

Cetor[®]

Patient information

Read this package leaflet carefully when you have some time to yourself. The text may have been amended.

General characteristics

The product is marketed under the name of Cetor[®].

The commercial packing of Cetor[®] consists of:

- A vial of Cetor[®] 500 U ('E')
- A 5 ml vial of water for injections
- An administration set consisting of: 10 ml disposable syringe ('Plastipak'), transfer needle, filter needle and butterfly-wing needle (Valu-Set).

The product is supplied in the form of powder for solution for intravenous injection. The active substance is C1-esterase inhibitor. After dissolution in the water for injections supplied, the product contains:

100 U C1-esterase inhibitor per ml; 5 ml = 500 U C1-esterase inhibitor.

The product also contains the following excipients: hepatitis B immunoglobulin, sodium chloride, saccharose, trisodium citrate dihydrate, L-valine, L-alanine and L-threonine.

Cetor[®] (C1-esterase inhibitor) is a serine protease inhibitor. It is a normal constituent in human blood. C1-esterase inhibitor plays a part in the body's reaction to inflammation and in blood coagulation. Insufficient C1-esterase inhibitor can result in oedema (swelling). The administration of Cetor[®] compensates for this deficiency thereby preventing or combating such swelling.

Cetor[®] is produced and marketed by Sanquin, Amsterdam,
tel: +31 20 512 3355. The marketing authorisation number is RVG 19303.

To be used with

Cetor[®] is intended for patients with (active) C1-esterase inhibitor deficiency. There are two forms of C1-esterase inhibitor deficiency, namely:

- a hereditary, congenital form that produces oedema. This disease is referred to as hereditary angio oedema (HAE);
- a form that occurs in older people, known as 'acquired C1-esterase inhibitor deficiency'.

Cetor[®] is used to treat both forms of C1-esterase inhibitor deficiency:

- in the treatment of swellings in the throat or in the gastrointestinal tract;
- to prevent an attack of angio oedema, for example, prior to surgery or the extraction of a tooth;
- if necessary, for the treatment of swellings located elsewhere than the throat and gastrointestinal tract.

Important advance information

Cases in which Cetor[®] should not be used:

Cetor[®] may not be administered when you are susceptible to one of the substances.

Special warnings and precautions for use of Cetor®:

- After being dissolved in the water for injections supplied, the product should be clear and must be free of lumps or particulate matter. Check this immediately prior to administration. The product may not be administered if any turbidity, lumps or particulate matter are visible.
- In some patients with **acquired** C1-esterase inhibitor deficiency, the angio oedema attacks occur with increasing frequency and severity. Such patients may produce antibodies to C1-esterase inhibitor. As a result, this product will be increasingly ineffective. Contact your physician if you should experience angio oedema attacks of increasing frequency and severity.
- Cetor® can induce an acute attack of hypersensitivity (anaphylactic shock). If you have previously used blood or a blood product and have been shown to be hypersensitive, this product may only be administered when there is no other option available (as in the case of a life-threatening attack). The administration of Cetor® to patients who are hypersensitive to blood or blood products should take place in a hospital or under close monitoring by a physician.
- Cetor® can produce allergic side effects (see under side effects). You are advised to discuss the following with the attending physician:
 - How do you recognise the side effects and what are the symptoms?
 - What should you do if side effects occur?
 - Is it necessary to keep a stock of certain medicines to combat or prevent the side effect?

Cetor® is a purified protein that has been extracted from donor blood. The donor blood used for this purpose is obtained from healthy, voluntary, nonremunerated donors. These individuals satisfy the requirements imposed on blood donors in The Netherlands.

All blood donors are tested for several pathogens, such as:

- the AIDS virus;
- the hepatitis B and C viruses (which cause jaundice);
- *Treponema pallidum* (the causative agent of syphilis).

These pathogens could not be detected in the donors. In addition, Cetor® has undergone a 'virus inactivation' process. The effect of this 'virus inactivation' is to kill or remove any viruses that may still be present.

The chance of transmitting pathogens through the use of blood products is extremely small.

Use during pregnancy and breast-feeding:

The use of Cetor® during pregnancy or while breast-feeding has not been investigated. Animal studies are not possible since Cetor® is prepared from human blood. The use of C1-esterase inhibitor products during pregnancy or while breast-feeding has never produced harmful effects. If you are pregnant, a nursing mother or if you wish to become pregnant, you are advised to contact your physician.

Driving and using machines:

Cetor® has no known effects on the ability to drive and to use machines.

Using other medicines:

No information is available concerning possible interactions between Cetor® and other medicines in the body.

Instructions for use**Dose**

The amount of Cetor® required to combat or prevent an attack of angio oedema can vary. This depends upon the severity and the nature of the attack. The attending physician will decide on the dosage that you require.

The usual amount is:

- for combating an attack, particularly in the case of swellings in the larynx and of painful

swellings: 1,000 U (approx. 2 vials). For details of the method of administration, see 'Instructions for use during treatment at home'.

- prior to surgery to prevent an attack, particularly with operations in the area of the head or neck: 1,000 U (approx. 2 vials).

If you are to undergo surgery or have a tooth extracted, inform your physician or dentist that you suffer from C1-esterase inhibitor deficiency and require Ceter®. He/she will ensure that Ceter® is administered to you, if necessary.

Instructions for use during treatment at home

Treatment at home may only be used with patients who have received appropriate training. These instructions for use are only intended to reinforce what you have already been taught. Follow the instructions given you by the physician or pharmacist. Examine the vials. They should not be cracked. Check that the date of expiry has not been exceeded.

Dissolving

The powder should be dissolved in the water for injections supplied (5 ml). During actual administration, the solution should not be too cold. The powder also dissolves more readily if both vials are brought to room temperature (15-25 °C) in advance.

Wash hands.....

(1) Remove plastic caps

(2) Disinfect rubber stoppers

Transfer needle: remove cover from one end

(3) Pierce the vial of water

Transfer needle:..... remove cover

(4) Invert, pierce..... vial of powder

Tilt vial.....

Remove empty vial and... needle

Swirl gently.....

Examine solution.....

- Wash your hands carefully with soap and water, and work on a clean, smooth surface.
- Remove the protective plastic caps from the vial of powder and the vial containing water for injections.
- Disinfect the rubber stopper of each vial. You can either use one of the supplied disinfection tissues for this purpose, or a piece of gauze soaked in 70% alcohol.
- Detach the removable section of the transfer needle's (i.e. the double-ended needle) protective cover. It is vital that the needle should not come into contact with any other object (neither touch it nor set it down) once the protective cover has been removed.
- Pierce the vial containing water for injections using this unshielded end of the transfer needle.
- Now detach the other removable section of the transfer needle's protective cover. Here also, it is vital that the needle should not come into contact with any other object.
- Invert the vial containing the transfer needle and immediately pierce the vial of powder with the needle.
- The water will now run into the vial of powder of its own accord. Tilt the vial of powder slightly so that the water runs down the wall of the vial. This improves dissolution of the product.
- As soon as all the water has flowed across, the empty vial and the overflow 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 a clear solution. This may either be light blue or colourless.
- Examine the solution by holding the vial up to the light. The solution should not be turbid and must be free of

lumps or particulate matter. Do not administer if you do see any turbidity, lumps or particulate matter.

Intravenous administration

Cetor[®] must be administered directly into a vein in the inside part of the arm (see figure 6). Cetor[®] should be administered as soon as possible, and no later than 3 hours after piercing the vial. The entire solution should be used in a single administration. Any residual solution should be handed in to the pharmacist.

- Remove the disposable syringe (Plastipak) from its packing.
 - Detach the removable section of the filter needle's protective cover.
 - Fit the filter needle to the disposable syringe.
 - Remove the protective cover from the filter needle. It is vital that the needle does not come into contact with any other object.
 - Pierce the vial. Hold the vial and the syringe upside down.
 - Draw the solution up, slowly.
 - Remove the filter needle. When doing so, hold the disposable syringe point uppermost.
 - Hold the syringe with the point uppermost and tap the syringe (with a finger or a pencil). This will cause any air in the syringe to move upwards. Remove air by (carefully) depressing the plunger. Set the syringe down carefully. The point of the syringe should not come into contact with any other object.
 - Fit a tourniquet to make the injection site easier to see.
 - Disinfect the injection site. You can either use the second of the disinfection tissues supplied for this purpose, or a piece of gauze soaked in 70% alcohol.
 - Remove the butterfly-wing needle (Valu-Set) from the packing. Remove the tube connector's plastic cap from the butterfly-wing needle's tube.
 - Remove the protective cover from the butterfly-wing needle. Ensure that the needle does not come into contact with any other object.
 - Introduce the needle into the vein. Hold the needle securely by folding the wings upwards until they meet. The tube attached to the butterfly-wing needle will fill with blood.
 - Release the tourniquet.
 - Allow the tube attached to the butterfly-wing needle to fill **completely** with blood.
 - Fit the tube attached to the butterfly-wing needle to the disposable syringe.
 - Empty the syringe completely over a period of about **5 minutes**.
- Filter needle: remove... cover from one end**
- Fit filter needle to... syringe**
- Filter needle: remove... cover**
- (5) Pierce the vial.....**
- Draw up the solution....**
- Remove filter needle....**
- Remove the air.....**
- Fitting the tourniquet..**
- Disinfecting the skin...**
- Tube: remove cap.....**
- Butterfly-wing needle:.. remove cover**
- Piercing the vein.....**
- Releasing the tourniquet**
- Blood fills tube.....**
- Fitting syringe to tube**
- (6) Administer gradually**

[diagrams 1-6]

Undesirable effects

The incidental occurrence of allergy (hypersensitivity) is possible. Slight hypersensitivity, such as hives (urticaria), can be treated with antihistamines (anti-allergy medications) and corticosteroids (anti-inflammatory drugs) if necessary.

In the event of a severe attack of hypersensitivity (anaphylactic shock), administration should be ceased immediately.

For further details, see 'Important advance information'. Notify your physician or pharmacist if you experience an undesirable effect that is **not** described in the package leaflet or if you feel the side effect is serious.

Storage instructions and date of expiry

The final date on which the vial of Cetor® and the vial of water for injections may be used is indicated on the label. After this date, the products may no longer be used and they must be returned to the pharmacist.

The vial of powder should be stored in its box, at a temperature of 2-8 °C. The refrigerator is suitable for this purpose. The vial of water for injections need not be stored in the refrigerator (2-8 °C). Since the solution needs to reach room temperature (15-25 °C) prior to use, it is useful to store the vial of water for injections in a separate place. This vial should be stored in its box at a temperature between 2-25 °C (avoid freezing).

Date on which the package leaflet was last revised:

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