



You can *do* this.

With hereditary angioedema (HAE), it takes courage to embrace a preventive approach. CINRYZE® (C1 esterase inhibitor [human]) was the first FDA-approved preventive treatment that can start at age 6, helping to reduce HAE attacks earlier in life.

Start with HAE attack prevention.

Not real patients.

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)



Not real patients.

CONSIDER STARTING WITH PREVENTION

In people with HAE, swelling attacks can affect areas of the body, including the hands and feet, stomach, face, and throat. These attacks can be unpredictable and swelling attacks of the throat can create potentially life-threatening situations.

Preventive therapy can help by reducing how often HAE attacks occur and how severe they are.

UNDERSTANDING HAE GUIDELINES

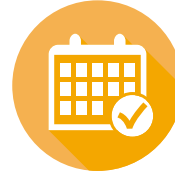
Current guidelines recommend



Talking to your doctor about the frequency and severity of your HAE attacks when developing a treatment plan



Having an acute treatment on hand in addition to exploring preventive therapy



Being evaluated for long-term preventive treatment at every doctor's visit or at least once a year

By considering a preventive approach, you can take an active role in managing and treating your or your loved one's HAE.

Important Safety Information

Tell your healthcare provider about all of your medical conditions, including if you

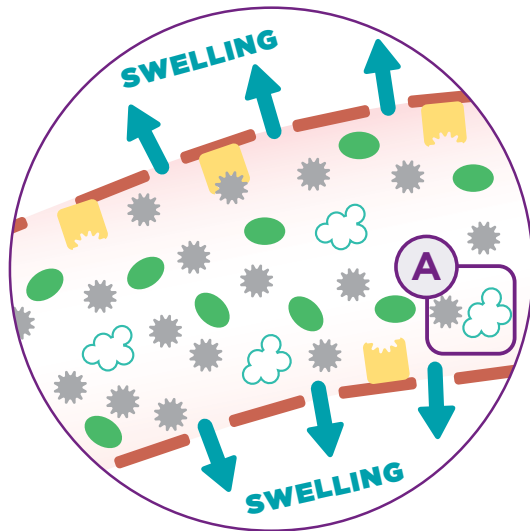
- have an indwelling catheter/access device in one of your veins.
- have a history of blood clots, heart disease, or stroke.
- are taking birth control pills or androgens.
- are pregnant or planning to become pregnant. It is not known if CINRYZE can harm your unborn baby.
- are breastfeeding or plan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

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HOW DOES CINRYZE® WORK?

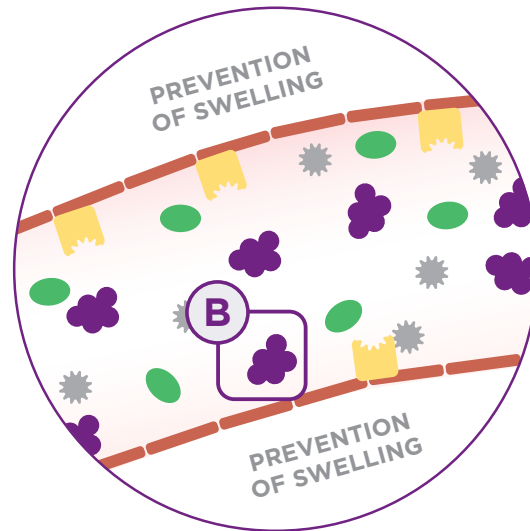
Most people with HAE don't have enough of a protein called C1 esterase inhibitor (C1-INH), or this protein does not work correctly, which leads to a cascade of events in the body. This cascade causes another protein, called plasma kallikrein, to trigger the release of a third protein, called bradykinin. 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® (C1 esterase inhibitor [human]) increases plasma levels of C1-INH, thereby preventing the generation of excess bradykinin to help reduce the risk of a swelling attack.

Untreated person with HAE during an attack

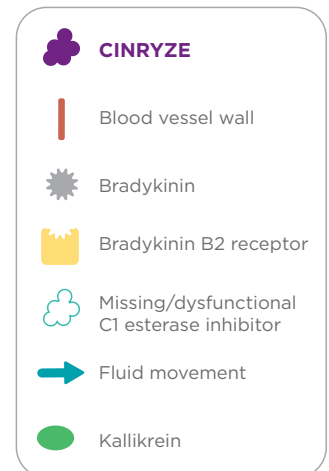


A Missing or dysfunctional C1-INH causes increased levels of bradykinin

Person with HAE responding to CINRYZE



B CINRYZE increases plasma levels of C1-INH to prevent the production of excess bradykinin





Not real patients.

How is CINRYZE® made?

CINRYZE is made from purified human plasma that is collected from plasma donors at US-licensed collection centers. Because CINRYZE is made from human blood, it may carry a risk of transmitting infectious viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. The donated human plasma goes through a complex purification process designed to reduce—but not eliminate—the risk of transmitting infectious diseases. The specific steps to minimize these risks include careful donor screening, testing for the presence of viruses, and pasteurization and nanofiltration.

Important Safety Information

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

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CINRYZE®
C1 esterase inhibitor (human)

PROVEN PREVENTIVE THERAPY FOR CHILDREN (6+)

In a clinical study, CINRYZE® (C1 esterase inhibitor [human]) helped prevent HAE attacks

Number of HAE attacks per month during 12-week observation period and 12-week treatment period

	Mean (average)
CINRYZE 500 U* (12 Patients)	1.2
CINRYZE 1,000 U (12 Patients)	0.7
Baseline observation (12 Patients)	3.7

- CINRYZE demonstrated a reduction in the number of HAE attacks (71.1% and 84.5% mean reduction with 500 U and 1,000 U, respectively) vs baseline observation attack rate

*Data generated with CINRYZE are expressed in Units (U), but dosing of CINRYZE is now expressed in International Units (IU).

The safety and efficacy of CINRYZE 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 1 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.

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

In children, CINRYZE® was proven to help reduce the severity of HAE attacks and reduce the use of acute treatment

Results from a clinical study in 12 children (7-11 years old) receiving CINRYZE (500 U and 1,000 U)

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

†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.

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

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PROVEN PREVENTIVE THERAPY FOR ADULTS AND TEENAGERS

In a clinical study, CINRYZE® (C1 esterase inhibitor [human]) helped prevent HAE attacks

Number of HAE attacks per month during 12-week placebo period and 12-week treatment period

	Mean (average)
CINRYZE (22 Patients)	6.1
PLACEBO (22 Patients)	12.7

- The majority of people had fewer attacks while taking CINRYZE than while taking placebo
- The response to CINRYZE varied
 - 20 people had fewer attacks, ranging from 100% to 1% fewer attacks
 - 4 people had no attacks
 - 2 people had more attacks, ranging from 8% to 85% more 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. Efficacy was measured as a reduction in the number of attacks while taking CINRYZE compared with placebo.

CINRYZE® was proven to help reduce the severity and duration of HAE attacks

Results from a clinical study in 24 patients (9-73 years old) receiving CINRYZE

Decrease in the average duration of attacks

Attacks lasted **2.1 days** while taking CINRYZE vs **3.4 days** while taking placebo

Fewer days of swelling

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

Decrease in the average severity of attacks

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)

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.

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.

HOW IS CINRYZE® ADMINISTERED?

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 and/or your caregiver(s) how to safely administer CINRYZE so that you feel more comfortable with the process. There are additional resources available from Takeda, such as the *CINRYZE Self-Administration Brochure*, which provides you with a step-by-step overview of the administration process. Do not attempt to self-administer unless you have been taught how by your healthcare provider.

Dosing of CINRYZE

	Adults and adolescents (≥12 years)	Children (6 to 11 years)
Dose	1,000 International Units (IU)* intravenous For people with HAE who have not responded adequately to 1,000 IU of CINRYZE, doses up to 2,000 IU (not exceeding 80 IU/kg) may be considered based on individual response	500 IU intravenous The dose may be adjusted according to individual response, up to 1,000 IU
Dosing regimen	Administered every 3 or 4 days	
Infusion rate	1 mL/min (10 minutes)	1 mL/min (5 minutes)

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Your healthcare provider may decide that a higher dose of CINRYZE is required. Be sure to always follow the specific instructions given by your healthcare provider.

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If you'd like additional or refresher training, Takeda offers administration training for people taking CINRYZE® (C1 esterase inhibitor [human]) and their caregiver(s). You can read more about this program on page 15.

“OnePath’s Path to Independence™ program arranged for a nurse to come to my home to train me how to self-administer. **She answered any questions that I had.**”

— A real HAE patient




FLEXIBLE ADMINISTRATION

By choosing to treat with CINRYZE® (C1 esterase inhibitor [human]), you are offered options to administer at home or away

Talk to your healthcare provider about which option is best for you and your lifestyle

- Self-administration
- Administration by a trained family member or caregiver
- Administration by a healthcare provider at an infusion center, a doctor's office, or in your home



You and your caregiver(s) 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

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.
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ONEPATH[®] PRODUCT SUPPORT SERVICES

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



With your CINRYZE treatment, OnePath offers:

- **Help with facilitating** an insurance benefits investigation, and explaining insurance coverage and financial assistance options (if applicable)
- **In-home administration training and support** for you and your caregiver(s) at no cost
- **Educational resources** and the OnePath Mobile App for you and your caregiver(s) at no cost
- **Resources specifically tailored for caregivers** to give them the information and support needed to make informed decisions about the health of those they care for

For questions about OnePath, call

1-866-888-0660

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

ADDITIONAL RESOURCES AND PROGRAMS FOR YOU



Path to Independence™ is a training program designed to help teach people with HAE, family members, and caregivers how to administer CINRYZE. Ask your OnePath PSM for more information about the Path to Independence Program, which is available at no cost.

Takeda Speaker Program Series

The Takeda speaker program offers educational events for you, your family members, and/or caregiver(s) to learn more about living with HAE and HAE treatments available from Takeda.

- Offerings include product programs presented by a healthcare professional and, when available, a patient ambassador will be featured

Your OnePath PSM can tell you about any upcoming events in your area.

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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Not a real patient.

For more information, visit www.cinryze.com



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