PREPARATION AND SELF-ADMINISTRATION INSTRUCTIONS FOR PATIENTS

CINRYZE®
C1 esterase inhibitor (human)

Shire
Hereditary Angioedema
Choosing to treat with CINRYZE® (C1 esterase inhibitor [human]) can offer you and your loved ones more options to administer at home or away. Through Path to Independence™, infusion nurses are available for hands-on training and ongoing support for patients and/or their caregivers throughout the infusion training process to help ensure that you are comfortable and confident in managing infusions.

**Patients and caregivers should only administer after being trained by a healthcare provider.**

Once you learn the administration process from a healthcare provider, you can follow the instructions in this brochure. Click [here](#) for Full Prescribing Information, which contains the step-by-step Instructions for Use as well.

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**Remember**, sticking to the prescribed treatment schedule that you and your doctor agreed upon is necessary to help prevent HAE attacks.

To help stay on track with treatment, use a calendar, planner, or journal to keep records of your infusion schedule, appointments, and supply order reminders.

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**INDICATION**

CINRYZE® (C1 esterase inhibitor [human]) is an injectable prescription medicine that is used to help prevent swelling and/or painful attacks in children (6 years of age and older), teenagers, and adults with Hereditary Angioedema (HAE).

**IMPORTANT SAFETY INFORMATION**

You should not use CINRYZE if you have had life-threatening immediate hypersensitivity reactions, including anaphylaxis, to the product.

Please see the complete Important Safety Information on page 11. For additional safety information, please click [here](#) for Full Prescribing Information and discuss with your doctor.
## DOSING

<table>
<thead>
<tr>
<th>DOSE</th>
<th>Adult and adolescent patients (≥12 years)</th>
<th>Pediatric patients (6 to 11 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1,000 U intravenous</td>
<td>500 U intravenous</td>
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<tr>
<td></td>
<td>For patients who have not responded adequately to 1,000 U of CINRYZE every 3 or 4 days, doses up to 2,500 U (not exceeding 100 U/kg) every 3 or 4 days may be considered based on individual patient response</td>
<td>The dose may be adjusted according to individual response, up to 1,000 U every 3 to 4 days</td>
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</table>

### DOSING REGIMEN

- Single dose can be administered every 3 or 4 days

### INFUSION RATE

- 1 mL/min (10 minutes)
- 1 mL/min (5 minutes)

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**Note:** Your healthcare provider may decide that you or your loved one may require higher doses of CINRYZE® (C1 esterase inhibitor [human]). You should always follow the specific instructions given by your healthcare provider.

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## PREPARATION OF CINRYZE®

Wash your hands before you begin. Ensure you are working on a flat surface and your work area is thoroughly cleaned and germ-free throughout the process.

- **Prior to preparation, CINRYZE should be stored at 2°C to 25°C (36°F to 77°F) and protected from light**
- **Visually inspect CINRYZE after preparation. CINRYZE should be colorless to slightly blue and free from particles. Do not administer if cloudy or discolored**
- **Each CINRYZE vial is for single use only. CINRYZE does not contain a preservative. Any vial that has been entered should be used promptly. Partially used vials should be discarded in accordance with biohazard procedures**
- **Do not mix CINRYZE with other materials**
- **Do not use if frozen**
- **Do not use after expiration date**
- **CINRYZE should be administered within 3 hours of preparation**

Call your healthcare provider if you have any questions on the preparation or self-administration of CINRYZE. **Patients should only self-administer after being trained by a healthcare provider.**
PREPARATION OF CINRYZE®

Supplies needed:

<table>
<thead>
<tr>
<th>Supplies needed</th>
<th>CINRYZE</th>
<th>Sterile Water for Injection, USP (diluent, 5 mL)</th>
<th>Mix2Vial® Transfer Devices</th>
<th>Alcohol Prep Pads (wipes)</th>
<th>110-mL Silicone-Free Syringe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult and adolescent 1,000 U dose</td>
<td>2 vials</td>
<td>2 vials</td>
<td>2</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Pediatric (age 6 to 11) 500 U dose</td>
<td>1 vial</td>
<td>1 vial</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

1. Let the vial(s) of CINRYZE® (C1 esterase inhibitor [human]) and the vial(s) of Sterile Water for Injection, USP (diluent) reach room temperature.

2. Remove the caps from the vial(s) of CINRYZE and the Sterile Water for Injection, USP (diluent) to show the center part of the rubber stopper.

3. Wipe the top of each vial with an alcohol wipe or swab and allow it to dry. Do not blow on the stopper to dry it faster. After cleaning, do not touch the rubber stopper with your hand or allow it to touch any surface.

4. Remove the protective covering from the top of the Mix2Vial® device package(s). Do not remove the device from the package.

5. Sterile Water for Injection, USP (diluent) vial must be penetrated before the CINRYZE vial to prevent loss of vacuum.

Place the Sterile Water for Injection, USP (diluent) vial on a flat surface and insert the blue end of the Mix2Vial device into the diluent vial, pushing down until the spike penetrates the rubber stopper and the device snaps in place. The Mix2Vial device must be positioned completely upright before penetrating the rubber stopper.

Remove the plastic package from the Mix2Vial device and discard it. Take care not to touch the exposed end of the device.

Please see the complete Important Safety Information on page 11. For additional safety information, please click here for Full Prescribing Information and discuss with your doctor.
6 Place the vial of CINRYZE® (C1 esterase inhibitor [human]) on a flat surface. Turn the Sterile Water for Injection, USP (diluent) vial upside down and insert the clear end of the Mix2Vial® device into the CINRYZE vial, pushing down until the spike penetrates the rubber stopper and the device snaps into place. The Mix2Vial device must be positioned completely upright before penetrating the rubber stopper. The Sterile Water for Injection, USP (diluent) will automatically flow into the vial of CINRYZE because the vacuum in the vial will draw the Sterile Water for Injection, USP (diluent) into the CINRYZE vial. If this does not happen, do not use the product.

7 Once all the Sterile Water for Injection, USP (diluent) is in the CINRYZE vial, gently swirl (do not shake) the CINRYZE vial until all the powder is dissolved. Disconnect the Sterile Water for Injection, USP (diluent) vial by turning it counterclockwise. Do not remove the clear end of the Mix2Vial device from the CINRYZE vial.

Look at the final solution before using it to make sure that CINRYZE is completely dissolved. The solution should be clear, colorless to slightly blue, and be without any evidence of cloudiness. Do not use if the solution is cloudy or otherwise discolored and call Shire Medical Information at 1-800-828-2088.

For a 500 Unit dose, prepare 1 vial of CINRYZE.

For doses of 1,000 Units or above, prepare additional vials of CINRYZE (1 vial for each 500 Unit dose required). Repeat steps 5-7 using a new Mix2Vial device for each 500 Unit dose of CINRYZE. Do not reuse the Mix2Vial transfer device.

Note: If your doctor has prescribed a dose other than 1,000 U, be sure to follow the preparation and administration instructions he or she has provided to you.

Call your healthcare provider if you have any questions on the preparation or self-administration of CINRYZE. Patients should only self-administer after being trained by a healthcare provider.
8 Utilizing a sterile, disposable 10 mL syringe, draw back the plunger to allow approximately 5 mL of air into the syringe.

9 Attach the syringe onto the clear end of the Mix2Vial® device by turning it clockwise.

10 Turn the CINRYZE® (C1 esterase inhibitor [human]) vial upside down and inject air into the vial. Slowly pull as much dissolved CINRYZE as possible into the syringe.

Continued on next page.

Please see the complete Important Safety Information on page 11. For additional safety information, please click here for Full Prescribing Information and discuss with your doctor.
While holding the vial upside down, detach the syringe from the vial by turning it counterclockwise and releasing it from the Mix2Vial® device.

Remove any air bubbles by gently tapping the syringe with your finger and slowly pushing the air out of the syringe.

**If preparing a 1,000 Unit dose (two vials), repeat steps 8-10 with a second vial of CINRYZE® (C1 esterase inhibitor [human]) to make one complete dose of 10 mL.**

Dispose of the vial(s) with the Mix2Vial device(s) attached.

CINRYZE should be administered at room temperature promptly after preparation in the syringe.

Call your healthcare provider if you have any questions on the preparation or self-administration of CINRYZE. **Patients should only self-administer after being trained by a healthcare provider.**
SELF-ADMINISTRATION OF CINRYZE®

A healthcare provider will teach you the proper technique to safely administer CINRYZE® (C1 esterase inhibitor [human]). It is important that CINRYZE is injected directly into a superficial vein (intravenous injection) and not injected into surrounding tissues or an artery.

CINRYZE should be administered at room temperature promptly after preparation in the syringe.

**Supplies needed:**

- Dissolved CINRYZE in 10-mL Silicone-Free Syringe
- Infusion Set With Winged Adapter (butterfly needle with tubing)
- Tourniquet
- Alcohol Prep Pads (wipes)
- Watch
- Medical Tape
- Bandages
- Sharps Container
- Syringe Filter

Please see the complete Important Safety Information on page 11. For additional safety information, please click here for Full Prescribing Information and discuss with your doctor.
1. Attach the syringe filter to the syringe.

2. Remove plastic cap and attach the infusion set to the syringe containing the dissolved CINRYZE® (C1 esterase inhibitor [human]) solution. Fill the tubing with dissolved CINRYZE by gently pushing the plunger of the syringe, being careful not to spill. This process replaces the air in the tubing with dissolved CINRYZE.

3. Apply a tourniquet and prepare the injection site by wiping the skin well with an alcohol wipe.

IMPORTANT SAFETY INFORMATION (continued)
Allergic reactions may occur with CINRYZE. Call your healthcare provider or get emergency support services right away if you have any of the following symptoms:

- wheezing
- difficulty breathing
- chest tightness
- turning blue (look at lips and gums)
- fast heartbeat
- swelling of the face
- faintness
- rash
- hives

Call your healthcare provider if you have any questions on the preparation or self-administration of CINRYZE. Patients should only self-administer after being trained by a healthcare provider.
As instructed by a healthcare provider, insert the butterfly needle of the infusion set tubing into the vein. Tape the needle to keep it in place.

Remove the tourniquet.

Make sure that the needle is in a vein.

Inject the dissolved CINRYZE® (C1 esterase inhibitor [human]) slowly over 5 minutes for a 500 Unit dose, or over 10 minutes for a 1,000 Unit dose (approximately 1 mL/min).

After infusing CINRYZE, remove the infusion set and discard. Cover the infusion site with a bandage. The amount of drug product left in the infusion set will not affect the treatment.

Dispose of all unused solution and empty vials. Used butterfly needle and syringe should be disposed of in an appropriate sharps container to ensure safe disposal and handling.

It is a good idea to record the lot number from the CINRYZE vial every time you use CINRYZE.

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IMPORTANT SAFETY INFORMATION
You should not use CINRYZE if you have had life-threatening immediate hypersensitivity reactions, including anaphylaxis, to the product.

Tell your healthcare provider about all of your medical conditions, including if you:
▷ have an indwelling catheter/access device in one of your veins.
▷ have a history of blood clots, heart disease, or stroke.
▷ are taking birth control pills or androgens.
▷ are pregnant or planning to become pregnant. It is not known if CINRYZE can harm your unborn baby.
▷ are breastfeeding or plan to breastfeed. It is not known if CINRYZE passes into your milk and if it can harm your baby.

Allergic reactions may occur with CINRYZE. Call your healthcare provider or get emergency support services right away if you have any of the following symptoms:
▷ wheezing
▷ difficulty breathing
▷ chest tightness
▷ turning blue (look at lips and gums)
▷ fast heartbeat
▷ swelling of the face
▷ faintness
▷ rash
▷ hives

Serious blood clots may occur with CINRYZE. Call your healthcare provider or get emergency support services right away if you have any of the following symptoms:
▷ pain and/or swelling of an arm or leg with warmth over the affected area
▷ discoloration of an arm or leg
▷ unexplained shortness of breath
▷ chest pain or discomfort that worsens on deep breathing
▷ unexplained rapid heart rate
▷ numbness or weakness on one side of the body

Because CINRYZE is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

The most common side effects seen with CINRYZE were headache, nausea, rash, and vomiting. These are not all the possible side effects of CINRYZE. Tell your healthcare provider about any side effect that bothers you or that does not go away. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

For additional safety information, please click here for Full Prescribing Information and discuss with your doctor.
Path to Independence™ is a training program designed to help teach patients, family members, or caregivers how to self-administer or administer CINRYZE.

For more information, contact your OnePath® Patient Support Manager at 1-866-888-0660.