ESMOZIN
Powder for solution for injection
and infusion 40mg/vial

ESMOZIN 40 MG

Esomeprazole Powder for solution for injection/infusion

Composition

Each vial contains esomeprazole 40 mg (as sodium salt).

Pharmaceutical form

Powder for solution for injection/infusion
White to off-white porous cake or powder

Therapeutic indications

Esmozin for injection and infusion is indicated as an alternative to oral therapy when oral intake is not appropriate:

- For gastroesophageal reflux disease in patients with esophagitis and/or severe symptoms of reflux.
- For healing of gastric ulcers associated with NSAID therapy.
- For prevention of gastric and duodenal ulcers associated with NSAID therapy, in patients at risk. Patients are considered to be at risk due to their age (≥60) and/or documented history of gastric and/or duodenal ulcers. Controlled studies do not extend beyond 6 months.
- Prevention of rebleeding following therapeutic endoscopy for acute bleeding gastric or duodenal ulcers.

Posology and method of administration

Gastric antisecretory treatment when the oral route is not possible

Patients who cannot take oral medication may be treated parenterally with 20-40 mg once daily. Patients with reflux oesophagitis should be treated with 40 mg once daily. Patients treated symptomatically for reflux disease should be treated with 20 mg once daily.
For healing of gastric ulcers associated with NSAID therapy the usual dose is 20 mg once daily. For prevention of gastric and duodenal ulcers associated with NSAID therapy, patients at risk should be treated with 20 mg once daily.

Usually the IV treatment duration is short and transfer to oral treatment should be made as soon as possible.

Prevention of rebleeding of gastric and duodenal ulcers

Following therapeutic endoscopy for acute bleeding gastric or duodenal ulcers, 80 mg should be administered as a bolus infusion over 30 minutes, followed by a continuous intravenous infusion of 8 mg/h given over 3 days (72 hours).
The parenteral treatment period should be followed by oral acid suppression therapy.

Method of administration

Injection

40 mg dose

The reconstituted solution should be given as an intravenous injection over a period of at least 3 minutes.

20 mg dose

Half of the reconstituted solution should be given as an intravenous injection over a period of approximately 3 minutes. Any unused solution should be discarded.

Infusion

40 mg dose

The reconstituted solution should be given as an intravenous infusion over a period of 10 to 30

minutes.

20 mg dose

Half of the reconstituted solution should be given as an intravenous infusion over a period of 10 to 30 minutes. Any unused solution should be discarded.

80 mg bolus dose

The reconstituted solution should be given as a continuous intravenous infusion over 30 minutes.

8 mg/h dose

The reconstituted solution should be given as a continuous intravenous infusion over a period of 71.5 hours (calculated rate of infusion of 8 mg/h. See "Shelf-life for shelf-life of the reconstituted solution").

Children and adolescents

Esmozin should not be used in children since no data is available.

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 "Pharmacokinetic properties").

Impaired hepatic function

GERD: Dose adjustment is not required in patients with mild to moderate liver impairment. For patients with severe liver impairment, a maximum daily dose of 20 mg Esmozin should not be exceeded (See "Pharmacokinetic properties").

Bleeding ulcers: Dose adjustment is not required in patients with mild to moderate liver impairment. For patients with severe liver impairment, following an initial bolus dose of 80 mg Esmozin for infusion, a continuous intravenous infusion dose of 4 mg/h for 71.5 hours may be sufficient (See "Pharmacokinetic properties").

Elderly

Dose adjustment is not required in the elderly.

Contraindications

Hypersensitivity to the active substance esomeprazole or to other substituted benzimidazoles or to any of the excipients of this medicinal product.

Special warnings and special 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 Esmozin may alleviate symptoms and delay diagnosis.

Concomitant administration with esomeprazole and drugs such as atazanavir and nelfinavir is not recommended (See "Interactions").

Co-administration of esomeprazole with atazanavir is not recommended (See "Interactions"). 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.

Results from studies in healthy subjects have shown a pharmacokinetic/pharmacodynamic interaction 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 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 discouraged (See also the "Interactions").

Bone fracture

Several published observational studies suggest that proton pump inhibitor (PPI) therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. The risk of fracture was increased in patients who received high-dose, defined as multiple daily doses, and long-term PPI therapy (a year or longer). Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated. Patients at risk for osteoporosis-related fractures should be managed according to established treatment guidelines (see Posology and method of administration and Undesirable effects).

***Clostridium difficile* associated diarrhoea**

Published observational studies suggest that proton pump inhibitor (PPI) therapy like esomeprazole may be associated with an increased risk of *Clostridium difficile* associated diarrhoea (CDAD), especially in hospitalised patients. This diagnosis should be considered for diarrhoea that does not improve (see "Undesirable effects").

Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.

Concomitant use of esomeprazole with Methotrexate

Literature suggests that concomitant use of PPIs with methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration a temporary withdrawal of the PPI may need to be considered in some patients (see "Interactions").

Hypomagnesaemia

Hypomagnesaemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures. In most patients, treatment of hypomagnesaemia required magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesaemia (e.g., diuretics), health care professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically. (See "Undesirable Effects").

Cutaneous lupus erythematosus and Systemic lupus erythematosus

Cutaneous lupus erythematosus (CLE) and systemic lupus erythematosus (SLE) have been reported in patients taking PPIs. These events have occurred as both new onset and an exacerbation of existing autoimmune disease. The majority of PPI-induced lupus erythematosus cases were CLE. The most common form of CLE reported in patients treated with PPIs was subacute CLE (SCLE) and occurred within weeks to years after continuous drug therapy in patients ranging from infants to the elderly. Generally, histological findings were observed without organ involvement. Systemic lupus erythematosus (SLE) is less commonly reported than CLE in patients receiving PPIs. PPI associated SLE is usually milder than non-drug induced SLE. Onset of SLE typically occurred within days to years after initiating treatment primarily in patients ranging from young adults to the elderly. The majority of patients presented with rash; however, arthralgia and cytopenia were also reported.

Avoid administration of PPIs for longer than medically indicated. If signs or symptoms consistent with CLE or SLE are noted in patients receiving Esmozin IV, discontinue the drug and refer the patient to the appropriate specialist for evaluation. Most patients improve with discontinuation of the PPI alone in 4 to 12 weeks. Serological testing (e.g., Antinuclear antibody) may be positive and elevated serological test results may take longer to resolve than clinical manifestations.

Interactions

Effects of esomeprazole on the pharmacokinetics of other drugs

The gastric acid suppression during treatment with Esmozin IV and other PPIs, might decrease or increase the absorption of drugs with a gastric pH dependent absorption. Like with other drugs that decrease the intragastric acidity, the absorption of drugs such as ketoconazole, itraconazole and erlotinib can decrease while the absorption of drugs such as digoxin can increase during treatment with esomeprazole. Concomitant treatment with omeprazole (20 mg daily) and digoxin in healthy subjects increased the bioavailability of digoxin by 10% (up to 30% in two out of ten subjects).
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. Concomitant oral administration of 30 mg esomeprazole resulted in a 45% decrease in clearance of the CYP2C19 substrate diazepam. Concomitant oral administration of 40 mg esomeprazole and phenytoin 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.
Concomitant oral administration of 40 mg esomeprazole to warfarin-treated patients in a clinical trial showed that coagulation times were within the accepted range. However, from post-marketed use cases of elevated INR of clinical significance have been reported during concomitant treatment with warfarin. Close monitoring is recommended when initiating and ending treatment with warfarin or other coumarin derivatives.
Results from studies in healthy subjects have shown a pharmacokinetic/pharmacodynamic interaction 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 resulting in decreased maximum inhibition of (ADP induced) platelet aggregation by an average of 14%. 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.
When clopidogrel was given together with a fixed dose combination of esomeprazole 20 mg + ASA 81 mg compared to clopidogrel alone in a 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 were the same in the clopidogrel and the clopidogrel + the combined (esomeprazole + ASA) product groups, likely due to the concomitant administration of low dose ASA.
Omeprazole as well as esomeprazole act as inhibitors of CYP 2C19. Omeprazole, given in doses of 40 mg to healthy subjects in a cross-over study, increased Cmax and AUC for cilostazol by 18% and 26% respectively, and one of its active metabolites by 29% and 69% respectively.
In healthy volunteers, concomitant oral administration of 40 mg esomeprazole and cisapride 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.
Concomitant administration of esomeprazole has been reported to increase the serum levels of tacrolimus.
Case reports, published population pharmacokinetic studies, and retrospective analyses suggest that concomitant administration of PPIs and methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite hydroxymethotrexate. However, no formal drug interaction studies of methotrexate with PPIs have been conducted (see Special warnings and special precautions for use).

Omeprazole has been reported to interact with some antiretroviral drugs. 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 antiretroviral drug. Other possible interaction mechanisms are via CYP 2C19. For some antiretroviral drugs, 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 drugs, such as saquinavir, increased serum levels have been reported. There are also some antiretroviral drugs for which unchanged serum levels have been reported when given with omeprazole. Due to the similar pharmacodynamic effects and pharmacokinetic properties of omeprazole and esomeprazole, concomitant administration with esomeprazole and antiretroviral drugs such as atazanavir and nelfinavir is not recommended.
Esomeprazole has been shown to have no clinically relevant effects on the pharmacokinetics of amoxicillin or quinidine. No in vivo interaction studies have been performed with the high dose iv regimen (80 mg+8 mg/h). The effect of esomeprazole on drugs metabolised by CYP2C19 may be more pronounced during this regimen, and patients should be monitored closely for adverse effects, during the 3-day i.v. treatment period.

Effects of other drugs on the pharmacokinetics of esomeprazole

Esomeprazole is metabolised by CYP2C19 and CYP3A4. Concomitant oral 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 CYP3A4, such as voriconazole, may result in more than doubling of the esomeprazole exposure. A dose adjustment of esomeprazole is not required in either situation. However, a dose adjustment should be considered in patients with severe hepatic impairment and if long-term treatment is indicated.
Drugs known to induce CYP2C19 pr CYP3A4 or both (such as rifampicin and St. John's wort) may lead to decreased esomeprazole serum levels by increasing the esomprazole metabolism.

Pregnancy and lactation

For Esomeprazole, limited data on exposed pregnancies are available. 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 Esomeprazole to pregnant women.
It is not known whether esomeprazole is excreted in human breast milk. No studies in lactating women have been performed. Therefore, Esomeprazole should not be used during breastfeeding.

Effects on ability to drive and use machines

Esmozin is not likely to affect the ability to drive or use machines.

Undesirable effects

The following adverse drug reactions have been identified or suspected in the clinical trials programme for esomeprazole administered orally or intravenously and post-marketing when administered orally. The reactions are classified according to frequency (common >1/100, <1/10; uncommon >1/1000, <1/100; rare >1/10000, <1/1000; very rare <1/10000); not known (cannot be estimated from the available data).

Blood and lymphatic system disorders

Rare: Leukopenia, thrombocytopenia
Very rare: Agranulocytosis, pancytopenia

Immune system disorders

Rare: Hypersensitivity reactions e.g. angioedema and anaphylactic reaction/shock
Not known: Systemic lupus erythematosus

Metabolism and nutrition disorders

Uncommon: Peripheral oedema

Rare: Hyponatraemia
Very Rare: Hypomagnesaemia; severe hypomagnesaemia may result in hypocalcaemia
Hypomagnesaemia may also result in 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
Uncommon: 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
Uncommon: Dry mouth
Rare: Stomatitis, gastrointestinal candidiasis
Very rare: Microscopic colitis
Hepatobiliary disorders
Uncommon: Increased liver enzymes
Rare: Hepatitis with or without jaundice
Very rare: Hepatic failure, encephalopathy in patients with pre-existing liver disease
Skin and subcutaneous tissue disorders
Common: Administration site reactions*
Uncommon: Dermatitis, pruritus, rash, urticaria
Rare: Alopecia, photosensitivity
Very rare: Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN)
Not known: Cutaneous lupus erythematosus
Musculoskeletal, connective tissue and bone disorders
Rare: Arthralgia, myalgia
Very rare: Muscular weakness
Renal and urinary disorders
Very rare: Interstitial nephritis
Reproductive system and breast disorders
Very rare: Gynaecomastia
General disorders and administration site conditions
Rare: malaise, increased sweating
Infection and Infestation
Not Known: In hospitalized patients, Clostridium difficile associated diarrhea
*Administration site reactions have mainly been observed in a study with high-dose exposure over 3 days (72 hours).
Irreversible visual impairment has been reported in isolated cases of critically ill patients who have received omeprazole (the racemate) intravenous injection, especially at high doses, but no causal relationship has been established.

Overdose

There is very limited experience to date with deliberate overdose. The symptoms described in connection with an oral dose of 280 mg were gastrointestinal symptoms and weakness. Single oral doses of 80 mg esomeprazole and intravenous doses of 308 mg esomeprazole over 24

hours 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.

Pharmacodynamic properties

Pharmacotherapeutic group: Proton pump inhibitor
ATC Code: A02BC05
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 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 GORD patients. The effect is similar irrespective of whether esomeprazole is administered orally or intravenously.
Using AUC as a surrogate parameter for plasma concentration, a relationship between inhibition of acid secretion and exposure has been shown after oral administration of esomeprazole.
During intravenous administration of 80 mg esomeprazole as a bolus infusion over 30 minutes followed by a continuous intravenous infusion of 8 mg/h for 23.5 hours, intragastric pH above 4, and pH above 6 was maintained for a mean time of 21 hours, and 11-13 hours, respectively, over 24 hours in healthy subjects.

Therapeutic effects of acid inhibition

Healing of reflux esophagitis with esomeprazole 40 mg occurs in approximately 78% of patients after 4 weeks, and in 93% after 8 weeks of oral treatment.
In a randomized, double blind, placebo-controlled clinical study, patients with endoscopically confirmed peptic ulcer bleeding characterised as Forrest Ia, Ib, IIa or IIb (9%, 43%, 38% and 10 % respectively) were randomized to receive Esomeprazole solution for infusion (n=375) or placebo (n=389). Following endoscopic haemostasis, patients received either 80 mg esomeprazole as an intravenous infusion over 30 minutes followed by a continuous infusion of 8 mg per hour or placebo for 72 hours. After the initial 72 hour period, all patients received open-label 40 mg oral Esomeprazole for 27 days for acid suppression. The occurrence of rebleeding within 3 days was 5.9% in the Esomeprazole treated group compared to 10.3% for the placebo group. At 30 days post-treatment, the occurrence of rebleeding in the Esomeprazole treated versus the placebo treated group was 7.7% vs 13.6%.

Other effects related to acid inhibition

During treatment with antisecretory drugs serum gastrin increases in response to the decreased acid secretion. Also chromogranin A (CgA) increases due to decreased gastric acidity. The increased CgA level may interfere with investigations for neuroendocrine tumours. Literature reports indicate that proton pump inhibitor treatment should be stopped 5 to 14 days before CgA measurement**.** Measurements should be repeated if levels have not normalised by this time.
An increased number of ECL cells possibly related to the increased serum gastrin levels, have been observed in patients during long term treatment with orally administered esomeprazole. In over 1,000 patients treated with Esomeprazole up to 6-12 months, the prevalence of ECL cell hyperplasia increased with time and dose. No patient developed ECL cell carcinoids, dysplasia, or neoplasia in the gastric mucosa.
During long-term oral 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*.

Pharmacokinetic properties

Distribution

The apparent volume of distribution at steady state in healthy subjects is approximately 0.22 L/kg body weight. Esomeprazole is 97% plasma protein bound.

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. Total exposure (AUC) 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 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.
Following repeated doses of 40 mg administered as intravenous injections, the mean peak plasma concentration is approx. 13.6 micromol/L. The mean peak plasma concentration after corresponding oral doses is approx. 4.6 micromol/L. A smaller increase (of approx. 30%) can be seen in the total exposure after intravenous administration compared to oral administration.
There is a dose-linear increase in total exposure following intravenous administration of esomeprazole as a 30-minute infusion (40 mg, 80 mg or 120 mg) followed by a continuous infusion (4 mg/h or 8 mg/h) over 23.5 hours.
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 3% of the population lacks a functional CYP2C19 enzyme and is called poor metabolisers. In these individuals the metabolism of esomeprazole is probably mainly catalysed by CYP3A4. After repeated once-daily administration of 40 mg oral esomeprazole, the mean total exposure was approximately 100% higher in poor metabolisers than in subjects with a functional CYP2C19 enzyme (extensive metabolisers). Mean peak plasma concentrations were increased by about 60%. Similar differences have been seen for intravenous administration of esomeprazole. 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 oral dose of 40 mg esomeprazole the mean total exposure is approximately 30% higher in females than in males. No gender difference is seen after repeated once-daily administration. Similar differences have been observed for intravenous administration of

esomeprazole. 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 total exposure of esomeprazole. Therefore, a maximum dose of 20 mg should not be exceeded in GERD patients with severe dysfunction. For patients with bleeding ulcers and severe liver impairment, following an initial bolus dose of 80 mg, a maximum continuous intravenous infusion dose of 4 mg/h for 71.5 hours may be sufficient.
Esomeprazole or its major metabolites do not show any tendency to accumulate with oncedaily 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.

List of excipients

Disodium edetate
Sodium hydroxide

Incompatibilities

This medicinal product should not be used with other medicinal products except those mentioned in Instruction for use and handling.

Shelf Life

Please refer to expiry date on the outer carton.

Shelf-life after reconstitution

Chemical and physical in-use stability has been demonstrated for 12 hours at 30°C or 24 hours at 2-8°C. From a microbiological point of view, the product should be used immediately.

Special precautions for storage

Store in the original package, in order to protect from light. Vials can however be stored exposed to normal in door light outside the box for up to 24 hours. Do not store above 30°C.

Pack Size

1 vial; Type I clear glass vial, sealed with a Type I bromobutyl rubber stopper and an aluminium cap with plastic flip-off seal

Instructions for use and handling

Injection

A solution for injection is prepared by adding 5 mL of 0.9% sodium chloride for intravenous use to the vial with esomeprazole. The reconstituted solution for injection is clear and colourless to very slightly yellow.
The degradation of reconstituted solution is highly pH dependent and the product must therefore only be reconstituted in the specified volume of 0.9% sodium chloride for intravenous use. The reconstituted solution should not be mixed or co-administered in the same infusion set with any other drug.
The reconstitution solution should be inspected visually for particulate matter and discoloration prior to administration. Only clear solution should be used.
The reconstituted solution should be used within 12 hours. From a microbiological point of view, the product should be used immediately. Do not store above 30^0C.
The reconstituted solution should be given as an intravenous injection over a period of at least 3 minutes.
Half of the volume should be given if 20 mg should be administrated. If the entire reconstituted content of the vial is not required for a single dose, any unused reconstituted solution should be discarded.

Infusion

A solution for infusion is prepared by dissolving the content of one vial with esomeprazole in up to 100 mL 0.9% sodium chloride for intravenous use.

The reconstituted solution for infusion is clear and colourless to very slightly yellow.
The degradation of reconstituted solution is highly pH dependent and the product must therefore only be reconstituted in the specified volume of 0.9% sodium chloride for intravenous use.
The reconstituted solution should not be mixed or co-administered in the same infusion set with any other drug.
The reconstituted solution should be administrated separately from other drugs.
The reconstituted solution should be inspected visually for particulate matter and discoloration prior to administration. Only clear solution should be used.
The reconstituted solution should be used within 12 hours. From a microbiological point of view, the product should be used immediately. Do not store above 30^0C.
The reconstituted solution should be given as an intravenous infusion over a period of 10 to 30 minutes.
Half of the volume should be given if 20 mg should be administrated. If the entire reconstituted content of the vial is not required for a single dose, any unused reconstituted solution should be discarded.
Infusion 80 mg
A solution for infusion is prepared by dissolving the content of two vials of esomeprazole 40 mg in up to 100 ml of 0.9% sodium chloride for intravenous use.

Name and Address of Manufacturer
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