Package leaflet: Information for the user

CEPROTIN 1,000 IU powder and solvent for solution for injection
human protein C

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 or pharmacist.
- 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 the side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What CEPROTIN is and what it is used for
2. What you need to know before you use CEPROTIN
3. How to use CEPROTIN
4. Possible side effects
5. How to store CEPROTIN
6. Contents of the pack and other information

1. What CEPROTIN is and what it is used for

CEPROTIN belongs to a class of medicines called antithrombotics. This medicine contains Protein C, a natural protein that is made in the liver and is present in your blood. Protein C plays a major role in prevention of excessive clot formation thus, prevent and/or treat intravascular thrombosis.

CEPROTIN is used in the treatment and prevention of thrombotic and haemorrhagic skin lesions (named purpura fulminans) in patients with severe congenital protein C deficiency. CEPROTIN may be used to treat a rare complication of a blood thinner medicine (anticoagulant medicine named coumarin) which may result in severe skin lesion (necrosis). Additionally, CEPROTIN may be used in the treatment of blood clot (venous thrombotic) events.

2. What you need to know before you use CEPROTIN

Do not use CEPROTIN

- if you are allergic to human protein C or any of the other ingredients of this medicine (listed in section 6) including mouse protein or heparin.

However, in the case of life-threatening thrombotic complications your doctor may still decide to continue treatment with CEPROTIN.

Warnings and precautions

Talk to your doctor or pharmacist before using CEPROTIN. Take special care with CEPROTIN if symptoms of allergy occur. Symptoms of allergy include rash, hives, breathing difficulties, low blood pressure, tightness of chest, and shock. If such symptoms occur during the administration of CEPROTIN, injection should be stopped. Such symptoms may constitute an allergic reaction to any of the components, to mouse protein or heparin. The preparation may contain traces of heparin and/or mouse protein as a result of the manufacturing process. If such a reaction occurs, your doctor will decide on the most appropriate treatment.

If the preparation is used in patients with severe congenital protein C deficiency, antibodies inhibiting protein C may develop that can inhibit protein C and therefore diminish the effect of the preparation. However, this has not been observed in the clinical studies to date.

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, and the testing of each donation and pools of plasma for signs of virus/infections. Manufacturers of these products also include 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, and for the non-enveloped hepatitis A virus. The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19. Parvovirus B 19 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 Protein C products.

Other medicines and CEPROTIN

No interactions with other medicinal products are currently known.
Nevertheless, please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

If you change to treatment with oral anticoagulants, treatment with CEPROTIN must continue until the blood level of the oral anticoagulation is adequate and stable.

CEPROTIN with food and drink

Not applicable.

Pregnancy and breast-feeding

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 taking this medicine.
Your doctor will decide if CEPROTIN may be used during pregnancy and lactation.

Driving and using machines

CEPROTIN has no influence on your ability to drive or to operate machines.

CEPROTIN contains Sodium

This medicine contains 44.9 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 2.2% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use CEPROTIN

CEPROTIN is intended for intravenous administration (infusion into a vein). It is given to you under close supervision of your doctor who is experienced in substitution therapy of coagulation

factors/inhibitors and where monitoring of protein C activity is possible. Dosage will vary depending on your condition and your body weight.

Dosage

The dose, administration frequency and duration of treatment depend on the severity of the protein C deficiency as well as on your clinical condition and on your plasma level of protein C. They should be adjusted accordingly on the basis of clinical effectiveness and laboratory assessment.

Treatment of acute episodes and short-term prophylaxis
A protein C activity of 100 % (1 IU/ml) should be achieved initially and the activity should be maintained above 25 % for the duration of the treatment.

An initial dose of 60 to 80 IU/kg should be administered. Your physician will take several blood drawings over time to determine how long protein C is remaining in your body.

The measurement of protein C activity using chromogenic substrates is recommended for the determination of your plasma level for protein C before and during treatment with CEPROTIN.

The dosage should be determined on the basis of laboratory measurements of the protein C activity. In the case of an acute thrombotic event these should be performed every 6 hours until your condition is stabilised, thereafter twice a day and always immediately before the next injection. It should be kept in mind that the half-life of protein C may be severely shortened in certain clinical conditions such as acute thrombosis with purpura fulminans and skin necrosis.

If the response to CEPROTIN injection is satisfactory, dosing may be gradually reduced to 12 hourly dosing ensuring trough protein C activity >25%.

If you receive prophylactic administration of protein C, higher trough levels may be warranted in situations of an increased risk of thrombosis (such as infection, trauma, or surgical intervention).

Long-term prophylaxis
For the long-term prophylactic treatment, a dose of 45 to 60 IU/kg every 12 hours is recommended. Measurement of the protein C activity should be performed to ensure trough levels of 25% or more.

In rare cases, subcutaneous infusion of 250 - 350 IU/kg has produced therapeutic plasma protein C levels in patients with no intravenous access.

If you have kidney and/or liver disease, please inform your doctor, because he may have to adjust your treatment accordingly.

Combination treatment
If you are switched to permanent prophylaxis with oral anticoagulants, protein C replacement is to be discontinued only when stable anticoagulation is obtained (see “Important information about some of the ingredients of CEPROTIN”).

At start of a combination treatment of anticoagulants (especially Vitamin K antagonists) with Protein C, stable activity levels of Protein C above 0.25 IU/ml should be maintained before starting the anticoagulation. Careful monitoring of the international normalized ratio (INR) is recommended. In the combination of Protein C Concentrate and anticoagulants, a Protein C trough level of about 10% or more is recommended to be maintained.

If you have APC resistance which is a thromboembolic risk factor present in up to 5 % of the population in Europe your doctor may need to adjust your treatment accordingly.

Administration

CEPROTIN will be administered to you by intravenous injection after reconstitution of the powder for solution for injection with Sterilised Water for Injections. It is strongly recommended that every time you receive a dose of CEPROTIN the name and batch number of the product are recorded in order to maintain a record of the batches used.

Reconstitute lyophilised CEPROTIN powder for solution for injection, with the supplied solvent (Sterilised Water for Injections) using the sterile transfer needle. Gently rotate the vial until all powder is dissolved.

After reconstitution, the solution is drawn through the sterile filter needle into a sterile disposable syringe. A separate unused filter needle must be used to withdraw each vial of reconstituted CEPROTIN. The solution should be discarded if particulate matter is visible.

The reconstituted solution should be administered immediately by intravenous injection.

CEPROTIN should be administered at a maximum injection rate of 2 ml per minute. In children with a body weight of less than 10 kg, the injection rate should not exceed a rate of 0.2 ml/kg/min.

All unused solution, empty vials and used needles and syringes must be discarded appropriately.

Frequency and duration of treatment depend on the severity of your protein C deficiency, on the results of determination of protein C levels in your plasma as well as on the location and extent of thrombosis.

In case of acute thrombosis CEPROTIN may be administered to you every 6 hours. As the tendency for thrombus formation decreases, the frequency may be reduced.

If you use more CEPROTIN than you should

It is recommended that you adhere to the dose level and frequency of administration as recommended by your doctor. In case you administered more CEPROTIN than recommended, please inform your doctor as soon as possible.

If you forget to use CEPROTIN

Not applicable.

If you stop using CEPROTIN

Do not stop using CEPROTIN without consulting your doctor.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

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

You may notice any of the following side effects after administration of CEPROTIN:

- As with any product administered by infusion into a vein allergic reactions including severe and potentially life-threatening reactions (anaphylaxis) are possible.
  You should be aware of the early signs of allergic reactions such as burning and stinging at the injection site, chills, flushing, rash, hives, breathing difficulty, nausea, headache, lethargy, low blood pressure, and tightness of the chest.

- The following side effects were rarely observed during clinical studies (less than 1 case in 1,000 administrations given to patients): itching (pruritus), rash and dizziness.
- In the postmarketing experience there have been reports of restlessness, excessive sweating, and pain and redness at the injection site.

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 Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store CEPROTIN

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.
Store in a refrigerator (2°C – 8°C). Do not freeze.
Keep the vial in the outer carton in order to protect from light.

The reconstituted solution should be used immediately.

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 to protect the environment.

6. Contents of the pack and other information

What CEPROTIN contains

Powder:
- The active substance is human protein C
- The other ingredients are human albumin, trisodium citrate dihydrate and sodium chloride. As solvent sterilised water for injections is used.

What CEPROTIN looks like and contents of the pack

CEPROTIN is presented as powder and solvent for solution for injection and is a white or cream coloured powder or friable solid. After reconstitution the solution is colourless to slightly yellowish and clear to slightly opalescent and essentially free from visible particles.

Each pack also contains one transfer needle and one filter needle.

Marketing Authorisation Holder and Manufacturer:

Takeda Manufacturing Austria AG
Industriestrasse 67
1221 Vienna
Austria
Tel.: +44 (0)3333 000181
E-mail: medinfoemea@takeda.com

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