with esomeprazole treatment.

Patients should be advised of the signs and symptoms of the severe skin reaction EM/SJS/TEN/DRESS and should seek medical advice from their medical practitioner immediately when observing any indicative signs or symptoms.

Esomeprazole should be discontinued immediately upon signs and symptoms of severe skin reactions and additional medical care/close monitoring should be provided as needed.

Re-challenge should not be undertaken in patients with EM/SJS/TEN/DRESS.

Excipients with known effect

ESOMEPRAZOLE 10 CIPLA GRANULES CIPLA contains sucrose and dextrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-

isomaltase insufficiency should not take ESOMEPRAZOLE 10 GRANULES CIPLA. ESOMEPRAZOLE 10 CIPLA GRANULES CIPLA may be harmful to the teeth.

4.5 Interaction with other medicines and other forms of interaction

Effects of esomeprazole on the pharmacokinetics of other medicines:

The gastric acid suppression during treatment with esomeprazole, might decrease or increase the absorption of medicines with a gastric pH dependent absorption. The absorption of medicines such as ketoconazole, itraconazole and erlotinib can decrease while the absorption of medicines such as digoxin can increase during treatment with esomeprazole. Concomitant treatment with omeprazole (20 mg daily) and digoxin increased the bioavailability of digoxin by 10 % (up to 30 % in 2 out of 10 subjects). Digoxin toxicity has been reported. Caution should be exercised when esomeprazole is given at high doses in elderly patients. Therapeutic monitoring of digoxin levels should be done.

Esomeprazole inhibits CYP2C19, the major esomeprazole metabolising enzyme. Concomitant administration of 30 mg esomeprazole resulted in a 45 % decrease in clearance of the CYP2C19 substrate diazepam. This interaction is unlikely to be of clinical relevance.
Concomitant administration of 40 mg esomeprazole resulted in a 13 % increase in trough plasma levels of phenytoin in epileptic patients; dose adjustment was not required in this study.

Concomitant administration of 40 mg esomeprazole to warfarin-treated patients showed that, despite elevation in the trough plasma concentration of the less potent R-isomer of warfarin, the coagulation times were within the accepted range.

From post marketed use, cases of elevated INR of clinical significance have been reported during concomitant treatment with warfarin. Close monitoring is recommended when warfarin is co-administered with esomeprazole at initiation of treatment, during the treatment and at ending

treatment.

A pharmacokinetic/ pharmacodynamic interaction between clopidogrel (300 mg loading dose/75 mg daily maintenance dose) and esomeprazole (40 mg p.o. daily) has been reported, resulting in decreased exposure to the active metabolite of clopidogrel by an average of 40 % and resulting in decreased maximum inhibition of (ADP induced) platelet aggregation by an average of 14 %. Based on these data, concomitant use of esomeprazole and clopidogrel should be avoided.

Omeprazole as well as esomeprazole act as inhibitors of CYP 2C19. Omeprazole given in doses of 40 mg, increased C_{max} and AUC for cilostazol by 18 % and 26 % respectively, and one of its metabolites by 29 % and 69 % respectively.

Esomeprazole can be suspected to have a similar effect.

Concomitant administration of 40 mg esomeprazole resulted in a 32 % increase in area under the plasma concentration-time curve (AUC) and a 31 % prolongation of elimination half-life ($t_{½}$) but no significant increase in peak plasma levels of cisapride. This interaction did not alter the influence of cisapride on cardiac electrophysiology.

When given together with proton pump inhibitors, methotrexate levels have been reported to increase in some patients. In high-dose methotrexate administration a temporary withdrawal of esomeprazole as in ESOMEPRAZOLE 10 GRANULES CIPLA may need to be considered.

Esomeprazole has been shown to have no clinically relevant effects on the pharmacokinetics of amoxicillin or quinidine.

Studies evaluating concomitant administration of esomeprazole and either naproxen (nonselective NSAID) or rofecoxib (COX-2-selective NSAID) did not identify any clinically relevant interaction.

Concomitant administration of esomeprazole may significantly reduce the plasma levels of atazanavir.

Omeprazole has been reported to interact with some antiretroviral medicines. Increased gastric pH during omeprazole treatment may change the absorption of the antiretroviral medicines. Other possible interaction mechanisms are via CYP2C19. For some antiretroviral medicines, such as atazanavir and nelfinavir, decreased serum levels have been reported when given together with omeprazole and concomitant administration is not recommended. For other antiretroviral medicines, such as saquinavir, increased serum levels have been reported of 80 to 100 %. There are also some antiretroviral medicines for which unchanged serum levels have been reported when given with omeprazole. Close monitoring or dose alteration is recommended.

Concomitant administration with esomeprazole and antiretroviral medicines such as atazanavir and nelfinavir is not recommended. Esomeprazole substantially decreases the concentration of atazanavir and nelfinavir (see **section 4.3**).

Co-administration of esomeprazole (40 mg once daily) reduced mean nelfinavir exposure by approximately 40 % and the mean exposure of the pharmacological active metabolite was reduced by approximately 75 to 90 %.

Tipranavir may decrease the concentration of esomeprazole. Co-administration is not recommended. However, if used concurrently, the dose of esomeprazole should be increased.

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.

Effects of other medicines on the pharmacokinetics of esomeprazole

Esomeprazole is metabolised by CYP2C19 and CYP3A4. Concomitant administration of esomeprazole and a CYP3A4 inhibitor, clarithromycin (500 mg twice daily), resulted in a doubling of the exposure (AUC) to esomeprazole.

Concomitant administration of esomeprazole and a combined inhibitor of CYP2C19 and CYP3A4, such as voriconazole, may result in more than tripling of the esomeprazole exposure. Dose adjustment of esomeprazole is not required.

Medicines known to induce CYP2C19 or CYP3A4 or both (such as rifampicin and St. John's Wort) may lead to decreased esomeprazole serum levels by increasing the esomeprazole metabolism.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety during pregnancy and lactation has not been established. With the racemic mixture omeprazole, data on a larger number of exposed pregnancies from epidemiological studies indicate no malformative nor foetotoxic effect. Animal studies with esomeprazole do not indicate direct or indirect harmful effects with respect to embryonal/foetal development. Animal studies with the racemic mixture do not indicate direct or indirect harmful effects with respect to pregnancy, parturition or postnatal development. Caution should be exercised when prescribing to pregnant women.

A moderate amount of data on pregnant women (between 300-1000 pregnancy outcomes) indicates no malformative or foeto/neonatal toxicity of esomeprazole.

Breast-feeding

It is not known whether esomeprazole is excreted in human breast milk. There is insufficient information on the effects of esomeprazole in newborns/infants. Esomeprazole should not be used during breast-feeding.

Fertility

Animal studies with the racemic mixture omeprazole, given by oral administration do not indicate effects with respect to fertility.

4.7 Effects on ability to drive and use machines

ESOMEPRAZOLE 10 GRANULES CIPLA may cause dizziness and blurred vision, thereby affecting the ability to drive or use machinery.

4.8 Undesirable effects

Summary of the safety profile

Headache, abdominal pain, diarrhoea and nausea are among those adverse reactions that have been most commonly reported in clinical trials (and also from post-marketing 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.

Tabulated list of adverse reactions

MedDRA system organ class	**Frequency**	**Side effects**
Blood and lymphatic system disorders	*Less frequent:*	Leukopenia, thrombocytopenia, agranulocytosis, pancytopenia
Immune system disorders	*Less frequent:*	Hypersensitivity reactions e.g. fever, angioedema, anaphylactic reaction/shock
Metabolism and nutrition disorders	*Less frequent:*	Peripheral oedema, hyponatraemia,
	Frequency unknown:	Hypomagnesaemia; severe hypomagnesaemia can correlate with hypocalca. Hypomagnesaemia may also be associated with hypokalaemia.

MedDRA system organ class	**Frequency**	**Side effects**
Psychiatric disorders	*Less frequent:*	Insomnia, agitation, confusion, depression, aggression, hallucination
Nervous system disorders	*Frequent:*	Headache
	Less frequent:	Dizziness, paraesthesia, somnolence, taste disturbance
Eye disorders	*Less frequent:*	Blurred vision
Ear and labyrinth disorders	*Less frequent:*	Vertigo
Respiratory, thoracic and mediastinal disorders	*Less frequent:*	Bronchospasm
Gastrointestinal disorders	*Frequent:*	Abdominal pain, diarrhoea, flatulence, nausea/vomiting, constipation, benign polyps in the stomach

	Less frequent:	Dry mouth, stomatitis, gastrointestinal candidiasis, gastrointestinal infections, microscopic colitis
Hepato-biliary disorders	*Less frequent:*	Increased liver enzymes, hepatitis with or without jaundice, hepatic encephalopathy encephalopathy in patients with existing liver disease, hepatic failure.
Skin and subcutaneous tissue disorders	*Less frequent:*	Dermatitis, pruritus, urticaria, rash, alopecia, photosensitivity, Erythema multiforme, Stevens-Johnson syndrome epidermal necrolysis (TEN), Drug reaction with eosinophilia and systemic symptoms (DRESS).
Musculoskeletal, connective tissue and bone disorders	*Less frequent:*	Arthralgia, myalgia, fracture of the hip, wrist or spine, Muscular weakness.
Renal and urinary disorders	*Frequency unknown:*	Interstitial nephritis, in some patients renal failure been reported concomitantly.
Reproductive system and breast disorders	*Less frequent:*	Gynaecomastia
General disorders and administration site conditions	*Less frequent:*	Malaise, hyperhidrosis

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website or to Cipla Medpro (Pty) Ltd. by email: drugsafetysa@cipla.com or telephone: 080 222 6662 (toll free).

4.9 Overdose

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 11.4.3 Other - Medicines acting on gastro-intestinal tract.
Pharmacotherapeutic group: Medicines for acid-related disorders, proton pump inhibitors.
ATC code: A02BC05

Mechanism of action

Esomeprazole, the S-isomer of omeprazole, reduces gastric acid secretion through specific inhibition of the acid pump in the parietal cell, where it is concentrated and converted to the active form in the acidic environment of the secretory canaliculi and inhibits the enzyme H^+K^+- ATPase – the acid pump. This effect on the final step of the gastric acid secretion is dose- dependent and provides for effective inhibition of both basal and stimulated acid secretion.

Pharmacodynamic effects

After oral dosing with esomeprazole 20 mg and 40 mg, the onset of effect occurs within 1 hour. After repeated administration with 20 mg esomeprazole once daily for 5 days, mean peak acid output after pentagastrin stimulation is decreased by 90 % when measured 6 to 7 hours after dosing on day 5.

After 5 days of oral dosing with 20 mg and 40 mg of esomeprazole, intragastric pH above 4 was maintained for a mean time of 13 hours and 17 hours, respectively over 24 hours in symptomatic Gastro-oesophageal Reflux Disease (GORD) patients. The proportion of patients maintaining an intragastric pH above 4 for at least 8, 12 and 16 hours were 76 %, 54 % and 24 % respectively for esomeprazole 20 mg. Corresponding proportions for esomeprazole 40 mg were 97 %, 92 % and 56 % respectively.

Using AUC as a surrogate parameter for plasma concentration, a relationship between inhibition of acid secretion and exposure has been shown.

Food intake had no significant influence on the effect of esomeprazole on intragastric acidity.

Other effects related to acid inhibition

During long-term treatment with antisecretory medicines, gastric glandular cysts occur. These changes are a physiological consequence of pronounced inhibition of acid secretion, are benign and appear to be reversible.

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 proton pump inhibitors 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.

5.2 Pharmacokinetic properties

Absorption

Esomeprazole is acid labile and is administered orally as enteric-coated granules. *In vivo* conversion to the R-isomer is negligible. Absorption of esomeprazole is rapid, with peak plasma levels occurring approximately 1 to 2 hours after dose. The absolute bioavailability is 89 % after repeated once-daily administration.

Distribution

The apparent volume of distribution at steady state in healthy subjects is approximately 0,22 litres/kg body weight. Esomeprazole is 97 % plasma protein bound.

Biotransformation

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 hydroxy- 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.

The parameters below reflect mainly the pharmacokinetics in individuals with a functional CYP2C19 enzyme (extensive metabolisers).

Elimination

Total plasma clearance is about 17 litres per hour after a single dose and about 9 litres per hour after repeated administration. The plasma elimination half-life is about 1,3 hours after repeated once-daily dosing. The area under the plasma concentration-time curve increases with repeated administration of esomeprazole. This increase is dose-dependent and results in a non-linear

dose-AUC relationship after repeated administration. This time and dose-dependency is due to a decrease of first pass metabolism and systemic clearance probably caused by an inhibition of the CYP2C19 enzyme by esomeprazole and/or its sulphone metabolite. 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 compound is found in urine.

Special patient populations

Approximately 1 to 2 % of the population lack a functional CYP2C19 enzyme and are called poor metabolisers. In these individuals the metabolism of esomeprazole is probably mainly catalysed by CYP3A4. After repeated once-daily administration of 40 mg esomeprazole, the mean area under the plasma concentration-time curve was approximately 100 % higher in poor metabolisers than in subjects having a functional CYP2C19 enzyme (extensive metabolisers). Mean peak plasma concentrations were increased by about 60 %.

The metabolism of esomeprazole is not significantly changed in elderly subjects (71 to 80 years of age).

Following a single dose of 40 mg esomeprazole the mean area under the plasma concentration-time curve is approximately 30 % higher in females than in males. No gender difference is seen after repeated once-daily administration. These findings have no implications for the dosage of esomeprazole.

The metabolism of esomeprazole in patients with mild to moderate liver dysfunction may be impaired. The metabolic rate is decreased in patients with severe liver dysfunction resulting

in a doubling of the area under the plasma concentration-time curve of esomeprazole.
Therefore, a maximum of 20 mg should not be exceeded in patients with severe dysfunction. Esomeprazole or its major metabolites do not show any tendency to accumulate with once-daily dosing.

No studies have been performed in patients with decreased renal function. Since the kidney is responsible for the excretion of the metabolites of esomeprazole, but not for the elimination of the parent compound, the metabolism of esomeprazole is not expected to be changed in patients with impaired renal function.

Following repeated dose administration of 20 mg and 40 mg esomeprazole, the total exposure (AUC) and the time to reach maximum plasma concentration (t_{max}) in 12 to 18 year-olds was similar to that in adults for both esomeprazole doses.

Following repeated dose administration of 10 mg and 20 mg esomeprazole, the total exposure (AUC) and the time to reach maximum plasma concentration (t_{max}) for the 10 mg dose was similar across the 1 to 11 year-olds and similar to the total exposure seen with the 20 mg dose in 12 to 18 year-olds and adults. The 20 mg dose resulted in higher exposure in 6 to 11 year- olds compared to 12 to 18 year-olds and adults.

Repeated dose administration of 5 mg esomeprazole resulted in insufficient exposure in 1 to 5 year-olds.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous citric acid

Crospovidone (Kollidon CL-M)

Dextrose anhydrous

Ferric oxide (yellow)

Hydroxy propyl cellulose (Klucel LF)

Hydroxy propyl methyl cellulose E-15 (HPMC E-15) Magnesium

stearate

Methacrylic acid and ethyl acrylate copolymer dispersion (Eudragit L30 D 55) PlasACRYL®

HTP-20

Polysorbate 80

Sugar spheres

Talc

Xanthan gum

PlasACRYL® HTP-20 composition

Glyceryl monostearate

Polysorbate 80

Triethyl citrate

Sugar spheres composition

Starch

Sucrose

Water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

To be used within 30 minutes after reconstitution.

6.4 Special precautions for storage

Store at or below 25 °C.

This medicine does not require any special storage conditions.

6.5 Nature and contents of container

ESOMEPRAZOLE 10 GRANULES CIPLA are packaged in 4-ply laminate of PET/aluminium foil sachets that are packed into outer cartons, in packs of 28's and 30's.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

CIPLA MEDPRO (PTY) LTD.

Building 9

Parc du Cap

Mispel Street

Bellville

7530

Customer Care: 080 222 6662

8. REGISTRATION NUMBER

56/11.4.3/0155

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First authorisation: 21 May 2024

Latest renewal: Not applicable.

10. DATE OF REVISION OF THE TEXT

16 July 2026