PACKAGE LEAFLET

Package leaflet: Information for the patient

Esomeprazole Tillomed 40 mg powder for solution for injection/infusion

esomeprazole

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Esomeprazole Tillomed is and what it is used for

Esomeprazole Tillomed contains a medicine called esomeprazole. This belongs to a group of medicines called "proton pump inhibitors". These work by reducing the amount of acid your stomach produces.

Esomeprazole Tillomed is used for the short-term treatment of certain conditions, when you are unable to have treatment by mouth. It is used to treat the following conditions:

Adults

- 'Gastroesophageal reflux disease' (GERD). This is where acid from the stomach enters the oesophagus (the passage between the throat and stomach) causing pain, inflammation and heartburn.
- Stomach ulcers caused by medicines called NSAIDs (Non-Steroidal Anti-Inflammatory Drugs). Esomeprazole can also be used to prevent stomach ulcers from developing if you are taking NSAIDs.
- Prevention of rebleeding following therapeutic endoscopy for acute bleeding from gastric or duodenal ulcers.

Children and adolescents aged 1-18 years

- 'Gastroesophageal reflux disease' (GERD). This is where acid from the stomach enters the oesophagus (the passage between the throat and stomach) causing pain, inflammation and heartburn.

2. What you need to know before Esomeprazole Tillomed is given to you

You must not be given Esomeprazole Tillomed:

▪ If you are allergic to esomeprazole or any of the other ingredients of this medicine (listed in section 6).

▪ If you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking esomeprazole or other related medicines.
▪ If you are allergic to other proton pump inhibitors (e.g. pantoprazole, lanzoprazole, rabeprazole, omeprazole).
▪ If you are taking a medicine containing nelfinavir (used to treat HIV infection).

You must not be given Esomeprazole Tillomed if any of the above apply to you. If you are not sure, talk to your doctor or nurse before you are given this medicine.

Warnings and precautions

Talk to your doctor or nurse before you are given Esomeprazole Tillomed if:

- you have severe liver problems
- you have severe kidney problems
- you have ever had a skin reaction after treatment with a medicine similar to Esomeprazole Tillomed that reduces stomach acid
- you are due to have a specific blood test (Chromogranin A).

Esomeprazole may hide the symptoms of other diseases. **Therefore, talk to your doctor immediately, if any of the following applies to you before or after you are given Esomeprazole Tillomed:**

- you are losing a lot of weight for no obvious reason and have difficulty swallowing.
- you get stomach pain or digestive disorders.
- You vomit food or blood.
- you pass black stools (bloody faeces).

Using a proton pump inhibitor like esomeprazole may slightly increase your risk of fractures in the hip, wrist or spine, especially if used over a period of more than one year. Tell your doctor if you have osteoporosis or if you are taking corticosteroids (which may increase the risk of osteoporosis).

If you get a rash on your skin, especially in areas exposed to the sun, tell your doctor as soon as you can, as you may need to stop your treatment with esomeprazole. Remember to also mention any other ill-effects like pain in your joints.

Serious skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), have been reported in association with esomeprazole treatment. Stop using esomeprazole and seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.

If at any time during treatment (even after several weeks) you develop a skin rash or any of these skin symptoms, stop taking this medicine and contact your doctor immediately.

Other medicines and Esomeprazole Tillomed

Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription. This is because esomeprazole can affect the way some medicines work and some medicines can have an effect on esomeprazole.

You must not be given esomeprazole if you are taking a medicine containing nelfinavir (used to treat HIV infection).

Tell your doctor or nurse if you are taking any of the following medicines:
- atazanavir (used to treat HIV infection)
- clopidogrel (used to prevent blood clots)
- ketoconazole, itraconazole or voriconazole (used to treat infections caused by a fungus)
- erlotinib (used to treat cancer)
- citalopram, imipramine or clomipramine (used to treat depression)
- diazepam (used to treat anxiety, relax muscles or for epilepsy)
- phenytoin (used in epilepsy). If you are taking phenytoin, you doctor will need to monitor you when you start or stop using esomeprazole.
- Medicines that are used to thin your blood, such as warfarin. Your doctor may need to monitor you when you start or stop using esomeprazole.
- Cilostazol (used to treat intermittent claudication - a pain in your legs when you walk caused by an insufficient blood circulation).
- Cisapride (used for indigestion and heartburn)
- Digoxin (used for heart problems)
- Methotrexate (a chemotherapy medicine used in high doses to treat cancer) - if you are taking a high dose methotrexate, your doctor may temporarily stop your esomeprazole treatment.
- tacrolimus (organ transplantation)
- rifampicin (used for treatment of tuberculosis)
- St. John's wort (*Hypericum perforatum*) (used to treat depression)

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before you are given this medicine.

Pregnancy

Your doctor will decide whether you can use esomeprazole during this time.

Breast-feeding

It is not known whether esomeprazole passes into breast milk. Therefore, you should not be given esomeprazole if you are breastfeeding.

Driving and using machines:

Esomeprazole is not likely to affect you being able to drive or use machines. However, side effects such as dizziness and blurred vision may uncommonly occur (see section 4). If affected, you should not drive or use machines.

3. How Esomeprazole Tillomed is given to you

Esomeprazole can be given to children and adolescents aged 1-18 years and adults, including the elderly.

Type of use

Adults

- Esomeprazole Tillomed will be given to you by your doctor who will decide how much you need.
- The recommended dose is 20 mg or 40 mg once a day.
- If you have severe liver problems, the maximum dose is 20 mg a day (GERD).

- The medicine will be given to you as an injection or infusion into one of your veins. This takes up to 30 minutes.
- The recommended dose for prevention of re-bleeding of gastric or duodenal ulcer is 80 mg administered as intravenous infusion over a period of 30 minutes, followed by a continuous infusion of 8 mg/hr given over 3 days. If you have severe liver problems, a continuous infusion of 4 mg/hr given over 3 days may be sufficient.

Children and adolescents aged 1 to 18 years

- Esomeprazole Tillomed will be given by the doctor who will decide how much is needed.
- For children 1-11 years of age, the recommended dose is 10 or 20 mg given once a day.
- For children 12-18 years of age, the recommended dose is 20 or 40 mg given once a day.
- The medicine will be given as an injection or infusion into a vein. This takes up to 30 minutes.

If you are given more Esomeprazole Tillomed than you should

If you think you have been given too much Esomeprazole Tillomed, talk to your doctor immediately.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you notice any of the following serious side effects, stop taking Esomeprazole Tillomed and contact a doctor immediately:

- Sudden wheezing, swelling of your lips, tongue and throat or body, skin rash, fainting or difficulties in swallowing (severe allergic reaction) (rare).
- Sudden onset of severe skin rash or reddening of the skin with blistering or peeling, which may occur even after several weeks of treatment. Severe blistering and bleeding of the lips, eyes, mouth, nose and genitals can also occur. The skin rashes can develop into severe, extensive skin damage (detachment of the epidermis and superficial mucous membranes) with life-threatening consequences. This could be “erythema multiforme”, "Stevens-Johnson syndrome", "toxic epidermal necrolysis" (very rare).
- Widespread rash, high body temperature and enlarged lymph nodes (DRESS syndrome or drug hypersensitivity syndrome), seen very rarely.
- Yellow skin, dark coloured urine and tiredness which can be symptoms of liver problems (rare).

Other side effects include:

Common: (may affect up to 1 in 10 people)

- Headache

- Effects on your stomach and/or intestines: diarrhoea, stomach pain, constipation, flatulence (bloating)
- Feeling sick (nausea) or being sick (vomiting)
- Injection site reaction
- Benign polyps in the stomach

Uncommon: (may affect up to 1 in 100 people)
- Swelling of the feet and ankles
- Sleep disorders (insomnia)
- Dizziness, tingling, fatigue
- Spinning sensation (vertigo)
- Visual disorders such as blurred vision
- Dry mouth
- Changes in blood tests used to measure liver function
- Skin rash, lumpy rash (hives) and itchy skin (pruritus)
- Bone fracture of the hip, wrist or spine (when esomeprazole is used in high doses and over a long period of time)

Rare: (may affect up to 1 in 1,000 people)
- Blood disorders such as a reduced number of white cells or platelets. This may cause weakness, bruising or make infections more likely.
- Low levels of sodium in the blood. This may cause weakness, being sick (vomiting) and muscle spasms.
- Excitement, confusion, depression
- Taste changes
- Suddenly feeling wheezy or short of breath (bronchospasm)
- An inflammation of the inside of the mouth
- An infection called "thrush" which can affect the gut and is caused by a fungus
- Liver problems, including jaundice which can cause yellowing of the skin, darkening of urine and tiredness
- Hair loss (alopecia)
- Skin rash on exposure to sunshine
- Joint pain (arthralgia) or muscle pain (myalgia)
- General feeling unwell and lacking energy
- Increased sweating

Very rare: (may affect up to 1 in 10,000 people)
- Changes in blood count including agranulocytosis (lack of white blood cells)
- Aggression
- Seeing, feeling or hearing things that are not real (hallucinations)
- Severe liver problems leading to liver failure and inflammation of the brain (encephalitis)
- Muscle weakness
- Severe kidney problems
- Enlargement of male breast

Not known: frequency cannot be estimated from the available data
- If you use esomeprazole for more than three months it is possible that the levels of magnesium in your blood may fall. Low levels of magnesium can manifest as fatigue,

involuntary muscle contractions, confusion, cramps, dizziness or increased heart rate. If you experience any of these symptoms, tell your doctor promptly. Low levels of magnesium can also lead to a reduction in potassium or calcium levels in the blood. Your doctor may perform regular blood tests to monitor your levels of magnesium.
- Inflammation in the gut (leading to diarrhoea)
- Rash, possibly with pain in the joints

Esomeprazole, may, in very rare cases, affect the white blood cells and lead to immune deficiency. If you have an infection with symptoms such as fever and a severely reduced general condition of health, or fever with symptoms of a local infection such as pain in the neck, throat or mouth, or difficulties in urinating, you must see your doctor as soon as possible so that a lack of white blood cells (agranulocytosis) can be ruled out by a blood test. It is important that you give information about your medication at this time.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance Website: www.hpra.ie. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Esomeprazole Tillomed

Keep this medicine out of the sight and reach of children.

The doctor or hospital pharmacist are responsible for storing, using and disposing of Esomeprazole Tillomed correctly.

Do not use this medicine after the expiry date, which is stated on the carton and vial after 'Exp'. The expiry date refers to the last day of that month.

Do not store above 25 °C.

Store in the original package, in order to protect from light. Vials can however be stored exposed to normal indoor light outside the box for up to 24 hours.

Do not refrigerate.

Chemical and physical in-use stability has been demonstrated for 12 hours at 30 °C.

From a microbiological point of view, unless the method of reconstitution precludes the risk of microbial contamination, the product should be used immediately.

If not used immediately, in-use storage times and conditions are the responsibility of user.

Do not use if solution shows signs of deterioration.

6. Contents of the pack and other information

What Esomeprazole Tillomed contains

The active substance is esomeprazole sodium. Each vial of powder for solution for injection/infusion contains 42.5 mg of esomeprazole sodium, equivalent to 40 mg of esomeprazole.

The other ingredients are: disodium edetate and sodium hydroxide (for pH-adjustment). Each vial contains less than 1 mmol sodium (23 mg) i.e. essentially ‘sodium-free’.

What Esomeprazole Tillomed looks like and contents of the pack

Esomeprazole Tillomed 40 mg powder for solution for injection/infusion is white to off white porous cake or powder. This is made into a solution before it is given to you.

Esomeprazole Tillomed is filled in 5 ml type-I, clear glass vial stoppered with dark grey bromobutyl rubber stopper and sealed with purple aluminium flip off seal.

Esomeprazole Tillomed is available in packs of 1, 10 and 50 vials.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Laboratorios Tillomed Spain S.L.U.
Calle Marcelo Spinola 8, planta 1, Puerta F,
28016, Madrid
Spain

Manufacturer

Tillomed Malta Limited
Malta Life Sciences Park,
LS2.01.06 Industrial Estate,
San Gwann, SGN 3000, Malta

This medicinal product is authorised in the Member States of the EEA under the following names:

Country	**Product Name**
Germany	Esomeprazol Tillomed 40 mg Pulver zur Herstellung einer Injektions-/Infusionslösung
Italy	Esomeprazolo Tillomed
France	ESOMEPRAZOLE TILLOMED 40 mg, poudre pour solution injectable/pour perfusion
Poland	Esomeprazole Zentiva
Austria	Esomeprazol Tillomed 40 mg Pulver zur Herstellung einer Injektions-/Infusionslösung
Netherlands	Esomeprazol Tillomed 40 mg poeder voor oplossing voor injectie /infusie
Ireland	Esomeprazole Tillomed 40 mg powder for solution for injection/infusion

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The following information is intended for medical or healthcare professionals only.

Esomeprazole Tillomed 40 mg powder for solution for injection/infusion contains 40 mg esomeprazole as sodium salt. Each vial contains disodium edetate and sodium hydroxide (< 1 mmol sodium).

The vials are for single use only. If the entire reconstituted content of the vial is not required for a single dose, any unused solution should be discarded.

For further information on dosage recommendations and storage conditions see sections 3 and 5 respectively.

Preparation and administration of the reconstituted solution

For the reconstitution of solution, withdraw the plastic cap of colour at the top of the vial of Esomeprazole Tillomed 40 mg powder for solution for injection/infusion and pierce the stopper in the centre of the designed circle, by maintaining the needle vertically, in order to be able to cross the stopper correctly.

The reconstituted solution for injection/infusion should be clear and colourless to very slightly yellow. It should be inspected visually for particulate matter and discoloration before administration and only clear solution should be used.

Do not refrigerate

Chemical and physical in-use stability has been demonstrated for 12 hours at 30 °C.

From a microbiological point of view, unless the method of reconstitution precludes the risk of microbial contamination, the product should be used immediately.

If not used immediately, in-use storage times and conditions are the responsibility of user.

Esomeprazole Tillomed 40 mg powder for solution for injection/infusion

To prepare a solution for injection

Injection 40 mg

For 8 mg/ml esomeprazole reconstituted solution: Prepare the solution by adding 5 ml of 0.9% sodium chloride for intravenous use to the esomeprazole 40 mg vial.

The reconstituted solution for injection should be administered intravenously over a period of at least 3 minutes.

For further information on dose administration, please see SmPC section 4.2.

To prepare a solution for infusion:

Infusion 40 mg (400 mcg/ml or 0.4 mg/ml)

Dissolve the content of one esomeprazole 40 mg vial in up to 100 ml of 0.9% sodium chloride for intravenous use.

Infusion 80 mg (800 mcg/ml or 0.8 mg/ml)

Dissolve the contents of two esomeprazole 40 mg vials in up to 100 ml of 0.9% sodium chloride for intravenous use.

For further information on dose administration, please see SmPC section 4.2.

Disposal

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