PACKAGE LEAFLET: INFORMATION FOR THE USER

Prolastin® 4000 mg, powder and solvent for solution for infusion
Prolastin® 5000 mg, powder and solvent for solution for infusion

Active ingredient: alpha$_1$-proteinase inhibitor, human

Read all of this leaflet carefully before you start using 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.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Prolastin is and what it is used for

Prolastin belongs to the class of compounds known as proteinase inhibitors.

Alpha$_1$-proteinase inhibitor (alpha$_1$-PI) is a substance formed in the body to inhibit substances known as elastases that damage the lungs. Where there is a hereditary deficiency of alpha$_1$-PI, there is an imbalance between alpha$_1$-PI and elastases. This may lead to progressive destruction of lung tissue and development of pulmonary emphysema. Pulmonary emphysema is an abnormal enlargement of the lungs, accompanied by destruction of the lung tissue. Prolastin is used to restore the balance between alpha$_1$-PI and elastases in the lung and consequently to prevent a further deterioration in the pulmonary emphysema.

Prolastin is used as long-term therapy in patients with alpha$_1$-proteinase inhibitor deficiency in particular forms as determined by your doctor.

2. What you need to know before you use Prolastin

Do not use Prolastin:

- if you are allergic (hypersensitive) to the active substance, alpha$_1$-proteinase inhibitor, or any of the other ingredients of Prolastin (listed in section 6).
- if you are known to have a deficiency of particular immunoglobulins (IgA), as severe allergic reactions, even to the point of anaphylactic shock, may occur in such cases.

Warnings and precautions:
- Talk to your doctor, pharmacist or nurse before using Prolastin.
- Tell your doctor if you have a severely weakened heart (heart failure). Special caution is necessary, as Prolastin can lead to a temporary increase in blood volume.

Allergic reactions (hypersensitivity)
Rarely hypersensitivity reactions to Prolastin may occur even if you have well tolerated alpha$_1$-proteinase inhibitor with previous administrations.
Your doctor will inform you about the signs of allergic reactions and what to do should they occur (see also section 4).
If you experience any sign of an allergic reaction during infusion of the medicine, tell your doctor or nurse immediately.

Information on safety with respect for risk to infections
When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These include:
- careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded,
- the testing of each donation and pools of plasma for signs of virus/infections,
- the inclusion of steps in the processing of the blood or plasma that can inactivate or remove viruses.

Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus. They may be of limited value against non-enveloped viruses such as hepatitis A and parvovirus B19. Parvovirus B19 infection may be serious for pregnant women (foetal infection) and for individuals whose immune system is depressed or who have some types of anaemia (e.g. sickle cell disease or haemolytic anaemia).

Your doctor may recommend that you consider vaccination against hepatitis A and B if you regularly/repeatedly receive human plasma–derived proteinase inhibitors.

It is strongly recommended that every time you receive a dose of Prolastin the name and batch number of the product are recorded in order to maintain a record of the batches used.

Smoking
Since the efficacy of Prolastin will be compromised by tobacco smoke in the lungs, cessation of smoking is strongly recommended.

Children and adolescents
No experience is available on use of Prolastin in children and young patients below the age of 18.

Other medicines and Prolastin
To date, there are no known interactions between Prolastin and other medicines.
Please nevertheless tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding
Ask your doctor or pharmacist for advice before taking any medicine.
There is no experience of use of Prolastin during pregnancy. Tell your doctor if you are pregnant or plan to become pregnant. It is not known whether Prolastin passes into breast milk. Ask your doctor for advice if you are breastfeeding.

Driving and using machines
There are no indications that Prolastin impairs the ability to drive or use machines.

Prolastin contains sodium
Prolastin 4000 mg contains approximately 441.6 mg sodium (main component of cooking/table salt).
Prolastin 5000 mg contains approximately 552.0 mg sodium (main component of cooking/table salt).
In case of a patient of 75 kg bodyweight a recommended dose is equivalent to 24.84 % of the recommended maximum daily dietary intake of sodium for an adult. Talk to your doctor or pharmacist if you have been advised to follow a low salt (sodium) diet.

3. How to use Prolastin

After reconstitution with the co-packed solvent, Prolastin is administered by intravenous infusion. A physician experienced with chronic obstructive lung diseases will supervise the first infusions with Prolastin.

<u>Home treatment</u>
After the first infusions, a healthcare professional might also administer Prolastin, but only after having received adequate training. Your attending physician decides whether you are suitable for home treatment and will make sure that the healthcare professional is instructed with regards to:

- how to prepare and administer the reconstituted solution for infusion (see illustrated instructions at the end of this leaflet),
- how to keep the medicine sterile (aseptic infusion techniques),
- how to keep a treatment diary,
- how to identify side effects, including signs of allergic reactions, and measures to be taken in case such effects occur (see also section 4).

Dose

The amount of Prolastin you are receiving is based on your body weight. A once-weekly dose of 60 mg active substance per kg of body weight (equivalent to 180 mL reconstituted solution for infusion containing 25 mg/mL alpha$_1$-proteinase inhibitor (human) in the case of a patient weighing 75 kg) is usually sufficient to keep protective levels of the serum alpha$_1$-proteinase inhibitor preventing further worsening of the pulmonary emphysema.

The doctor in charge of your treatment will decide on its duration. There are no indications to date of any need to limit the duration of treatment.

If you have the impression that the effect of Prolastin is too strong or too weak, talk to your doctor or pharmacist.

If you use more Prolastin than you should

Consequences of overdose are not known to date.

- Tell your doctor or healthcare professional if you think you have used more Prolastin than you should. He or she will take the appropriate measures.

If you forget to use Prolastin

- Talk to your physician to decide if the missed dose should be administered.
- Do not take a double dose to make up for a forgotten infusion.

If you stop using Prolastin

If treatment with Prolastin is stopped, your condition may worsen. Please talk to the doctor in charge of your treatment if you wish treatment with Prolastin to be ended prematurely.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

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

If side effects occur during infusion of Prolastin, the infusion should be suspended or discontinued, depending on the nature and severity of the side effect.

Possible serious side effects

Rarely (may affect up to 1 in 1,000 people) **hypersensitivity** reactions may occur, in some very rare cases (may affect up to 1 in 10,000 people) these reactions can present as anaphylactic reactions of any kind, even if you experienced no signs of allergy on previous infusions.

Tell your doctor or nurse **immediately**, if you observe any of the following signs:

- rash, hives, itching,
- difficulty swallowing,
- swelling of your face or mouth,
- flushing,
- difficulty in breathing (dyspnoea),
- fall in blood pressure,
- alteration of heart rate,
- chills.

Your doctor or healthcare professional will decide whether to slow or to stop the infusion and institute the suitable therapy as necessary.
In case of home treatment, **stop the infusion immediately** and contact your doctor or healthcare professional.

The following side effects have been observed during treatment with Prolastin:

Uncommon*:* (may affect up to 1 in 100 people)*:*
- chills, fever, flu-like symptoms, pain in the chest
- hives (urticaria)
- dizziness, dazed state, headache
- difficulty breathing (dyspnoea)
- rash
- nausea
- joint pain (arthralgia)

Rare*:* (may affect up to 1 in 1,000 people):
- hypersensitivity reactions
- fast pulse (tachycardia)
- low blood pressure (hypotension)
- high blood pressure (hypertension)
- back pain

Very rare*:* (may affect up to 1 in 10,000 people):
- allergic shock

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. 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 Prolastin

Do not store above 25°C**.**
Do not freeze.

The reconstituted solution should not be refrigerated and should always be used within 3 hours of its preparation. Any unused medicinal product should be discarded.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

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

Do not use Prolastin after the expiry date which is stated on the vial label and the carton.

6. Contents of the pack and other information

What Prolastin contains

- The active substance is alpha$_1$-proteinase inhibitor, human (i.e. derived from human blood or plasma)
- The other ingredients are sodium chloride, sodium dihydrogen phosphate, water for injections (solvent/diluent).

What Prolastin looks like and contents of the pack

Alpha$_1$-proteinase inhibitor is a white or pale yellow or pale brown powder or friable mass.
After it has been reconstituted with water for injections, the solution should be clear to slightly opalescent, colourless, pale green, pale yellow or pale brown and free from visible particles.
1 mL of the reconstituted solution contains 25 mg alpha$_1$-proteinase inhibitor.

One single pack contains:
Prolastin 4000 mg, powder and solvent for solution for infusion
- 1 vial with powder containing 4000 mg alpha1-proteinase inhibitor, human.
- 1 vial with 160 mL solvent (water for injections).
- 1 transfer device for reconstitution.

Prolastin 5000 mg, powder and solvent for solution for infusion
- 1 vial with powder containing 5000 mg alpha1-proteinase inhibitor, human.
- 1 vial with 200 mL solvent (water for injections).
- 1 transfer device for reconstitution.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

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Manufacturer
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Can Guasch, 2 - Parets del Vallès
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This medicinal product is authorised in the Member States of the EEA under the following names:

Prolastin [4000 mg/5000 mg]: Austria, Ireland, Italy, France, Germany, Greece, Netherlands, Poland, Portugal.
Prolastina [4000 mg/5000 mg]: Denmark, Finland, Norway, Spain, Sweden.
Pulmolast [4000 mg/5000 mg]: Belgium.

This leaflet was last revised in.

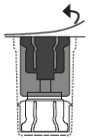
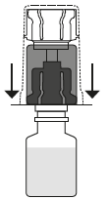
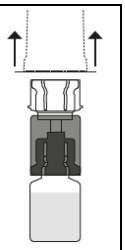
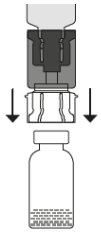
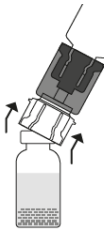
Product Authorisation Number: PA1405/002/002
Product Authorisation Number: PA1405/002/003

Detailed information on this medicine is available on the website of the Health Products Regulatory Authority (HPRA) www.hpra.ie.

Information for healthcare professionals and for patients suitable for home treatment:

Preparation of the reconstituted solution for infusion:

1. Use aseptic technique (clean and sanitized) in order to maintain sterility. Perform the reconstitution procedure on a flat work surface.
2. Ensure that the vials of Prolastin powder and the solvent (sterile Water for Injections) are at room temperature (20-25ºC).
3. Remove the protective cap from both the Prolastin vial and the solvent vial and clean the collar rims and the stoppers with an alcohol swab. Allow the rubber stoppers to dry.

4. Open the sterile transfer device package by peeling away the lid completely. Do not remove the device from the package. 	5. Place the solvent vial upright on the even surface and hold it securely. Without removing the outer package press the blue end of the transfer adapter straight down until the spike penetrates the stopper and snaps. Avoid rotating. 	6. Remove the clear outer packaging from the transfer adapter and discard it. 
7. Place the Prolastin powder vial upright on the surface. Turn the unit consisting of the adapter and the solvent vial upside down by 180°. Push it with the clear/white end of the adapter straight down – without rotating - until the spike penetrates the stopper and snaps. 	8. Due to the vacuum in the powder vial the solvent transfer will start automatically. Wait for complete transfer of the solvent. Remove the adapter with the connected solvent vial in an approximate angle of 45°. 	9. Gently swirl the Prolastin vial until the powder is completely dissolved. Do not shake to avoid foaming. Do not touch the stopper. Proceed with the administration of the product by aseptic technique. 

10. If more than one vial of product will be needed to achieve the required dose, repeat instructions above using the additional package containing a new transfer adapter. Do not reuse the adapter.

Total dissolution should be obtained within approximately 15 minutes.
Only clear to slightly opalescent solutions, colourless, pale green, pale yellow or pale brown and free from visible particles should be used. Prolastin should not be mixed with other solutions for infusion. The reconstituted solution should always be used within 3 hours of its preparation.

The reconstituted solution should be administered by slow intravenous infusion, using a suitable infusion set (not included). The infusion rate should not exceed 0.08 mL/kg of body weight (equivalent to 6 mL in a patient weighing 75 kg) per minute.