

RECONSTITUTION
AND ADMINISTRATION
INSTRUCTIONS FOR
**HEALTHCARE
PROFESSIONALS**





TRUST THE POWER OF PREVENTION WITH CINRYZE®

Whether your patients are new to treatment or are continuing their journey, remind them that compliance is an important part of CINRYZE® (C1 esterase inhibitor [human]) therapy.

Encourage your patients to follow the treatment schedule you provide, and explain that missing a dose of CINRYZE can result in HAE attacks.

For further support, remind patients about the personalized product support services provided by OnePath®, including the Path to Independence™ self-administration training program, and encourage them to work with their Case Manager.

Indication

CINRYZE® (C1 esterase inhibitor [human]) is indicated for routine prophylaxis against angioedema attacks in adolescent and adult patients with Hereditary Angioedema (HAE).

Important Safety Information

CINRYZE is contraindicated in patients who have manifested life-threatening immediate hypersensitivity reactions, including anaphylaxis to the product.

Please see additional Important Safety Information on the last page.

Before prescribing CINRYZE, please read the Full Prescribing Information available at www.cinryze.com.

DOSING

- ▶ Dose of CINRYZE® (C1 esterase inhibitor [human]) for routine prophylaxis against HAE attacks is 1,000 Units every 3 or 4 days
- ▶ CINRYZE comes in 500 Unit vials, so 2 vials are needed to administer a single dose
- ▶ CINRYZE should be infused over 10 minutes (an infusion rate of 1 mL/min)

INSTRUCTIONS FOR USE

The following procedures are provided as general guidelines for the reconstitution and administration of CINRYZE. Use either the Mix2Vial® transfer device or a commercially available double-ended needle.

CINRYZE is a freeze-dried powder that is supplied in a vacuum-sealed vial.

Always work on a flat, clean surface and wash your hands before performing the following procedures.

Reconstitution, product administration, and handling of the administration set and needles must be done with caution. Percutaneous puncture with a needle contaminated with blood can transmit infectious viruses including HIV (AIDS) and hepatitis. Obtain immediate medical attention if injury occurs. Place needles in a sharps container after single use. Discard all equipment, including any reconstituted CINRYZE, in an appropriate container.


C1 esterase inhibitor (human)

PREPARATION AND HANDLING

Prior to reconstitution, CINRYZE® (C1 esterase inhibitor [human]) should be stored at 2°C to 25°C (36°F to 77°F) and protected from light.

A silicone-free syringe is recommended for reconstitution and administration of CINRYZE.

Visually inspect CINRYZE prior to administration. The reconstituted product should be colorless to slightly blue and free from particulate matter; do not use if solution is turbid or discolored.

Each vial of CINRYZE is for single use only. CINRYZE contains no preservative, and 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

SUPPLIES NEEDED:



2 Vials of CINRYZE
(500 Units each)



**2 Vials of Sterile Water
for Injection, USP**
(diluent, 5 mL each)



**2 Mix2Vial®
Transfer Devices**



Alcohol Prep Pads
(wipes)

CINRYZE must be administered at room temperature within 3 hours of reconstitution.

Before prescribing CINRYZE, please read the Full Prescribing Information available at www.cinryze.com.

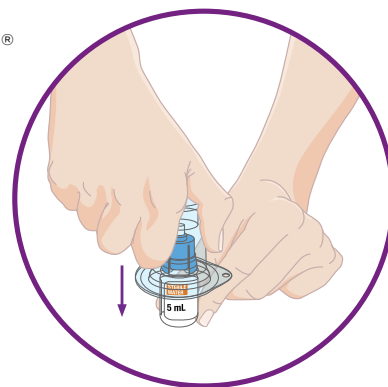
RECONSTITUTION

Two vials of reconstituted CINRYZE® (C1 esterase inhibitor [human]) are combined for a single dose. Sterile Water for Injection, USP (diluent) is required and is not supplied with CINRYZE.

- 1 Use Aseptic technique during the reconstitution procedure.
- 2 Bring CINRYZE and Sterile Water for Injection, USP (diluent) to room temperature if refrigerated.
- 3 Remove caps from the CINRYZE and Sterile Water for Injection, USP (diluent) vials.
- 4 Cleanse stoppers with an alcohol wipe and allow them to dry prior to use.
- 5 Remove protective covering from the top of the Mix2Vial® device, but do not remove the device from the package.
- 6 **Note: Sterile Water for Injection, USP (diluent) vial must be accessed prior to the CINRYZE vial to prevent loss of vacuum.**

Insert the blue end of the Mix2Vial device into the diluent vial, pushing down until the spike penetrates the center of the diluent vial stopper and the Mix2Vial device snaps into place.

The Mix2Vial device must be positioned completely vertical prior to penetrating the stopper. Remove the plastic package and discard it. Take care not to touch the exposed end of the device.



CINRYZE®
C1 esterase inhibitor (human)

- 7 Invert the Sterile Water for Injection, USP (diluent) vial and insert the clear end into the CINRYZE® (C1 esterase inhibitor [human]) vial, pushing down until the spike penetrates the rubber stopper and the Mix2Vial® device snaps into place.

The Mix2Vial device must be positioned completely vertical prior to penetrating the stopper. The Sterile Water for Injection, USP (diluent) will automatically flow into the CINRYZE vial, because the vacuum in the vial will draw in the Sterile Water for Injection, USP (diluent). If there is no vacuum in the vial, do not use the product.



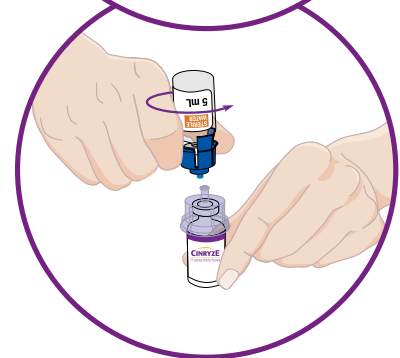
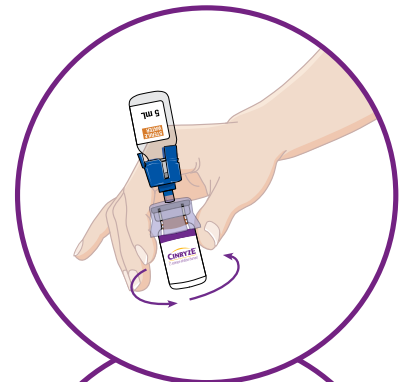
- 8 Gently swirl (do not shake) the CINRYZE vial until all powder is completely dissolved.

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.

One vial of reconstituted CINRYZE contains 5 mL of C1 esterase inhibitor at a concentration of 100 Units/mL. **Reconstitute two vials of CINRYZE for one dose.**

Repeat steps 1 to 8 with a second Mix2Vial device to reconstitute the second vial of CINRYZE. Do not reuse the Mix2Vial transfer device.



Before prescribing CINRYZE, please read the Full Prescribing Information available at www.cinryze.com.

ADMINISTRATION

After reconstitution, the solution should be colorless to slightly blue and free from particulate matter. Do not use if solution is turbid or otherwise discolored.

SUPPLIES NEEDED:



**2 Vials of Reconstituted
CINRYZE**



**One 10-mL
Silicone-Free Syringe**



**Infusion Set With
Winged Adapter**
(butterfly needle with tubing)



Tourniquet



**Alcohol Prep Pads
(wipes)**



Watch



Medical Tape



Bandages

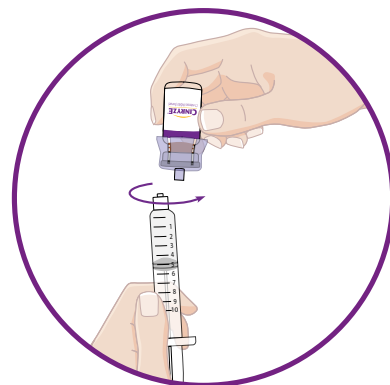


Sharps Container

- 1 Use Aseptic technique.
- 2 Utilizing a sterile, disposable syringe, draw back the plunger to admit 5 mL air.
- 3 Attach the syringe onto the top of the clear end of the Mix2Vial® device by turning it clockwise.



- 4 Invert the vial and inject air into the solution and then slowly withdraw the reconstituted CINRYZE® (C1 esterase inhibitor [human]) into the syringe.
- 5 Detach the syringe from the vial by turning it counterclockwise and releasing it from the clear end of the Mix2Vial device.



Before prescribing CINRYZE, please read the Full Prescribing Information available at www.cinryze.com.

- 6** **Using the same syringe, repeat steps 3 to 6 with a second vial of CINRYZE® (C1 esterase inhibitor [human]) to make the complete dose.** CINRYZE should be administered promptly after preparation in the syringe and should not be used if the solution is turbid or discolored or if particles are observed.
- 7** Attach the infusion set and inject intravenously. As a guideline, administer 1,000 Units (reconstituted in 10 mL) of CINRYZE at a rate of 1 mL per minute over 10 minutes.
- 8** Dispose of all unused solution and the empty vials in an appropriate container for handling waste. Used needles and syringes should be disposed of in a sharps container to ensure safe disposal and handling.

Important Safety Information

Hypersensitivity Reactions: Severe hypersensitivity reactions may occur during or after administration of CINRYZE® (C1 esterase inhibitor [human]). Consider treatment methods carefully, because hypersensitivity reactions and HAE attacks may have similar symptoms. In case of hypersensitivity, discontinue CINRYZE infusion and institute appropriate treatment. Have epinephrine immediately available for treatment of an acute severe hypersensitivity reaction.

Thromboembolic Events: Serious arterial and venous thromboembolic (TE) events have been reported at the recommended dose of C1 Esterase Inhibitor (Human) products, including CINRYZE, following administration in patients with HAE. Risk factors may include presence of an indwelling venous catheter/access device, prior history of thrombosis, underlying atherosclerosis, use of oral contraceptives, certain androgens, morbid obesity, and immobility. Benefits of CINRYZE for routine prophylaxis of HAE attacks should be weighed against the risks of TE events in patients with underlying risk factors. Monitor patients with known risk factors for TE events during and after CINRYZE administration.

Transmissible Infectious Agents: 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. ALL infections thought by a physician possibly to have been transmitted by CINRYZE should be reported to Shire Medical Information at 1-866-888-0660.

Adverse Reactions: The only serious adverse reaction observed in clinical studies of CINRYZE was cerebrovascular accident. The most common adverse reactions observed were headache, nausea, rash, and vomiting. Postmarketing adverse reactions include local infusion site reactions and hypersensitivity. Postmarketing thromboembolic events have been reported, including catheter-related and deep venous thromboses, transient ischemic attack, and stroke.

Before prescribing CINRYZE, please read the Full Prescribing Information available at www.cinryze.com.



CINRYZE, Path to Independence, OnePath, and the associated logos are either registered trademarks or trademarks of Shire or its affiliates.

Mix2Vial is a registered trademark of Medimop Medical Projects, Ltd. in the United States and other jurisdictions.

© 2016 Shire. All rights reserved. S11383 06/2016

