
Preparation and Administration of Cinryze® (Human C1-esterase inhibitor) Medication

500 IU powder and solvent for solution
for injection

Instructions for Patients and Caregivers

This resource is only for use by patients for whom the decision to prescribe Cinryze has already been made. Takeda is providing this risk management material as part of its commitment to the EMA to implement the approved Risk Management Plan. This material fulfils the condition of the marketing authorisation and has been approved by the competent authority.

Please refer to the Package Leaflet for further product information.

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What Cinryze is and what it is used for

Cinryze contains the human protein called "C1-esterase inhibitor" as the active substance.

C1-esterase inhibitor is a naturally occurring protein that is normally present in the blood. If you have a low amount of C1-esterase inhibitor in your blood or your C1-esterase 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 children, Cinryze can raise the amount of C1-esterase inhibitor in the blood and either prevent (prior to undergoing medical or dental procedures) these swelling attacks from occurring or stop swelling attacks once they have begun.

In adults, adolescents and children (aged 6 years and above), Cinryze can raise the amount of C1-esterase inhibitor in the blood and routinely prevent swelling attacks from occurring.

Dosing for children (2 – 11 years)

The recommended dose of Cinryze is as follows:

	2 to 11 years 10-25 kg	2 to 11 years >25 kg
Treatment of swelling attacks	A dose of 500 IU (one vial) of Cinryze should be injected at the first sign of a swelling attack. A second injection of 500 IU may be given if the patient's symptoms do not improve after 60 minutes.	A dose of 1000 IU (two vials) of Cinryze should be injected at the first sign of a swelling attack. A second injection of 1000 IU may be given if the patient's symptoms do not improve after 60 minutes.
Prevention of swelling attacks before surgery	A dose of 500 IU (one vial) of Cinryze should be injected up to 24 hours before a medical, dental, or surgical procedure.	A dose of 1000 IU (two vials) of Cinryze should be injected up to 24 hours before a medical, dental, or surgical procedure.

Cinryze is not for use in children below 6 years of age for routine prevention of angioedema attacks.

	6 to 11 years
Routine prevention of swelling attacks	A dose of 500 IU (one vial) of Cinryze should be injected every 3 or 4 days for routine prevention of swelling attacks. The dosing interval may be adjusted depending upon the patient's response to Cinryze.

Adults and adolescents (12 years and above)

Treatment of swelling attacks

- A dose of 1000 IU (two vials) of Cinryze should be injected at the first sign of a swelling attack.
- A second injection of 1000 IU may be given if symptoms do not improve after 60 minutes.
- If you are experiencing a severe attack, particularly a swelling of the voice-box (larynx), or if initiation of treatment is delayed, the second 1000 IU dose may be given earlier than 60 minutes after the first dose, depending on your clinical response.

Routine prevention of swelling attacks

- A dose of 1000 IU (two vials) of Cinryze should be injected every 3 or 4 days for routine prevention of swelling attacks.
- The dosing interval may be adjusted depending on your response to Cinryze.

Prevention of swelling attacks prior to surgery

- A dose of 1000 IU (two vials) of Cinryze should be injected up to 24 hours before a medical, dental, or surgical procedure.

Preparation of Cinryze (Human C1-esterase inhibitor)

Note: There are limited data on the use of this medicine in home or self-administration.

- Your doctor has decided that you should be trained to administer Cinryze (a medication containing Human C1-esterase inhibitor as the active substance, which is used to treat Hereditary Angioedema attacks (HAE)), or you have a family member who can be trained to administer your Cinryze at home.
- **Do not attempt to administer unless you have been trained by your treating physician.**
- Cinryze powder vials and water for injection vials must be stored below 25°C. Do not freeze. Store in the original package in order to protect from light.
- Reconstitution, product administration and handling of the administration set and needles must be done with caution. Use the transfer device provided with Cinryze.
- Once you learn how to administer, you can follow the instructions in this guide.
- Do not use Cinryze after the expiry date on the vial.
- Ensure that the area where you will prepare Cinryze is thoroughly cleaned before you begin. Wash your hands and keep the area clean and germ-free while preparing the solution.

Preparation and handling

Cinryze (Human C1-esterase inhibitor) is intended for intravenous administration after reconstitution with water for injection. Each vial of Cinryze is for single use only.

Preparation and handling



1 or 2 Vials of Cinryze
(500 IU each)



1 or 2 Vials of water for injection
(diluent, 5 ml each)



1 or 2 Transfer devices



Disinfection swabs
(not included in the pack)



Mat



1 Disposable 10 ml syringe

Reconstitution

For a dose of 500 IU:

One (1) powder vial, 1 solvent vial, 1 filter transfer device, 1 disposable 10 ml syringe, 1 venipuncture set and 1 protective mat are needed. Store the remaining vial and administration equipments for the next dose.

For a dose of 1000 IU:

Two (2) powder vials, 2 solvent vials, 2 filter transfer devices, 1 disposable 10 ml syringe, 1 venipuncture set and 1 protective mat are needed.

Each powder vial should be reconstituted with 5 ml water for injection. One vial of reconstituted Cinryze corresponds to a dose of 500 IU.

Two vials of reconstituted Cinryze correspond to a dose of 1000 IU.

1. Work on the mat provided and wash your hands before performing the following procedures.
2. Ensure you work in a clean environment during the reconstitution procedure.
3. Remove the powder vial (Cinryze) and solvent vials (water for injection) from the original package.
4. Ensure that powder vial (Cinryze) and solvent vial (water for injection) are at room temperature (15°C – 25°C) prior to administration.



Note: Please be aware that to prepare a dose of 1000 IU you will need to prepare two vials of Cinryze by performing steps 5 to 15 from this section twice.

5. Release the powder vial label by peeling down the purple strip, indicated by the arrow. The peel-off stickers containing the batch number are marked by a black triangle on the top left corner. Please keep the batch number for your records.



6. Remove the cap from the vial of Cinryze to show the centre part of the rubber stopper. Place the vial of Cinryze on a flat surface. Try to avoid touching the rubber stopper.



7. Remove the cap from the vial of water for injection, to show the centre part of the rubber stopper. Place the vial of water for injection on a flat surface. Try to avoid touching the rubber stopper.



8. Wipe the stopper of the vial of Cinryze with a disinfection swab and allow it to dry. Do not blow on the stopper. After cleaning, do not touch the rubber stopper with your hands or allow it to touch any other surface.



9. Wipe the stopper of the vial of water for injection, with the same disinfection swab and allow it to dry. Do not blow on the stopper. After cleaning, do not touch the rubber stopper with your hands or allow it to touch any other surface.



10. **Note: The vial of water for injection must be penetrated before the vial of Cinryze to prevent loss of vacuum.**

Remove the upper protective covering from the transfer device package. Do not remove the transfer device from the package.



11. With the vial of water for injection on a flat surface, place the blue end of the transfer device (which must be completely upright) over it, pushing down until the spike penetrates the rubber stopper and the device snaps into place.



12. Remove the plastic package and discard it.

Be careful not to touch the exposed end of the transfer device.



13. Place the vial of Cinryze on a flat surface. Turn the transfer device and the vial of water for injection upside down and with them positioned completely upright, insert the clear end of the transfer device into the vial of Cinryze, pushing down until the spike penetrates the rubber stopper and the device snaps into place. The water for injection will automatically flow into the vial of Cinryze because of the vacuum in the vial. **If this does not happen, do not use the product.**



14. Once all the water for injection, is in the vial of Cinryze, gently swirl (do not shake) the vial of Cinryze until all the powder is dissolved. Check through the visible area of the vial, where the label is attached.



15. Disconnect the vial of water for injection, by turning it anti-clockwise (left). **Do not remove the clear end of the transfer device from the vial of Cinryze.** Look at the final solution before using it to make sure that Cinryze is completely dissolved. Once dissolved, the solution in the vial of Cinryze should be colourless to slightly blue and clear. Do not use the product if the solution is cloudy or discoloured, or contains any particles.



Note: One vial of dissolved Cinryze contains 500 IU of Human C1-esterase inhibitor in 5 ml, resulting in a concentration of 100 IU/ml.

If you are preparing a dose of 1000 IU, prepare the second vial of Cinryze by repeating steps 5 – 15 using a new transfer device. Do not reuse the transfer device or the swab.

If you are preparing a dose of 500 IU, continue to Step 16.

16. Once the correct amount (500 IU or 1000 IU) of Cinryze powder has been reconstituted remove the 10 ml syringe supplied in the administration set. Draw back the plunger to the 5 ml mark, so that it contains 5 ml of air.



17. Attach the syringe onto the clear end of the transfer device by turning it clockwise (right).



18. Turn the vial of Cinryze gently upside down and inject the air into the vial by pushing the plunger gently.



19. Then slowly draw the reconstituted Cinryze solution up into the syringe by pulling back gently on the plunger.



20. While holding the vial upside down, detach the syringe from the vial by turning it anti-clockwise (left) and releasing it from the transfer device.

If you are making a dose of 1000 IU, using the same syringe, draw back the plunger to the 10 ml mark so that it contains 5 ml of air. Repeat steps 17 to 20 with a second vial of Cinryze to make one complete dose of 1000 IU (10 ml).

If you are preparing a dose of 500 IU, continue to Step 21.



21. With the syringe pointing upwards, remove any air bubbles by gently tapping the syringe with your fingers and slowly pushing the air out of the syringe.

Inspect the Cinryze solution, do not use if particles are observed.

22. Dispose of the vials with the transfer device attached to them. **Note: the reconstituted Cinryze solution should be used immediately.**



Administration (intravenous injection) of Cinryze (Human C1-esterase inhibitor,)

Do not attempt to administer unless you have been trained by your healthcare provider.

Cinryze has to be administered directly into a vein. It is recommended that self-administration only takes place when someone who is familiar with the process is present, in case of an accident.

Ensure that the area is thoroughly cleaned before you begin to inject Cinryze.

Other materials needed

Before injecting you will need to have the following materials:



Dissolved Cinryze
in 10 ml syringe



1 Venipuncture set
(butterfly needle with tubing)



Tourniquet



Disinfection swabs
(not included in the pack)



Sharps container
(not included in the pack)



Medical tape
(not included in the pack)



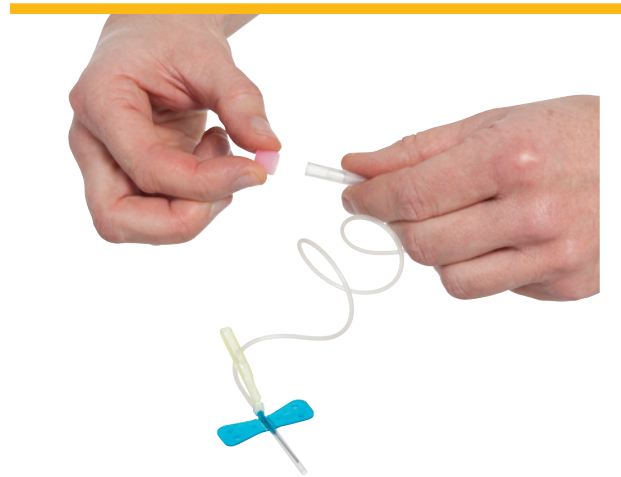
Plasters and dry swabs
(not included in the pack)



Watch
(not included in the pack)

1. Remove the cap from the end of the venipuncture set which attaches to the syringe containing the dissolved Cinryze. Leave the cap on the butterfly needle.

Note: Prior to use, remember to stretch the tube enough to remove any kinks and ensure smooth flow of the dissolved Cinryze.



2. Attach the venipuncture set to the syringe containing the dissolved Cinryze.



3. Fill the tubing with dissolved Cinryze by gently pushing down the plunger of the syringe until a small drop of liquid is seen at the edge of the needle.

Be careful not to spill the dissolved Cinryze. This process replaces the air in the tubing with dissolved Cinryze.



4. Apply a tourniquet above the site of the injection.



5. Prepare the injection site by carefully wiping the skin with a disinfection swab. Always use a new sterile needle each time you use Cinryze. Never re-use needles or syringes.



6. Remove the cap from the butterfly needle and, as instructed by your healthcare provider, insert the needle into a vein at as shallow an angle as possible.



7. Remove the tourniquet and make sure that the needle is in a vein by pulling back the plunger gently (you should see backflow of blood into the butterfly tube).

To avoid needle movement during the injection, tape the winged adapter to your skin using medical tape.

Inject the dissolved Cinryze slowly at a rate of 1ml per minute (10 minutes for 1000 IU or 5 minutes for 500 IU). Keep your arm straight and still during the injection.

At the end of the injection the small amount of drug product left in the venipuncture set will not affect your treatment.

In case of failure to gain venous access; if you develop excessive bleeding, pain, swelling or severe bruising; or if you fail to inject Cinryze into a vein correctly, please contact your healthcare provider immediately.

8. After injecting Cinryze, remove the venipuncture set and cover the injection site with a dry swab. Press on the site with the dry swab for a couple of minutes after the needle is removed and before covering with a small plaster.
9. Dispose of all unused solution, empty vials, and the used needles and syringe in a sharps container for the disposal of waste that might injure others if not handled properly. In the event of a carer receiving a needlestick injury, he/she is advised to go to A&E straight away, taking with them the medication that was being administered.



Important information

Your HAE doctor or nurse should provide you with a diary to bring with you every time you meet with him/her. In the diary, you should record the batch number and expiry dates from each vial of Cinryze you use (found on the label); the date of treatment; and the reason for treatment (pre-procedural, treatment of attack or routine prevention). The time of treatment, dose received, response to treatment and any adverse reactions should also be recorded.

- Like all medicines, Cinryze can cause side effects, although not everybody gets them. This can include allergic-type reactions. 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). Please refer to the Package Leaflet for further product information.
- In case of failure to gain venous access; if you develop excessive bleeding, pain, swelling or severe bruising; or if you fail to inject Cinryze into a vein correctly, please contact your healthcare provider immediately.
- For more detailed information please consult the Patient Information Leaflet (PIL) in the Cinryze product package.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in the package leaflet.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any side effects not listed in the patient information leaflet. You can also report side effects directly to HPRA Pharmacovigilance via the website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

