

Produktinformationen för Axiago 10 mg enterogranulat till oral suspension i dospåse, MTnr 24627, gäller vid det tillfälle då läkemedlet godkändes. Informationen kommer inte att uppdateras eftersom läkemedlet inte marknadsförs i Sverige. Av samma anledning finns inte någon svensk produktinformation.

Den engelska produktinformationen kommer dock att uppdateras för de produkter där Sverige är referensland.

Om läkemedelsnamnet i följande produktinformation inte stämmer med namnet på dokumentet, beror det på att läkemedlet i Sverige är godkänt under ett annat namn.

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

AXIAGO 10 mg gastro-resistant granules for oral suspension, sachet

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains: 10 mg esomeprazole (as magnesium trihydrate).

Excipients: Sucrose 6.8 mg and glucose 2.8 g

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Gastro-resistant granules for oral suspension, sachet

Pale yellow fine granules. Brownish granules may be visible.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Axiago oral suspension is primarily indicated for:

Children 1-11 years old

Gastroesophageal Reflux Disease (GERD)

- treatment of endoscopically proven erosive reflux esophagitis
- symptomatic treatment of gastroesophageal reflux disease (GERD)

Children over 4 years of age

In combination with antibiotics in treatment of duodenal ulcer caused by *Helicobacter pylori*

Axiago oral suspension may also be used by patients having difficulty swallowing dispersed Axiago gastro-resistant tablets. For indications in patients from the age of 12 years reference is made to the Axiago gastro-resistant tablet SmPC.

4.2 Posology and method of administration

Posology

Paediatric population.

Children 1 – 11 years with a bodyweight of ≥ 10 kg

Gastroesophageal Reflux Disease (GERD)

- *Treatment of endoscopically proven erosive reflux esophagitis*

Weight ≥ 10 - <20 kg: 10 mg once daily for 8 weeks.

Weight ≥ 20 kg: 10 mg or 20 mg once daily for 8 weeks.

- *Symptomatic treatment of gastroesophageal reflux disease (GERD)*
10 mg once daily for up to 8 weeks.

Doses over 1 mg/kg/day have not been studied.

Children over 4 years of age

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 kg	Combination with two antibiotics: Axiago 10 mg, amoxicillin 25 mg/kg body weight and clarithromycin 7.5 mg/kg body weight are all administered together twice daily for one week.
30 - 40 kg	Combination with two antibiotics: Axiago 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: Axiago 20 mg, amoxicillin 1 g and clarithromycin 500 mg are all administered together twice daily for one week.

Children below the age of 1 year

The experience of treatment with esomeprazole in infants < 1 year is limited and treatment is therefore not recommended (see section 5.1).

Adults and adolescents from the age of 12 years

For posology in patients from the age of 12 years reference is made to the Nexium gastroresistant tablet SmPC.

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 (See section 5.2).

Impaired hepatic function

Dose adjustment is not required in patients with mild to moderate liver impairment. For patients ≥12 years with severe liver impairment, a maximum dose of 20 mg Axiago should not be exceeded. For children 1-11 years with severe liver impairment, a maximum dose of 10 mg should not be exceeded (See section 5.2).

Method of administration

For a 10 mg dose empty the contents of a 10 mg sachet into a glass containing 15 ml water. For a 20 mg dose empty the contents of two 10 mg sachets into a glass containing 30 ml water. Do not use carbonated water. Stir the contents until the granulate has been dispersed and leave for a few minutes to thicken. Stir again and drink within 30 minutes. The granules must not be chewed or crushed. Rinse with 15 ml water to obtain all granules.

For patients who have a nasogastric or gastric tube in place: see section 6.6 for preparation and administration instructions.

4.3 Contraindications

Known hypersensitivity to esomeprazole, substituted benzimidazoles or any other constituents of the formulation.

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 Axiago may alleviate symptoms and delay diagnosis.

Patients on long-term treatment (particularly those treated for more than a year) should be kept under regular surveillance. Long-term treatment is indicated in adults and adolescents (12 years and older, see section 4.1).

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

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.

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

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 observed between clopidogrel and omeprazole (see section 4.5). The clinical relevance of this interaction is uncertain. As a precaution, concomitant use of esomeprazole and clopidogrel should be discouraged.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction studies have only been performed in adults.

Effects of esomeprazole on the pharmacokinetics of other drugs

Medicinal products with pH dependent absorption

The decreased intragastric acidity during treatment with esomeprazole, might increase or decrease the absorption of drugs if the mechanism of absorption is influenced by gastric acidity. In common with the use of other inhibitors of acid secretion or antacids, the absorption of ketoconazole and itraconazole can decrease during treatment with esomeprazole.

Omeprazole has been reported to interact with some protease inhibitors. The clinical importance and the mechanisms behind these reported interactions are not always known. Increased gastric pH during omeprazole treatment may change the absorption of the protease inhibitors. Other possible interaction mechanisms are via inhibition of CYP 2C19. 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 resulted 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 resulted in a decrease of approximately 30% in the atazanavir exposure as compared with the exposure observed 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 was reduced by 75-92%. 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 had no effect on the exposure of amprenavir (with and without concomitant ritonavir). Treatment with omeprazole 40 mg qd had no effect on the exposure of lopinavir (with concomitant ritonavir). Due to the similar pharmacodynamic effects and pharmacokinetic properties of omeprazole and esomeprazole, concomitant administration with esomeprazole and atazanavir is not recommended and concomitant administration with esomeprazole and nelfinavir is contraindicated..

Drugs 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. Concomitant administration of 30 mg esomeprazole resulted in a 45% decrease in clearance of the CYP2C19 substrate diazepam. Concomitant administration of 40 mg esomeprazole resulted 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. Omeprazole (40 mg once daily) increased voriconazole (a CYP2C19 substrate) $C_{\max}$ and AUC_τ by 15% and 41%, respectively

Concomitant administration of 40 mg esomeprazole to warfarin-treated patients in a clinical trial 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.

In healthy volunteers, 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 ($t_{1/2}$) but no significant increase in peak plasma levels of cisapride. The slightly prolonged QTc interval observed after administration of cisapride alone, was not further prolonged when cisapride was given in combination with esomeprazole.

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 or rofecoxib did not identify any clinically relevant pharmacokinetic interactions during short-term studies.

In a crossover clinical study, clopidogrel (300 mg loading dose followed by 75 mg/day) alone and with omeprazole (80 mg at the same time as clopidogrel) were administered for 5 days. The exposure to the active metabolite of clopidogrel was decreased by 46% (Day 1) and 42% (Day 5) when clopidogrel and omeprazole were administered together. Mean inhibition of platelet aggregation (IPA) was diminished by 47% (24 hours) and 30% (Day 5) when clopidogrel and omeprazole were administered together. In another study it was shown that administering clopidogrel and omeprazole at different times did not prevent their interaction that is likely to be driven by the inhibitory effect of omeprazole on CYP2C19. Inconsistent data on the clinical implications of this PK/PD interaction in terms of major cardiovascular events have been reported from observational and clinical studies.

Effects of other drugs on the pharmacokinetics of esomeprazole

Esomeprazole is metabolised by CYP2C19 and CYP3A4. Concomitant administration of esomeprazole and a CYP3A4 inhibitor, clarithromycin (500 mg b.i.d.), resulted in a doubling of the exposure (AUC) to esomeprazole. Concomitant administration of esomeprazole and a combined inhibitor of CYP2C19 and CYP 3A4 may result in more than doubling of the esomeprazole exposure. The CYP2C19 and CYP3A4 inhibitor voriconazole increased omeprazole AUC_{τ} 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. Long-term treatment is indicated in adults and adolescents (12 years and older, see section 4.1).

4.6 Pregnancy and lactation

For Axiago, clinical data on exposed pregnancies are insufficient. 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/fetal 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.

It is not known whether esomeprazole is excreted in human breast milk. No studies in lactating women have been performed. Therefore Axiago should not be used during breast-feeding.

4.7 Effects on ability to drive and use machines

No effects have been observed.

4.8 Undesirable effects

The following adverse drug reactions have been identified or suspected in the clinical trials programme for esomeprazole and post-marketing. None was found to be dose-related. The reactions are classified according to frequency:

Very common $\geq 1/10$; common $\geq 1/100$ to $< 1/10$; uncommon $\geq 1/1,000$ to $< 1/100$; rare $\geq 1/10,000$ to $< 1/1,000$; very rare $< 1/10,000$; not known (cannot be estimated from the available data).

General disorders and administration site conditions

Rare: Malaise, increased sweating

Respiratory, thoracic and mediastinal disorders

Rare: Bronchospasm

Blood and lymphatic system disorders

Rare: Leukopenia, thrombocytopenia

Very rare: Agranulocytosis, pancytopenia

Nervous system disorders

Common: Headache

Uncommon: Dizziness, paraesthesia, somnolence

Rare: Taste disturbance

Immune system disorders

Rare: Hypersensitivity reactions e.g. fever, angioedema and anaphylactic reaction/shock

Skin and subcutaneous tissue disorders

Uncommon: Dermatitis, pruritus, rash, urticaria

Rare: Alopecia, photosensitivity

Very rare: Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN)

Hepatobiliary disorders

Uncommon: Increased liver enzymes

Rare: Hepatitis with or without jaundice

Very rare: Hepatic failure, encephalopathy in patients with pre-existing liver disease

Gastrointestinal disorders

Common: Abdominal pain, constipation, diarrhoea, flatulence, nausea/vomiting

Uncommon: Dry mouth

Rare: Stomatitis, gastrointestinal candidiasis

Metabolism and nutrition disorders

Uncommon: Peripheral oedema
Rare: Hyponatraemia
Very rare: Hypomagnesaemia

Musculoskeletal, connective tissue and bone disorders

Rare: Arthralgia, myalgia
Very rare: Muscular weakness

Renal and urinary disorders

Very rare: Interstitial nephritis

Psychiatric disorders

Uncommon: Insomnia
Rare: Agitation, confusion, depression
Very rare: Aggression, hallucinations

Reproductive system and breast disorders

Very rare: Gynaecomastia

Eye disorders

Rare: Blurred vision

Ear and labyrinth disorders

Uncommon: Vertigo

4.9 Overdose

There is very limited experience to date with deliberate overdose. The symptoms described in connection with 280 mg were gastrointestinal symptoms and weakness. Single doses of 80 mg esomeprazole were uneventful. No specific antidote is known. 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: proton pump inhibitor
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.

Site and 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.

Effect on gastric acid secretion

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 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 was 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 97%, 92% and 56%.

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

Therapeutic effects of acid inhibition

Healing of reflux esophagitis with esomeprazole 40 mg occurs in approximately 78% of patients after four weeks, and in 93% after eight weeks.

Other effects related to acid inhibition

During treatment with antisecretory drugs serum gastrin increases in response to the decreased acid secretion.

An increased number of ECL cells possibly related to the increased serum gastrin levels, have been observed in some patients during long term treatment with esomeprazole.

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.

Pediatric population

GERD - 1 to 11 Years of Age

In a multicenter, parallel-group study, 109 pediatric patients with endoscopically proven GERD (1 to 11 years of age) were treated with AXIAGO once daily for up to 8 weeks to evaluate safety and tolerability. Dosing by patient weight was as follows:

Weight <20 kg: once daily treatment with esomeprazole 5 mg or 10 mg

Weight ≥20 kg: once daily treatment with esomeprazole 10 mg or 20 mg

Patients were endoscopically characterized as to the presence or absence of erosive esophagitis. Fifty-three patients had erosive esophagitis at baseline. Of the 45 patients who had follow-up endoscopy, 43 (93.3%) of these patients had their erosive esophagitis healed through 8 weeks.

GERD – 0 to 11 months of age

In a placebo-controlled study (98 patients aged 1-11 months) efficacy and safety in patients with signs and symptoms of GERD were evaluated. Esomeprazole 1 mg/kg once daily was given for 2 weeks (open-label phase) and 80 patients were included for an additional 4 weeks (doubleblind, treatment-withdrawal phase). There was no significant difference between esomeprazole and placebo for the primary endpoint time to discontinuation due to symptom

worsening.

In a placebo-controlled study (52 patients aged < 1 month) efficacy and safety in patients with symptoms of GERD were evaluated. Esomeprazole 0.5 mg/kg once daily was given for a minimum of 10 days. There was no significant difference between esomeprazole and placebo in the primary endpoint, change from baseline of number of occurrences of symptoms of GERD.

Results from the paediatric studies further show that 0.5 mg/kg and 1.0 mg/kg esomeprazole in < 1 month old and 1 to 11 month old infants, respectively, reduced the mean percentage of time with intra-oesophageal pH < 4.

The safety profile appeared to be similar to that seen in adults.

5.2 Pharmacokinetic properties

Absorption and distribution

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 1-2 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. 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.

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

Metabolism and excretion

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.

Total plasma clearance is about 17 l/h after a single dose and about 9 l/h after repeated administration. The plasma elimination half-life is about 1.3 hours after repeated once-daily dosing. The pharmacokinetics of esomeprazole has been studied 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. 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.

Special patient populations

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 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%. These findings have no implications for the posology of esomeprazole.

The metabolism of esomeprazole is not significantly changed in elderly subjects (71-80 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 posology 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.

Paediatric

Adolescents 12-18 years:

Following repeated dose administration of 20 mg and 40 mg esomeprazole in adolescents 12-18 years of age, the total exposure (AUC) and the time to reach maximum plasma drug concentration ($t_{\max}$) was similar to that in adults.

Children 1 – 11 years:

Following repeated dose administration of 10 mg esomeprazole, the total exposure (AUC) was similar within the age range 1 to 11 years and the exposure was similar to the exposure seen with the 20 mg dose in adolescents and adults.

Following repeated dose administration of 20 mg esomeprazole, the total exposure (AUC) was higher in 6 to 11 year-olds compared to the same dose in adolescents and adults.

5.3 Preclinical safety data

Preclinical bridging studies reveal no particular hazard for humans based on conventional studies of repeated dose toxicity, genotoxicity, and toxicity to reproduction. 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 observed after long-term treatment in the rat with inhibitors of gastric acid secretion.

No new or unexpected toxicity findings were observed in juvenile rats and dogs, after administration of esomeprazole for up to 3 months, as compared to the adult animals.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Esomeprazole granules:

Glycerol monostearate 40-55,

Hydroxypropyl cellulose

Hypromellose

Magnesium stearate

Methacrylic acid –ethyl acrylate copolymer (1:1) dispersion 30%

Polysorbate 80

Sugar spheres (sucrose and maize starch)

Talc

Triethyl citrate

Excipient granules:

Citric acid anhydrous (for pH adjustment)

Crospovidone

Glucose

Hydroxypropyl cellulose

Yellow iron oxide(E172)

Xanthan gum

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

To be used within 30 minutes after reconstitution.

6.4 Special precautions for storage

No special storage instructions.

6.5 Nature and content of container

Carton containing 28 sachets. Sachets (containing granules): Laminate consisting of three layers: polyethylene terephthalate (PET), aluminium, low density polyethylene (LDPE) which protects the granules against moisture.

6.6 Special precautions for disposal and other handling

For patients who have a nasogastric or gastric tube in place

1. For a 10 mg dose, add the contents of a 10 mg sachet into 15 ml of water
2. For a 20 mg dose add the contents of two 10 mg sachets into 30 ml of water.
3. Stir
4. Leave for a few minutes to thicken

5. Stir again
 6. Draw the suspension into a syringe
 7. Inject through the enteric tube, French size 6 or larger, into the stomach within 30 minutes after reconstitution.
 8. Refill the syringe with 15 ml water for a 10 mg dose and 30 ml for a 20 mg dose.
 9. Shake and flush any remaining contents from the enteric tube into the stomach
- Any unused suspension should be discarded.

7 MARKETING AUTHORISATION HOLDER

To be completed nationally

8 MARKETING AUTHORISATION NUMBER(S)

To be completed nationally

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

To be completed nationally

Date of latest renewal: 10 March 2010

10 DATE OF REVISION OF THE TEXT

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