Package leaflet: Information for the user

Cofact 250 IU, human prothrombin complex, 250 IU factor IX per vial, powder and solvent for solution for injection.
Cofact 500 IU, human prothrombin complex, 500 IU factor IX per vial, powder and solvent for solution for injection.

Human prothrombine complex = factor II/VII/IX/X

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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This include any possible side effect not listed in this leaflet. See section 4.

What is in this leaflet:

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

1. What Cofact is and what it is used for

Cofact is supplied as a powder and a solvent for a solution for injection (vial of 10 or 20 ml).

Cofact contains the coagulation factors II, VII, IX and X.

These factors are normal constituents of human blood. If there is a deficiency of one or more of these factors, blood coagulation disorders will take place. As a result of this, bleeding may occur. The administration of Cofact serves to supplement this deficiency, thereby combating or preventing bleeding.

Cofact can be used for:

The treatment of haemorrhages or the prevention of peri-operative haemorrhages as the result of

- acquired deficiency of the prothrombin complex coagulation factors. For example, in cases of deficiency caused by the treatment with vitamin K antagonists or by an overdose of vitamin K antagonists, when acute correction of the deficiency is required.
- congenital deficiencies of one of the vitamin K dependent coagulation factors, when purified and specific coagulation factors are not available.

2. What you need to know before you use Cofact

Do not use Cofact

- If you are allergic (hypersensitive) to coagulation factors or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

- When previous use of a blood product has shown you to be hypersensitive, Cofact should only be administered when nothing else is possible (such as in the case of life threatening situations). The treatment must take place in a hospital or under the careful supervision of a doctor.
- Cofact counteracts the effects of coumarin derivatives (medicines that prevent the coagulation of blood, the so-called anticoagulants). If the reason for the use of Cofact is 'an overdose with coumarin derivatives', you will usually also be given vitamin K.
- Your doctor will check whether the administration of Cofact poses a risk of thrombosis (the formation of blood clots in the blood vessels, see side effects). The following individuals have a greater chance of developing thrombosis:
    - individuals who have suffered a heart attack
    - individuals who have had (or still have) other diseases of the coronary arteries
    - individuals with liver diseases
    - newborn infants
    - individuals who have recently undergone surgery.

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 and other types of infections.

The measures taken are considered effective for enveloped viruses such as HIV, HBV, HCV and for non-enveloped virus HAV. The measures taken may be of limited value against other non-enveloped viruses such as Parvovirus B19. Parvovirus B19 infection may be serious for pregnant women (fetal infection) and for individuals whose immune system is depressed or who have some types of anaemia (e.g. sickle cell disease or haemolytic anaemia).

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

Other medicines and Cofact

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines, including medicines obtained without a prescription.

No information is available concerning possible interactions between Cofact and other medicines, with the exception of anticoagulants.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine.

The use of Cofact during pregnancy or while breast-feeding has not been investigated. Investigation with animals is not possible, because Cofact is manufactured from human blood. To date, no adverse events have been reported after the use of coagulation factors during pregnancy or breast-feeding. If you are pregnant, a nursing mother, or if you wish to become pregnant, you are advised to contact your doctor.

Driving and using machines

No effects of Cofact are expected to influence the ability to drive or to use machinery.

3. How to use Cofact

Your doctor will determine the quantity of Cofact that you require for the treatment or prevention of haemorrhages as a result of using anticoagulants or in case of a congenital deficiency of one of the vitamin K dependent coagulation factors.

The exact dose is dependent on

- the severity of your condition
- your weight
- the coagulation factors that you need
- the quantity of these factors in your blood (your blood level).

In case of congenital coagulation factor deficiency, it is important to regularly determine the blood levels of the coagulation factors.

Determination of INR value for the treatment or the prevention of haemorrhages as a result of using anticoagulants:

As a result of the use of an anticoagulant, it will take longer for your blood to clot. This increases the possibility of haemorrhages. The thrombo test (TT) will be used to determine the desired degree of anticoagulation activity during the declotting therapy. The result is expressed in INR (International Normalised Ratio). In the event of haemorrhages or to prevent haemorrhages, it is important that your INR is brought to a certain level.

The following must be done to obtain the desired INR level:

1. The administration of the anticoagulant must be stopped;
2. Vitamin K must be administered. In the case of an extreme severe loss of blood (shock), the vitamin K must be administered in a vein (intravenously).
3. Cofact must be administered until the desired INR has been reached. The doctor will use special tables for determining the dose.
4. It is important that your INR is regularly measured following the administration of Cofact and for some considerable time thereafter.

Instructions for use:

The powder should be dissolved in the accompanying water for injections. Both vials should be brought to room temperature (15-25 °C) beforehand. Dissolving will then be easier. Furthermore, the solution should not be too cold during administration.

1. Remove the protective plastic caps from the vial containing the powder and the vial containing the water for injections.
2. Disinfect the rubber stoppers of the vials with a piece of gauze soaked in 70% alcohol.
3. Detach the removable section of the transfer needle's protective sheath. Pierce the vial containing the water for injections using this unshielded end of the transfer needle. Now detach the other removable section of the transfer needle's protective sheath.
4. Invert the vial containing the transfer needle and immediately pierce the needle into the vial containing the powder. The water runs into the vial containing the powder on its own accord. Slightly tilt the vial containing the powder so that the water runs down the side of the vial. This improves the dissolution of the product. As soon as the water has flowed across, the empty vial and the transfer needle should be removed in a single action.

Dissolve the powder by swirling gently (do not shake!). The powder dissolves within 10 minutes to produce an almost completely clear, blue-coloured solution. The solution should not be turbid and must be free of lumps. Once dissolved, the product can be stored for 3 hours at room temperature (15-25 °C). If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user. The solution is intended to be used at one time.

Administration

The solution should be administered as soon as possible, at the most within 3 hours. Before administration, check if the product is clear and free of particles or lumps.

1. Draw the dissolved product out of the vial, using a syringe.
2. Cofact should be administered into a vein (intravenously).
3. Administer the dissolved product slowly (approx. 2 ml per minute).

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

4. Possible side effects

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

At high doses, the use of Cofact can lead to thrombosis, caused by the formation of clots in the blood vessels.

Patients with a deficiency of one of the coagulation factors II, VII, IX or X may develop antibodies against these factors as a result of using Cofact. In that case, the activity of the product will not be optimal.

In theory, allergy (hypersensitivity) may occur. In case of hypersensitivity, the administration must be immediately stopped.

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 the national reporting system, Nederlands Bijwerkingen Centrum Lareb (Website: www.lareb.nl). By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cofact

Store in a refrigerator (2°C - 8°C). Do not freeze. Keep the vial in the outer carton in order to protect from light.

Cofact can be stored at or below 25°C up to six months, for example while travelling, without impairing its efficacy. The date when taken to room temperature should be marked on the package. If not used during six months storage at room temperature the product must be discarded.

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 carton.

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.

6. Contents of the pack and other information

What Cofact contains

- The active substances are the coagulation factors II, VII, IX and X and further active substances are protein C&S.
- A vial of Cofact 250 IU contains 250 IU Factor IX; 140 – 350 IU Factor II; 70 - 200 IU Factor VII and 140 - 350 IU Factor X; 111 – 390 IU protein C; 10 – 80 IU protein S.
- A vial of Cofact 500 IU contains 500 IU Factor IX; 280 - 700 IU Factor II; 140 - 400 IU Factor VII and 280 - 700 IU Factor X; 222 – 780 IU protein C; 20 – 160 IU protein S.

After being dissolved in the supplied water for injection, the ready made solution for injection contains:

- Not less than 14 IU and not more than 35 IU factor II per ml;

- Not less than 7 IU and not more than 20 IU factor VII per ml;
- 25 IU factor IX per ml;
- Not less than 14 IU and not more than 35 IU factor X per ml;
- Not less than 11 IU and not more than 39 IU protein C per ml;
- Not less than 1 IU and not more than 8 IU protein S per ml.

The other ingredients are trisodium citrate dihydrate, sodium chloride and antithrombin.

What Cofact looks like and contents of the pack

The commercial package of Cofact consists of a box containing:

- A Cofact vial to be used for a 10 ml or 20 ml solution.
- A vial with 10 ml or 20 ml of water for injections.
- Requisite for dissolving the product: a transfer needle.

Cofact powder for injection is a bluish powder. Ready made solution for injection is a bluish solution.

Marketing authorisation holder and manufacturer

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Marketing authorisation number RVG 17060.

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The following information is intended for healthcare professionals only:

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