

SUMMARY OF PRODUCT CHARACTERISTICS

Sompraz 20/40
(Esomeprazole Magnesium Tablets 20/40 mg)

1. NAME OF THE MEDICINAL PRODUCT

Sompraz 20/40

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sompraz 20/40

Each enteric coated tablet contains:

Esomeprazole Magnesium Equivalent to

Esomeprazole..... 20/40 mg

An excipient with known effect:

Sompraz 20: Sucrose 30 mg/tablet

Sompraz 40: Sucrose 60 mg/tablet

For the full list of excipients, see **section 6.1**

3. PHARMACEUTICAL FORM

Gastro-Resistant Tablets

Description (Sompraz 20): Light brick red to brown colored, oval, biconvex, film coated tablets with 'E5' debossed on one side and plain on other side.

Description (Sompraz 40): Light brick red to brown colored, oval, biconvex, film coated tablets with 'E6' debossed on one side and plain on other side.

4. CLINICAL PARTICULARS ^{1,2}

4.1 Therapeutic indications

Sompraz 20mg tablets are indicated in adults for:

- Gastroesophageal Reflux Disease (GERD)
 - treatment of erosive reflux esophagitis
 - long-term management of patients with healed esophagitis to prevent relapse
 - symptomatic treatment of gastroesophageal reflux disease (GERD)
- In combination with appropriate antibacterial therapeutic regimens for the eradication of *Helicobacter pylori* and
 - healing of *Helicobacter pylori* associated duodenal ulcer and
 - prevention of relapse of peptic ulcers in patients with *Helicobacter pylori* associated ulcers.

- Patients requiring continued NSAID therapy
 - healing of gastric ulcers associated with NSAID therapy.
 - prevention of gastric and duodenal ulcers associated with NSAID therapy, in patients at risk.
- Treatment of Zollinger Ellison Syndrome

Sompraz 20mg tablets are indicated in adolescents from the age of 12 years for:

- Gastroesophageal Reflux Disease (GERD)
 - treatment of erosive reflux esophagitis
 - long-term management of patients with healed esophagitis to prevent relapse
 - symptomatic treatment of gastroesophageal reflux disease (GERD)
- In combination with antibiotics in treatment of duodenal ulcer caused by *Helicobacter pylori*

Sompraz 40mg is indicated in adults for:

- Gastroesophageal Reflux Disease (GERD)
 - treatment of erosive reflux esophagitis.

Prolonged treatment after i.v. induced prevention of rebleeding of peptic ulcers. Treatment of Zollinger Ellison Syndrome

Sompraz 40mg tablets are indicated in adolescents from the age of 12 years for:

- Gastroesophageal Reflux Disease (GERD)
 - treatment of erosive reflux esophagitis

4.2 Posology and method of administration

Sompraz is available in the strength of 20 and 40 mg tablets and may not be suitable for all dosage recommendations given below. Therefore, other suitable available strengths and dosage forms of esomeprazole should be used in such cases.

Posology

Adults

Sompraz 20mg:

- *Gastroesophageal Reflux Disease (GERD)*

- treatment of erosive reflux esophagitis

40 mg once daily for 4 weeks.

An additional 4 weeks treatment is recommended for patients in whom esophagitis has not healed or who have persistent symptoms.

- long-term management of patients with healed esophagitis to prevent relapse

20 mg once daily.

- symptomatic treatment of gastroesophageal reflux disease (GERD)

20 mg once daily in patients without esophagitis. If symptom control has not been achieved after 4 weeks, the patient should be further investigated. Once symptoms have resolved, subsequent symptom control can be achieved using 20 mg once daily. An on demand regimen taking 20 mg once daily, when needed, can be used. In NSAID treated patients at risk of developing gastric and duodenal ulcers, subsequent symptom control using an on demand regimen is not recommended.

- *In combination with appropriate antibacterial therapeutic regimens for the eradication of Helicobacter pylori and*

- healing of *Helicobacter pylori* associated duodenal ulcer and

- prevention of relapse of peptic ulcers in patients with *Helicobacter pylori* associated ulcers

20 mg **Sompraz** with 1 g amoxicillin and 500 mg clarithromycin, all twice daily for 7 days.

- *Patients requiring continued NSAID therapy*

- healing of gastric ulcers associated with NSAID therapy:

The usual 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.

- *Treatment of Zollinger Ellison Syndrome*

The recommended initial dosage is **Sompraz** 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 to 160 mg esomeprazole daily. With doses above 80 mg daily, the dose should be divided and given twice daily.

Sompraz 40mg

Adults

- Gastroesophageal Reflux Disease (GERD)
 - Treatment of erosive reflux esophagitis 40 mg once daily for 4 weeks.An additional 4 weeks treatment is recommended for patients in whom esophagitis has not healed or who have persistent symptoms.

Prolonged treatment after i.v. induced prevention of rebleeding 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 **Sompraz** 40 mg twice daily. The dosage should then be individually adjusted and treatment continued as long as clinically indicated. Based on the clinical data reported, the majority of patients can be controlled on doses between 80 to 160 mg esomeprazole daily. With doses above 80 mg daily, the dose should be divided and given twice daily.

Special Populations

Renal impairment

Dose adjustment is not required in patients with impaired renal function. Due to limited reported experience in patients with severe renal insufficiency, such patients should be treated with caution (see **section 5.2**).

Hepatic impairment

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 (see **section 5.2**).

Elderly

Dose adjustment is not required in the elderly.

Paediatric population

- Adolescents from the age of 12 years

Gastroesophageal Reflux Disease (GERD)

- treatment of erosive reflux esophagitis

40 mg once daily for 4 weeks

An additional 4 weeks treatment is recommended for patients in whom esophagitis has not healed or who have persistent symptoms.

- long-term management of patients with healed esophagitis to prevent relapse
20 mg once daily.
- symptomatic treatment of gastroesophageal reflux disease (GERD)
20 mg once daily in patients without esophagitis. If symptom control has not been achieved after 4 weeks, the patient should be further investigated. Once symptoms have resolved, subsequent symptom control can be achieved using 20 mg once daily.

Treatment of duodenal ulcer caused by Helicobacter pylori

When selecting appropriate combination therapy, consideration should be given to official national, regional and local guidance regarding bacterial resistance, duration of treatment (most commonly 7 days but sometimes up to 14 days), and appropriate use of antibacterial agents. The treatment should be supervised by a specialist.

The posology recommendation is:

Weight	Posology
30 - 40 kg	Combination with two antibiotics: esomeprazole 20 mg, amoxicillin 750 mg and clarithromycin 7.5 mg/kg body weight are all administered together twice daily for one week.
40 kg	Combination with two antibiotics: esomeprazole 20 mg, amoxicillin 1 g and clarithromycin 500 mg are all administered together twice daily for one week.

- *Children below the age of 12 years*

For posology in patients aged 1 to 11 reference is made to the esomeprazole sachet SmPC.

Method of administration

The tablets should be swallowed whole with liquid. The tablets should not be chewed or crushed. For patients who have difficulty in swallowing, the tablets can also be dispersed in half a glass of non-carbonated water. No other liquids should be used as the enteric coating may be dissolved. Stir until the tablets disintegrate and drink the liquid with the pellets immediately or within 30 minutes. Rinse the glass with half a glass of water and drink. The pellets must not be chewed or crushed.

For patients who cannot swallow, the tablets can be dispersed in non-carbonated water and administered through a gastric tube. It is important that the appropriateness of the selected syringe and tube is carefully tested.

For preparation and administration instructions:

No special requirements for disposal.

Administration through gastric tube

- 1) Put the tablet into an appropriate syringe and fill the syringe with approximately 25 ml water and approximately 5 ml air. For some tubes, dispersion in 50 ml water is needed to prevent the pellets from clogging the tube.
- 2) Immediately shake the syringe for approximately 2 minutes to disperse the tablet.
- 3) Hold the syringe with the tip up and check that the tip has not clogged.
- 4) Attach the syringe to the tube whilst maintaining the above position.
- 5) Shake the syringe and position it with the tip pointing down. Immediately inject 5–10 ml into the tube. Invert the syringe after injection and shake (the syringe must be held with the tip pointing up to avoid clogging of the tip).
- 6) Turn the syringe with the tip down and immediately inject another 5–10 ml into the tube. Repeat this procedure until the syringe is empty.
- 7) Fill the syringe with 25 ml of water and 5 ml of air and repeat step 5 if necessary to wash down any sediment left in the syringe. For some tubes, 50 ml water is needed.

4.3 Contraindications

Sompraz is contraindicated in:

- Hypersensitivity to esomeprazole, to substituted benzimidazoles or to any of the excipients listed in **section 6.1**.
- Esomeprazole should not be used concomitantly with nelfinavir (see **section 4.5**).

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.

Long term use

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 physician if their symptoms change in character.

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.

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. 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), healthcare professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.

Risk of fracture

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. Proton pump inhibitors 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.

Subacute cutaneous lupus erythematosus (SCLE)

Proton pump inhibitors are associated with very infrequent reported 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 esomeprazole. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

Combination with other medicinal products

Co-administration of esomeprazole with atazanavir is not recommended (see **section 4.5**). 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 reported between clopidogrel and esomeprazole (see **section 4.5**). The clinical relevance of this interaction is uncertain. As a precaution, concomitant use of esomeprazole and clopidogrel should be discouraged.

When prescribing esomeprazole for on demand therapy, the implications for interactions with other pharmaceuticals, due to fluctuating plasma concentrations of esomeprazole should be considered (see **section 4.5**).

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 physician 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.

Interference with laboratory tests

Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, esomeprazole 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 proton pump inhibitor treatment.

Excipients

Sompraz contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Sompraz contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Effects of esomeprazole on the pharmacokinetics of other drugs

Protease inhibitors

Omeprazole has been reported to interact with some protease inhibitors. The clinical importance and the mechanisms behind these reported interactions are not reported. Increased gastric pH during omeprazole treatment may change the absorption of the protease inhibitors. Other possible interaction mechanisms are via inhibition of CYP2C19.

For atazanavir and nelfinavir, decreased serum levels have been reported when given together with omeprazole and concomitant administration is not recommended. Co-administration of omeprazole (40 mg once daily) with atazanavir 300 mg/ritonavir 100 mg to healthy volunteers has been reported to result in a substantial reduction in atazanavir exposure (approximately 75% decrease in AUC, $C_{\max}$ and $C_{\min}$). Increasing the atazanavir dose to 400 mg did not compensate for the impact of omeprazole on atazanavir exposure. The co-administration of omeprazole (20 mg qd) with atazanavir 400 mg/ritonavir 100 mg to healthy volunteers has been reported to result in a decrease of approximately 30% in the atazanavir exposure as compared with the exposure reported with atazanavir 300 mg/ritonavir 100 mg qd without omeprazole 20 mg qd. Co-administration of omeprazole (40 mg qd) reduced mean nelfinavir AUC, $C_{\max}$ and $C_{\min}$ by 36-39 % and mean AUC, $C_{\max}$ and $C_{\min}$ for the pharmacologically active metabolite M8 has been reported to be reduced by 75-92%. Due to the similar pharmacodynamic effects and pharmacokinetic properties of omeprazole and esomeprazole, concomitant administration with esomeprazole and atazanavir is not recommended (see

section 4.4) and concomitant administration with esomeprazole and nelfinavir is contraindicated (see **section 4.3**).

For saquinavir (with concomitant ritonavir), increased serum levels (80-100%) have been reported during concomitant omeprazole treatment (40 mg qd). Treatment with omeprazole 20 mg qd had no effect on the exposure of darunavir (with concomitant ritonavir) and amprenavir (with concomitant ritonavir). Treatment with esomeprazole 20 mg qd reportedly had no effect on the exposure of amprenavir (with and without concomitant ritonavir). Treatment with omeprazole 40 mg qd reportedly had no effect on the exposure of lopinavir (with concomitant ritonavir).

Methotrexate

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.

Tacrolimus

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.

Medicinal products with pH dependent absorption

Gastric acid suppression during treatment with esomeprazole and other PPIs might decrease or increase the absorption of medicinal products with a gastric pH dependent absorption. As with other medicinal products that decrease intragastric acidity, the absorption of medicinal products such as ketoconazole, itraconazole and erlotinib can decrease and the absorption of digoxin can increase during treatment with esomeprazole. Concomitant treatment with omeprazole (20 mg daily) and digoxin in healthy subjects reportedly increased the bioavailability of digoxin by 10% (up to 30% in two out of ten subjects). Digoxin toxicity has been rarely reported. However, caution should be exercised when esomeprazole is given at high doses in elderly patients. Therapeutic drug monitoring of digoxin should then be reinforced.

Medicinal products metabolised by CYP2C19

Esomeprazole inhibits CYP2C19, the major esomeprazole-metabolising enzyme. Thus, when esomeprazole is combined with drugs metabolised by CYP2C19, such as diazepam, citalopram, imipramine, clomipramine, phenytoin etc., the plasma concentrations of these drugs may be increased and a dose reduction could be needed. This should be considered especially when prescribing esomeprazole for on-demand therapy.

Diazepam

Concomitant administration of 30 mg esomeprazole has been reported to result in a 45% decrease in clearance of the CYP2C19 substrate diazepam.

Phenytoin

Concomitant administration of 40 mg esomeprazole has been reported to result in a 13% increase in trough plasma levels of phenytoin in epileptic patients. It is recommended to monitor the plasma concentrations of phenytoin when treatment with esomeprazole is introduced or withdrawn.

Voriconazole

Omeprazole (40 mg once daily) has been reported to increase voriconazole (a CYP2C19 substrate) $C_{\max}$ and AUC τ by 15% and 41%, respectively.

Cilostazol

Omeprazole as well as esomeprazole act as inhibitors of CYP2C19. Omeprazole, given in doses of 40 mg to healthy subjects has been reported to increase $C_{\max}$ and AUC for cilostazol by 18% and 26% respectively, and one of its active metabolites by 29% and 69% respectively.

Cisapride

In healthy volunteers, concomitant administration of 40 mg esomeprazole has been reported to result in a 32% increase in area under the plasma concentration-time curve (AUC) and a 31% prolongation of elimination half-life ($t_{1/2}$) but no significant increase in peak plasma levels of cisapride. The slightly prolonged QTc interval reported after administration of cisapride alone, has not been reported to be further prolonged when cisapride was given in combination with esomeprazole (see **section 4.4**).

Warfarin

Concomitant administration of 40 mg esomeprazole to warfarin-treated patients in a reported clinical study showed that coagulation times were within the accepted range. However, post-marketing, a few isolated cases of elevated INR of clinical significance have been reported during concomitant treatment. Monitoring is recommended when initiating and ending concomitant esomeprazole treatment during treatment with warfarin or other coumarine derivatives.

Clopidogrel

Pharmacokinetic (PK)/ pharmacodynamic (PD) interaction has been reported between clopidogrel (300 mg loading dose/75 mg daily maintenance dose) and esomeprazole (40 mg p.o. daily) resulting in decreased exposure to the active metabolite of clopidogrel by an average

of 40% and a decreased maximum inhibition of (ADP induced) platelet aggregation by an average of 14%.

When clopidogrel was given together with a fixed dose combination of esomeprazole 20 mg + ASA 81 mg compared to clopidogrel alone in a reported study in healthy subjects, there was a decreased exposure by almost 40% of the active metabolite of clopidogrel. However, the maximum levels of inhibition of (ADP induced) platelet aggregation in these subjects have been reported to be same in the clopidogrel and the clopidogrel + the combined (esomeprazole + ASA) product groups.

Inconsistent data on the clinical implications of a PK/PD interaction of esomeprazole in terms of major cardiovascular events have been reported from both observational and clinical studies. As a precaution concomitant use of clopidogrel should be discouraged.

Investigated medicinal products with no clinically relevant interaction

- *Amoxicillin and quinidine*

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

- *Naproxen or rofecoxib*

No clinically relevant pharmacokinetic interactions have been reported on concomitant administration of esomeprazole and either naproxen or rofecoxib.

Effects of other medicinal products on the pharmacokinetics of esomeprazole

Medicinal products which inhibit CYP2C19 and/or CYP3A4

Esomeprazole is metabolised by CYP2C19 and CYP3A4. Concomitant administration of esomeprazole and a CYP3A4 inhibitor, clarithromycin (500 mg b.i.d.), reported a doubling of the exposure (AUC) to esomeprazole. Concomitant administration of esomeprazole and a combined inhibitor of CYP2C19 and CYP3A4 may result in more than doubling of the esomeprazole exposure. The CYP2C19 and CYP3A4 inhibitor voriconazole has been reported to increase esomeprazole AUC by 280%. A dose adjustment of esomeprazole is not regularly required in either of these situations. However, dose adjustment should be considered in patients with severe hepatic impairment and if long-term treatment is indicated.

Medicinal products which induce CYP2C19 and/or CYP3A4

Drugs 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.

Paediatric population

Interaction studies have only been reported in adults.

4.6 Fertility, pregnancy, and lactation

Pregnancy

Reported clinical data on exposed pregnancies with esomeprazole are insufficient. No malformative or foetotoxic effect has been reported with racemic mixture of omeprazole. No direct or indirect harmful effects with respect to embryonal/foetal development have been reported in animals. No direct or indirect harmful effects with respect to pregnancy, parturition or postnatal development have been reported with the racemic mixture. Caution should be exercised when prescribing to pregnant women.

A moderate amount of reported data on pregnant women indicates no malformative or foeto/neonatal toxicity of esomeprazole.

No direct or indirect harmful effects with respect to reproductive toxicity have been reported in animals (see **section 5.3**).

Breast-feeding

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

Fertility

No effects with respect to fertility has been reported with the racemic mixture omeprazole in animals.

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) has been reported (see **section 4.8**). If affected patients should not drive or use machines.

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 reported.

Tabulated list of adverse reactions

None of the adverse events have been reported to be dose-related. The reactions are classified according to frequency very common >1/10; common >1/100 to <1/10; uncommon >1/1,000 to <1/100; rare >1/10,000 to <1/1,000; very rare <1/10,000; not known (cannot be estimated from the available reported data).

System Class	Organ	Frequency	Undesirable Effect
Blood and lymphatic system disorders		Rare	Leukopenia, thrombocytopenia
		Very rare	Agranulocytosis, pancytopenia
Immune system disorders		Rare	Hypersensitivity reactions e.g. fever, angioedema and anaphylactic reaction/shock
Metabolism and nutrition disorders		Uncommon	Peripheral oedema
		Rare	Hyponatraemia
		Not known	Hypomagnesaemia (see section 4.4); severe hypomagnesaemia can correlate with hypocalcaemia. Hypomagnesaemia may also be associated with hypokalaemia.
Psychiatric disorders		Uncommon	Insomnia
		Rare	Agitation, confusion, depression
		Very rare	Aggression, hallucinations
Nervous system disorders		Common	Headache
		Uncommon	Dizziness, paraesthesia, somnolence
		Rare	Taste disturbance
Eye disorders		Rare	Blurred vision
Ear and labyrinth disorders		Uncommon	Vertigo
Respiratory, thoracic and mediastinal disorders		Rare	Bronchospasm
Gastrointestinal disorders		Common	Abdominal pain, constipation, diarrhoea, flatulence, nausea/vomiting, fundic gland polyps (benign)
		Uncommon	Dry mouth
		Rare	Stomatitis, gastrointestinal candidiasis
		Not known	Microscopic colitis
		Uncommon	Increased liver enzymes

Hepatobiliary disorders	Rare	Hepatitis with or without jaundice
	Very rare	Hepatic failure, encephalopathy in patients with pre-existing liver disease
Skin and subcutaneous tissue disorders	Uncommon	Dermatitis, pruritus, rash, urticaria
	Rare	Alopecia, photosensitivity
	Very rare	Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), Drug reaction with eosinophilia and systemic symptoms (DRESS)
	Not known	Sub-acute cutaneous lupus erythematosus (see section 4.4)
Musculoskeletal and connective tissue disorders	Uncommon	Fracture of the hip, wrist or spine (see section 4.4)
	Rare	Arthralgia, myalgia
	Very rare	Muscular weakness
Renal and urinary disorders	Very rare	Interstitial nephritis; in some patients renal failure has been reported concomitantly.
Reproductive system and breast disorders	Very rare	Gynaecomastia
General disorders and administration site conditions	Rare	Malaise, increased sweating

Reporting of suspected 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. Healthcare professionals are asked to report any side effects or safety related issues to: pharmacovigilance.africasme@sunpharma.com and also via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) <https://pv.pharmacyboardkenya.org> and For product defects, packaging issues, or any quality concerns, contact: Complaintdesk.Tandalja@sunpharma.com.

4.9 Overdose

There is very limited reported experience to date with deliberate overdose. The symptoms described in connection with 280 mg have been reported to be gastrointestinal symptoms and weakness. Single doses of 80 mg esomeprazole have been reported to be uneventful. No specific antidote is known. Esomeprazole is extensively plasma protein bound and is therefore not readily dialyzable. As in any reported case of overdose, treatment should be symptomatic and general supportive measures should be utilized.

5. PHARMACOLOGICAL PROPERTIES^{1,2}

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs for acid-related disorders proton pump inhibitors

ATC code: A02B C05

Esomeprazole is the S-isomer of omeprazole and reduces gastric acid secretion through a specific targeted mechanism of action. It is a specific inhibitor of the acid pump in the parietal cell. Both the R- and S-isomer of omeprazole have similar pharmacodynamic activity.

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.

Pharmacodynamic effects

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

After five days of oral dosing with 20 mg and 40 mg of esomeprazole, intragastric pH above 4 has been reportedly maintained for a mean time of 13 hours and 17 hours, respectively over 24 hours in symptomatic GERD patients. The proportion of patients maintaining an intragastric pH above 4 for at least 8, 12 and 16 hours respectively were for esomeprazole 20 mg 76%, 54% and 24%. Corresponding proportions for esomeprazole 40 mg were reported to be 97%, 92% and 56%.

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

Healing of reflux esophagitis with esomeprazole 40 mg has been reported to occur in approximately 78% of patients after four weeks, and in 93% after eight weeks.

One week treatment with esomeprazole 20 mg b.i.d. and appropriate antibiotics, results in successful eradication of *H. pylori* in approximately 90% of patients.

After eradication treatment for one week, there is no need for subsequent monotherapy with antisecretory drugs for effective ulcer healing and symptom resolution in uncomplicated duodenal ulcers.

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 tumour. 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.

An increased number of ECL cells possibly related to the increased serum gastrin levels, have been reported in both children and adults during long-term treatment with esomeprazole. The reported findings are considered to be of no clinical significance.

During long-term treatment with antisecretory drugs, gastric glandular cysts have been reported to occur at a somewhat increased frequency. These changes are a physiological consequence of pronounced inhibition of acid secretion, are benign and appear to be reversible. Decreased gastric acidity due to any means including proton pump inhibitors, increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with proton pump inhibitors may lead to slightly increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacter* and, in hospitalized patients, possibly also *Clostridium difficile*.

Paediatric population

In a reported study in paediatric GERD patients (<1 to 17 years of age) receiving long-term PPI treatment, 61% of the children developed minor degrees of ECL cell hyperplasia with no known clinical significance and with no development of atrophic gastritis or carcinoid tumours.

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 reported approximately 1-2 hours after dose. The absolute bioavailability is reported to be 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 reported to be 50% and 68% respectively.

Food intake both delays and decreases the absorption of esomeprazole although this has no significant influence reported on the effect of esomeprazole on intragastric acidity.

Distribution

The apparent volume of distribution at steady state in healthy subjects is reported to be approximately 0.22 l/kg body weight. Esomeprazole is reported to be 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.

Elimination

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

Total plasma clearance is reported to be about 17 l/h after a single dose and about 9 l/h after repeated administration. The plasma elimination half-life is reported to be 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 reported to be excreted as metabolites in the urine, the remainder in the faeces. Less than 1% of the parent drug is reported to be found in urine.

Linearity/non-linearity

The pharmacokinetics of esomeprazole has been reported in doses up to 40 mg b.i.d. The area under the plasma concentration-time curve increases with repeated administration of esomeprazole. This increase is dose-dependent and results in a more than dose proportional increase in AUC 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.

Special patient populations

Poor metabolisers

Approximately $2.9 \pm 1.5\%$ of the population lack a functional CYP2C19 enzyme and are called poor metabolisers. In these individuals the metabolism of esomeprazole is probably mainly catalyzed by CYP3A4. After repeated once daily administration of 40 mg esomeprazole, the mean area under the plasma concentration-time curve has been reported to be approximately 100% higher in poor metabolisers than in subjects having a functional CYP2C19 enzyme (extensive metabolisers). Mean peak plasma concentrations were reported to be increased by about 60%. These reported findings have no implications for the posology of esomeprazole.

Gender

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

Hepatic impairment

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 reported 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.

Renal impairment

No studies have been reported 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.

Elderly

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

Paediatric population (Adolescents 12-18 years)

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

5.3 Preclinical safety data

Reported 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 reported in clinical studies, but reported in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use were as follows:

Reported carcinogenicity studies in the rat with the racemic mixture 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 reported after long-term treatment in the rat with inhibitors of gastric acid secretion.

6. PHARMACEUTICAL PARTICULARS

6.1 *List of excipients*

Sugar spheres, hydroxypropyl cellulose, cross povidone, hypromellose phthalate, diethyl phthalate, acetone, macrogel, microcrystalline cellulose, sodium stearyl fumarate, opadry brown.

6.2 *Incompatibilities*

Not Applicable

6.3 *Shelf life*

24 Months

6.4 *Special precautions for storage*

Store up to 30°C, protected from light.

6.5 *Nature and contents of the container*

SOMPRAZ 20/40 is available in cold form blister of 10 tablets

6.6 *Special precautions for disposal and other handling*

No Special Requirements

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESS

Sun Pharmaceutical Industries Limited

8. MARKETING AUTHORISATION NUMBER

Sompraz 20: 15444

Sompraz 40: 14858

9. DATE OF FIRST REGISTRATION/ RENEWAL OF THE REGISTRATION

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10. DATE OF REVISION OF THE TEXT

April 2026

REFERENCES

1. Summary of Product Characteristics of Nexium (esomeprazole) 20 mg Gastro-resistant Tablets, AstraZeneca UK Limited, October 2023.
2. Summary of Product Characteristics of Nexium (esomeprazole) 40 mg Gastro-resistant Tablets, AstraZeneca UK Limited, October 2023.

Information compiled in April 2026

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