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Caring for someone with hereditary angioedema (HAE)

Information and resources to help support a loved one taking CINRYZE

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 additional Important Safety Information on adjacent pages. For additional safety information, please [click here](#) for Full Prescribing Information and discuss with your doctor.

CINRYZE®
C1 esterase inhibitor (human)

THE ROLE OF THE CAREGIVER IN HAE

As a caregiver, you play an important role in caring for and supporting your loved one with hereditary angioedema (HAE). HAE is a rare genetic disease that can cause localized swelling attacks in the body.

In this brochure, you'll find information to help you better understand:

- The signs, symptoms, and triggers of HAE
- How CINRYZE® (C1 esterase inhibitor [human]) can help in the prevention of HAE attacks
- How to manage HAE and access available product support services

Signs and symptoms of an HAE attack

Caring for someone with HAE may come with many responsibilities and challenges. HAE can cause swelling attacks that can be unpredictable, debilitating, and potentially life-threatening.

Because each person experiences HAE attacks differently, it's important to learn the symptoms and triggers. Even if they are taking preventive therapy, you should make sure your child or loved one is familiar with HAE symptoms so they recognize an attack as soon as possible.

Important Safety Information

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.

Please see additional Important Safety Information on adjacent pages.

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2 Information and discuss with your doctor.



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“When I was trained on how to administer CINRYZE, the nurse from OnePath® also trained my daughter. **I stress to her how important it is that she stay on treatment and to stick to the dosing schedule.**”

– A real HAE patient

WHAT TO KNOW ABOUT HAE

HAE swelling attacks can affect areas of the body, including:



Skin, or subcutaneous tissue: areas include the hands, face, feet, or genitals



Stomach: mild to severe pain and may be accompanied by vomiting and diarrhea



Throat: can interfere with breathing, which can be life-threatening, if left untreated

Common HAE attack triggers

Although attacks often occur without a known cause, there may be certain things that trigger them. It's important to be aware of these potential triggers because attacks may happen even in people taking preventive treatment.

Triggers may include:



Stress



Surgery



Dental procedures



Hormonal changes



Infection



Strenuous physical activities



Minor trauma (an injury or shock to the body)



Prolonged sitting or standing

Important Safety Information

Allergic reactions may occur with CINRYZE® (C1 esterase inhibitor [human]). 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

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THE IMPORTANCE OF PREVENTION

Preventive therapy, such as CINRYZE® (C1 esterase inhibitor [human]), can help by reducing how often HAE attacks occur and how severe they are. The decision to start preventive therapy involves many considerations including the frequency and severity of your child's or loved one's HAE attacks.

Along with preventive treatment with CINRYZE, your child's or loved one's doctor may also recommend having an acute therapy on hand in case an HAE attack occurs. Acute therapy should be administered as soon as the symptoms of an HAE attack are recognized.

You can help your loved one or child by keeping them on track with taking their medications as prescribed and by working closely with their doctor on their treatment plan.

Important Safety Information

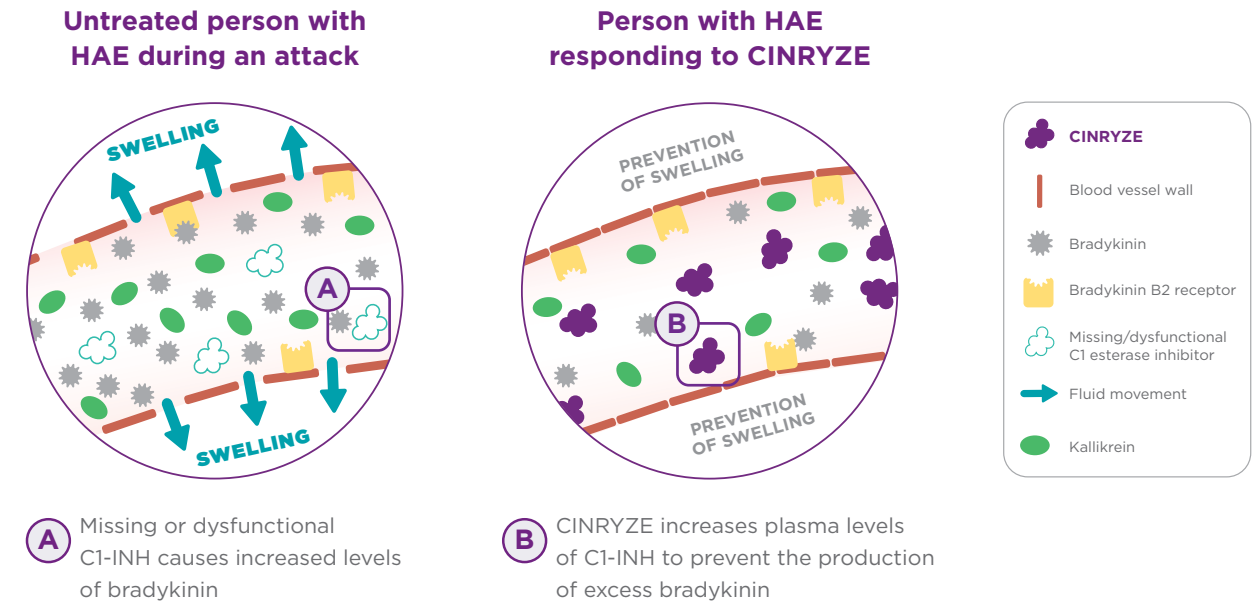
Serious blood clots may occur with CINRYZE. Call your healthcare provider or get emergency support services right away if you have any of the following symptoms:

- pain and/or swelling of an arm or leg with warmth over the affected area
- chest pain or discomfort that worsens on deep breathing
- discoloration of an arm or leg
- unexplained rapid heart rate
- unexplained shortness of breath
- numbness or weakness on one side of the body

How does CINRYZE® work?

Most people with HAE don't have enough of a protein called C1 esterase inhibitor (C1-INH), or this protein does not work correctly, which leads to a cascade of events in the body. This cascade causes another protein, called plasma kallikrein, to trigger the release of a third protein, called bradykinin. The release of too much bradykinin causes small blood vessels to release fluid in certain parts of the body, resulting in the localized swelling and pain of an HAE attack.

CINRYZE increases plasma levels of C1-INH, thereby preventing the generation of excess bradykinin to help reduce the risk of a swelling attack.



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PROVEN PREVENTIVE THERAPY FOR CHILDREN (6+)

The safety and efficacy of CINRYZE® (C1 esterase inhibitor [human]) were evaluated in a 36-week clinical trial in 12 children 7 to 11 years old with HAE. Children were observed for 12 weeks to establish the baseline observation attack rate and then were given one dose of CINRYZE (500 U or 1,000 U) every 3 or 4 days for 12 weeks and then switched to the other dose for the last 12 weeks. Efficacy was measured as reduction in the number of attacks at 12 weeks for each treatment dose compared with the baseline observation attack rate.

Results from a clinical study in children receiving CINRYZE (500 U and 1,000 U)

- Reduction in the number of HAE attacks vs baseline observation attack rate
 - **71.1%** and **84.5% mean reduction** with 500 U and 1,000 U, respectively
- Average change in the severity of attacks per month vs baseline observation
 - **-5.2** and **-5.8** with 500 U and 1,000 U, respectively
- Change in the number of attacks requiring acute treatment per month vs baseline observation
 - **-1.6** and **-1.9** with 500 U and 1,000 U, respectively

Baseline observation attack rate was the number of attacks during the 12-week study period when patients were not receiving any treatment.

Severity of attacks were measured on a 3-point scale (1=mild, 2=moderate, and 3=severe). Results are the decrease in the total of the maximum symptom severity score for each attack.

CINRYZE® was the first preventive therapy indicated to help prevent HAE attacks in children 6 to 12 years old.



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Important Safety Information

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.

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CINRYZE®
C1 esterase inhibitor (human)

PROVEN PREVENTIVE THERAPY FOR ADULTS AND TEENAGERS

In a clinical study, CINRYZE® (C1 esterase inhibitor [human]) was proven to help prevent HAE attacks, as well as reduce the severity and duration of HAE attacks.

The safety and efficacy of CINRYZE were evaluated in a 24-week clinical trial in 24 patients (9 to 73 years old) diagnosed with HAE. People in the study were divided into 2 groups. Group 1 received CINRYZE 1,000 U for the first 12 weeks and were switched to placebo for the last 12 weeks. Group 2 received placebo for the first 12 weeks and were switched to CINRYZE 1,000 U for the last 12 weeks. The main measure was the number of attacks experienced by patients taking CINRYZE compared with the number of attacks experienced by patients taking placebo.

Results from a clinical study with CINRYZE in adults and teenagers

<p>Fewer attacks while taking CINRYZE than while taking placebo</p>	<ul style="list-style-type: none"> • Average number of HAE attacks per month experienced in 12 weeks was 6.1 attacks for patients taking CINRYZE, while patients taking placebo experienced 12.7 attacks • 20 people had fewer attacks, ranging from 100% to 1% fewer attacks <ul style="list-style-type: none"> — 4 people had no attacks • 2 people had more attacks, ranging from 8% to 85% more attacks
<p>Decrease in the average duration of attacks</p>	<p>Attacks lasted 2.1 days while taking CINRYZE vs 3.4 days while taking placebo</p>
<p>Fewer days of swelling</p>	<p>66% reduction in days of swelling, from an average of 10.1 days of swelling over 12 weeks while taking CINRYZE, to 29.6 days while taking placebo</p>
<p>Decrease in the average severity of attacks</p>	<p>On a 3-point scale (1=mild, 2=moderate, 3=severe), attacks while taking CINRYZE were ranked as less severe than were attacks while taking placebo (1.3 vs 1.9)</p>



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CINRYZE®
C1 esterase inhibitor (human)

ADMINISTERING CINRYZE®

CINRYZE® (C1 esterase inhibitor [human]) is administered by intravenous (or IV) injection, meaning it is injected into a vein in the arm. A healthcare provider can teach you how to safely administer CINRYZE to your child or loved one if that is an administration option you've chosen. Please see our *CINRYZE Self-Administration Brochure* available in the CINRYZE Welcome Kit or at CINRYZE.com for a step-by-step overview of the administration process.

You should only administer CINRYZE after being trained by a healthcare provider.

Storing CINRYZE

- Do not freeze CINRYZE. CINRYZE should be stored in a refrigerator or at room temperature between 36°F to 77°F (2°C to 25°C)
- CINRYZE should be protected from light
- Do not use CINRYZE after the expiration date on the vial

If you'd like additional or refresher training, Takeda offers assistance for caregivers who will be administering CINRYZE to a child or loved one. You can read more about this program on page 17.

Important Safety Information

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.

Help make administering CINRYZE a part of your child's routine

There are many things you can do to support your child and help them stay on track with their CINRYZE treatment



Explain to your child why they are taking CINRYZE and that it can help prevent HAE swelling attacks



Have your child use their own personal calendar to help them stay on track with their treatment

- Your child can use stickers to mark when an injection is due and when an injection has been finished



Use a reminder app, like the OnePath Mobile App, so everyone knows when the next injection is due

If your child is worried about pain or needles, there are steps you can take to ease their concerns and help them stay calm during an injection, like providing distractions (for example, listening to music or reading a book) and using different ways to help them relax.

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SUPPORTING A CHILD WITH HAE

There are steps you can take that can help you be as prepared as possible to support your child throughout their HAE journey.



Find a physician who is knowledgeable about HAE, experienced in managing people with HAE, and familiar with treatment options. The US Hereditary Angioedema Association (HAEA) has a doctor referral tool on their website that can help you find a doctor familiar with HAE near you. Visit www.haea.org.



Monitor your child's progress over time, including the frequency and severity of their HAE attacks, and share this information with your child's doctor to help make sure their treatment plan is meeting your child's needs.

- Keep a record of all attacks, regardless of severity, and include information such as the time of day, the part(s) of the body affected, and any potential triggers



Encourage your child to participate in extracurricular activities that he or she enjoys.



If your child is enrolled in OnePath®, **the Path to Independence™ program is available to help train you or another family member on how to administer CINRYZE® (C1 esterase inhibitor [human]) at home**. See page 17 for more information.



Make sure that people who are involved in the care of your child have an understanding of HAE and its treatment.

- Educate teachers, school nurses, other healthcare providers, babysitters, coaches, and friends who have frequent contact with your child
- Contact your local emergency department to make sure they are aware of HAE treatment options and have acute treatments on hand
- Have your child carry identification to alert healthcare providers about their HAE in case of an emergency
 - Be sure to include contact information for your child's healthcare provider and a list of their medications

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ONEPATH® PRODUCT SUPPORT SERVICES

When CINRYZE® (C1 esterase inhibitor [human]) has been prescribed to your loved one and they are enrolled in OnePath, they will be connected with a dedicated Patient Support Manager (PSM) who will work to help with access to medication, in addition to providing other product support services.



OnePath offers eligible patients:

- **Help with facilitating** an insurance benefits investigation and explaining insurance coverage and financial assistance options (if applicable)
- **In-home administration training** for patients and caregiver(s) at no cost
- **Educational resources**, as well as the OnePath Mobile App for patients and caregiver(s)

For questions about OnePath, call

1-866-888-0660

OnePath is available Monday through Friday, from 8:30 AM to 8:00 PM ET.

PATH TO INDEPENDENCE™

Path to Independence is a training program designed to help teach people with HAE, family members, and caregivers how to administer CINRYZE. This program includes a network of specially trained infusion nurses who are available to help eligible patients and/or their caregiver(s) learn:



- Proper preparation of CINRYZE and IV administration techniques
- Appropriate methods for storage, handling, and disposal of CINRYZE
- How to order medication and supplies

Contact your OnePath PSM to request administration training or for more information about the Path to Independence program, which is available at no cost.



If self-administration of CINRYZE is an option for your loved one, you can take the training with them to support administration of CINRYZE at home.

You can also connect with other people living with HAE by reaching out to the US Hereditary Angioedema Association (HAEA) by calling 1-866-798-5598, visiting www.haea.org, or emailing mentors@haea.org.



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For more information, visit www.cinryze.com



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