

PATIENT / USER INFORMATION LEAFLET

Cinryze 500 Units powder and solvent for solution for injection C1 inhibitor (human)

Read all of this leaflet carefully before you start taking this medicine.

- 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 any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Cinryze is and what it is used for
2. Before you take Cinryze
3. How to take Cinryze
4. Possible side effects
5. How to store Cinryze
6. Further information

1. WHAT CINRYZE IS AND WHAT IT IS USED FOR

Cinryze contains the human protein called “C1 inhibitor” as the active substance.

C1 inhibitor is a naturally occurring protein that is normally present in the blood. If you have a low amount of C1 inhibitor in your blood or your C1 inhibitor is not working properly, this can lead to swelling attacks (called angioedema). Symptoms may include stomach pains and swelling of the:

- hands and feet
- face, eyelids, lips or tongue
- voice-box (larynx), which may make breathing difficult
- genitals

In adults and adolescents, Cinryze can raise the amount of C1 inhibitor in the blood and either prevent these swelling attacks from occurring or stop swelling attacks once they have begun.

2. BEFORE YOU TAKE CINRYZE

Do not take Cinryze

- If you are allergic (hypersensitive) to C1 inhibitor or any of the other ingredients of Cinryze (see section 6, “Further information”). It is important to tell your doctor if you think you have ever had an allergic reaction to any of the ingredients in Cinryze.

Take special care with Cinryze

- Before you start treatment with Cinryze, it is important that you tell your doctor if you have, or have had, problems with your blood clotting (thrombotic events). You will be carefully monitored if this is the case.
- If you begin to suffer from rashes, tightness of the chest, wheezing, or a fast heart beat once you have taken Cinryze, you should tell your doctor **immediately**.

- 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 and hepatitis C viruses, and for the non-enveloped hepatitis A and parvovirus B19 viruses.

Your doctor may recommend that you consider having vaccinations against hepatitis A and B if you regularly or repeatedly receive C1 inhibitor products that have been taken from human plasma.

It is strongly recommended that every time you receive a dose of Cinryze the name and batch number of the product are recorded by your nurse or doctor in order to maintain a record for the batches used.

Children

Cinryze is not for use in children before adolescence.

Taking Cinryze with other medicines

Always tell your doctor about other medicines you are taking or have recently taken, including those bought without a prescription.

Pregnancy and breast-feeding

If you think you might be pregnant, are planning to get pregnant, or are breast-feeding, ask your doctor for advice before taking Cinryze. There is limited information on the safety of Cinryze use during pregnancy and breast-feeding. Your doctor will discuss with you the risks and benefits of taking this medicine.

Driving and using machines

No studies on the effects of the medicine on driving or using machines have been performed.

Important information about some of the ingredients of Cinryze

This medicine contains up to 41 mg of sodium in the recommended 10 ml dose. This should be taken into account by people on a controlled sodium diet.

3. HOW TO TAKE CINRYZE

A doctor or nurse may prepare and inject Cinryze for you.

The usual dose of Cinryze for adults, adolescents, the elderly, or patients suffering from kidney or liver problems is as follows:

Treatment of swelling attacks

- A dose of 1000 Units of Cinryze should be injected at the first sign of a swelling attack.

- A second injection of 1000 Units may be given if your symptoms do not improve after 60 minutes.
- If you are experiencing a severe attack, particularly a laryngeal attack, or if initiation of treatment is delayed, the second 1000 Units dose may be given earlier than 60 minutes after the first dose, depending on your clinical response.
- Cinryze should be injected intravenously.

Prevention of swelling attacks

- A dose of 1000 Units of Cinryze should be injected every 3 or 4 days for routine prevention of swelling attacks.
- The dosing interval may be adjusted by your doctor depending upon your response to Cinryze.
- Cinryze should be injected intravenously.

Prevention of swelling attacks prior to surgery

- A dose of 1000 Units of Cinryze should be injected up to 24 hours before a medical, dental, or surgical procedure.
- Cinryze should be injected intravenously.

Reconstitution and method of administration

Cinryze is usually injected into a vein (intravenously) by your doctor or nurse. You or your carer might also administer Cinryze as an injection, but only after receiving adequate training. If your doctor decides that you may be suitable for such home-treatment, he/she will give you detailed instructions. You will be required to keep a diary in order to document each treatment received at home and to bring it to each of your visits to the doctor. Regular review of your/your carer's injection technique will be performed to ensure continued appropriate handling.

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

4. POSSIBLE SIDE EFFECTS

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

Tell your doctor **immediately** if you experience any of the following symptoms after taking this medicine. Although they are rare, the symptoms can be severe.

- Sudden wheeziness, difficulty in breathing, swelling of eyelids, face or lips, rash or itching (especially affecting the whole body).

The frequency of possible side effects listed below is defined using the following convention:

- very common (affects more than 1 user in 10)
- common (affects 1 to 10 users in 100)
- uncommon (affects 1 to 10 users in 1,000)
- rare (affects 1 to 10 users in 10,000)
- very rare (affects less than 1 user in 10,000)
- not known (frequency cannot be estimated from the available data).

Common side effects: rash.

Uncommon side effects: high blood sugar, dizziness, headache, blood clot, painful veins, hot flush, cough, nausea, vomiting, stomach pain, diarrhoea, skin flaking, itching or redness, joint swelling and pain, muscle pain, injection site rash or pain, chest discomfort, and fever.

If any of the side effects gets serious or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE CINRYZE

Keep out of the reach and sight of children.

Do not use Cinryze after the expiry date which is stated on the carton or vials after "EXP". Store and transport refrigerated (2°C - 8°C). Do not freeze. Store in the original package in order to protect from light.

Once reconstituted, Cinryze solution should be used immediately.

Medicines must not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Cinryze contains

The active substance is C1 inhibitor produced from the plasma of human donors. Each powder vial contains 500 units of C1 inhibitor. After reconstitution, one vial contains 500 Units (U) of C1 inhibitor (human) per 5 ml. Two vials of reconstituted Cinryze are combined for a single dose, corresponding to a concentration of 100 U/ml.

The total protein content of the reconstituted solution is 15 ± 5 mg/ml.

One Unit is equivalent to the mean quantity of C1 inhibitor present in 1 ml of normal human plasma.

The other ingredients (excipients) are:

Powder vial: sodium chloride, sucrose, sodium citrate, L-valine, L-alanine and L-threonine.

Solvent vial: water for injections.

What Cinryze looks like and contents of the pack

Cinryze is a white powder contained in a vial.

After it has been dissolved in the water for injections the solution is clear and colourless to slightly blue.

Each pack of Cinryze contains:

2 vials of Cinryze 500 Units powder for solution for injection

2 vials of water for injections (5 ml each)

The administration set contains:

2 filter transfer devices

1 disposable 10 ml syringe

1 venipuncture set

2 disinfection swabs

1 protective mat

Marketing Authorisation Holder:

ViroPharma SPRL
Rue Montoyer 47
B - 1000 Brussels Belgium

Manufacturer:

Sanquin Blood Supply Foundation
Plesmanlaan 125
1066 CX Amsterdam
The Netherlands

This leaflet was last approved in 06/2011.

Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu/>. There are also links to other websites about rare diseases and treatments.

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

Reconstitution and administration of Cinryze

Reconstitution, product administration and handling of the administration set and needles must be done with caution.

Use either the filter transfer device provided with Cinryze or a commercially available double-ended needle.

Preparation and handling

Cinryze is intended for intravenous administration after reconstitution with water for injections. Cinryze vial is for single use only.

Reconstitution

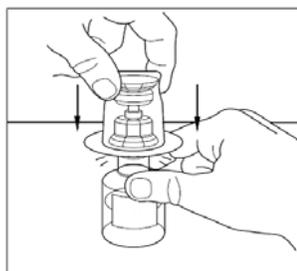
Each product vial should be reconstituted with 5 ml water for injections.

Two vials of reconstituted Cinryze are combined for ONE dose (1000 Units).

1. Work on the mat provided and wash your hands before performing the following procedures.
2. Aseptic technique should be used during the reconstitution procedure.
3. Bring the powder vial and the solvent vial to room temperature (15°C - 25°C).
4. Remove plastic caps from the powder and solvent vials.
5. Cleanse stoppers with an alcohol wipe and allow them to dry prior to use.
6. Remove protective covering from the top of the transfer device package. Do not remove the device from the package.



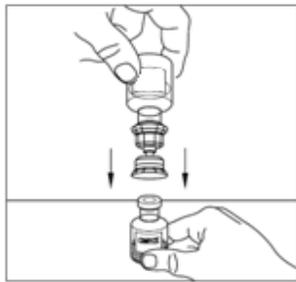
7. Note: the transfer device must be attached to the solvent vial before being attached to the powder vial, so that the vacuum in the powder vial is not lost. Place the solvent vial on a flat surface and insert the blue end of the transfer device into the solvent vial, pushing down until the spike penetrates through the centre of the solvent vial stopper and the device snaps in place. The transfer device must be vertical prior to penetrating the stopper closure.



8. Remove the plastic package from the transfer device and discard it. Take care not to touch the exposed end of the transfer device.



9. Place the powder vial on a flat surface. Invert the transfer device and the solvent vial containing water for injections and insert the clear end of the transfer device into the powder vial, pushing down until the spike penetrates the rubber stopper and the transfer device snaps into place. The transfer device must be vertical prior to penetrating the stopper closure of the powder vial. The vacuum in the powder vial will draw in the solvent. If there is no vacuum in the vial, do not use the product.



10. Gently swirl the powder vial until all powder is dissolved. Do not shake the powder vial. Make sure all the powder is completely dissolved.



11. Disconnect the solvent vial by turning it anti-clockwise. Do not remove the clear end of the transfer device from the powder vial.

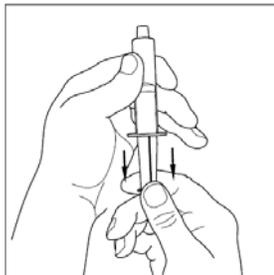


ONE vial of reconstituted Cinryze contains 500 Units of C1 inhibitor in 5 ml, resulting in a concentration of 100 Units/ml.

TWO vials of Cinryze powder must be reconstituted to make one dose (1000 Units/10 ml). Therefore repeat instructions 1 to 11 above using an additional package containing a transfer device to reconstitute the second of two powder vials. Do not reuse the transfer device.

Administration process

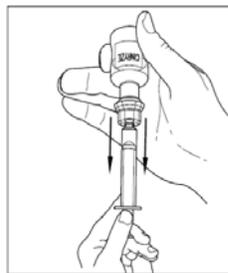
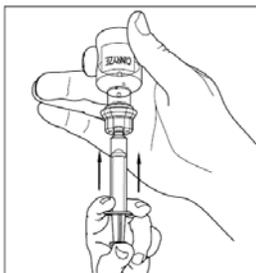
1. Aseptic technique should be used during the administration procedure.
2. After reconstitution, the Cinryze solutions are colourless to slightly blue and clear. Do not use the product if the solutions are turbid or discoloured.
3. Using a sterile, disposable 10 ml syringe, draw back the plunger to allow approximately 5 ml of air into the syringe.



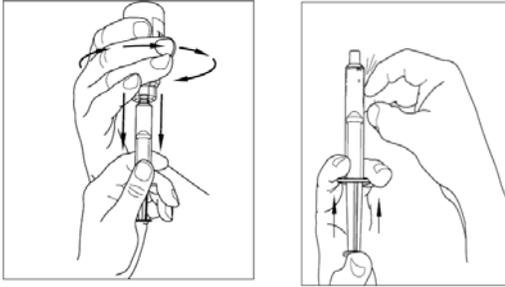
4. Attach the syringe onto the top of the clear end of the transfer device by turning it clockwise.



5. Invert the vial and inject air into the solution and then slowly withdraw the reconstituted Cinryze solution into the syringe.



6. Detach the syringe from the vial by turning it anti-clockwise and releasing it from the clear end of the transfer device.



7. Using the same syringe, repeat steps 4 to 7 with a second vial of reconstituted Cinryze to make one complete 10 ml dose.
8. Attach a needle to the syringe containing Cinryze solution and inject intravenously into the patient. Administer 1000 Units (reconstituted in 10 ml of water for injections) of Cinryze by intravenous injection at a rate of 1 ml per minute over 10 minutes.

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