Hereditary angioedema (HAE) symptoms can range in severity. Some attacks may be mild or temporarily disabling, but others can become more dangerous due to throat swelling. Swelling in the throat can interfere with breathing, creating a potentially life-threatening situation.

Preventive therapies may help reduce the frequency and severity of attacks. Guidelines developed by HAE experts recommend talking to your doctor about the frequency and severity of your HAE attacks when developing a treatment plan. Remember, there is no way to tell if the next HAE attack will be severe. Your treatment plan should be individualized to meet your needs.
CINRYZE®—PROVEN PREVENTION OF HAE ATTACKS SINCE 2008

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.

For additional safety information, please click here for Full Prescribing Information and discuss with your doctor.
WHAT IS HAE?

Most cases of HAE are caused by an insufficient amount of or defective C1 esterase inhibitor (C1-INH), a protein in the blood that helps to prevent swelling experienced during HAE attacks.

The lack of C1-INH may contribute 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. Having too much bradykinin causes the blood vessels to release fluid, resulting in localized swelling.

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® (C1 esterase inhibitor [human]) 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.

For additional safety information, please click here for Full Prescribing Information and discuss with your doctor.
 HOW DOES CINRYZE® WORK?

CINRYZE® (C1 esterase inhibitor [human]), which is administered by intravenous (IV) infusion, increases plasma levels of C1 inhibitor activity, thereby preventing the generation of bradykinin and reducing the swelling that causes attacks.

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
ADULT AND ADOLESCENT PATIENTS

The safety and effectiveness of CINRYZE® (C1 esterase inhibitor [human]) were evaluated in a 24-week clinical trial in 22 adult and adolescent patients. Patients in the study were diagnosed with HAE and had a history of at least two attacks per month. Patients were divided into two groups: one group received CINRYZE for the first 12 weeks and switched to placebo for the last 12 weeks; the other group received placebo for the first 12 weeks and switched to CINRYZE for the last 12 weeks.

The main measure was the number of attacks experienced by each patient when taking CINRYZE compared with the number of attacks experienced by each patient when taking placebo.

PEDIATRIC PATIENTS

The safety and efficacy of CINRYZE were evaluated in a 36-week clinical trial in 12 pediatric patients aged 7 to 11 years old. Patients were observed for 12 weeks 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 attack rate.

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
- 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

For additional safety information, please click [here](#) for Full Prescribing Information and discuss with your doctor.
CINRYZE® HELPED PREVENT ATTACKS

The majority of patients had fewer attacks while on CINRYZE® (C1 esterase inhibitor [human]) than while on placebo.

The response to CINRYZE varied:
- 20 patients had fewer attacks, ranging from 100% to 1% fewer attacks
  - 4 patients had no attacks
- 2 patients had more attacks, ranging from 8% to 85% more attacks

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

<table>
<thead>
<tr>
<th>ADULT AND ADOLESCENT PATIENTS</th>
<th>Number of HAE attacks experienced in 12 weeks</th>
<th>Mean (average)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CINRYZE® (22 PATIENTS)</td>
<td>6.1</td>
<td></td>
</tr>
<tr>
<td>PLACEBO (22 PATIENTS)</td>
<td>12.7</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PEDIATRIC PATIENTS</th>
<th>Number of HAE attacks during 12-week treatment</th>
<th>Mean (average)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CINRYZE 500 U (12 PATIENTS)</td>
<td></td>
<td>1.2</td>
</tr>
<tr>
<td>CINRYZE 1,000 U (12 PATIENTS)</td>
<td></td>
<td>0.7</td>
</tr>
<tr>
<td>Baseline* (12 PATIENTS)</td>
<td></td>
<td>3.7</td>
</tr>
</tbody>
</table>

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

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.
Since having my first infusion, I am happy to say that the frequency of my attacks has been reduced.

THE FIRST C1-INH THERAPY INDICATED TO HELP PREVENT HAE ATTACKS IN CHILDREN (AS YOUNG AS 6), TEENAGERS, AND ADULTS
CINRYZE® IS PROVEN TO REDUCE THE SEVERITY AND DURATION OF ATTACKS

ADULT AND ADOLESCENT PATIENTS
During treatment with CINRYZE® (C1 esterase inhibitor [human]), compared to placebo, adult and adolescent patients experienced:

- 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)

PEDIATRIC PATIENTS (7-11 years)
In pediatric patients, both doses of CINRYZE (500 U and 1,000 U) vs. baseline attack rate were shown to:

- Lessen the severity of attacks and reduce the use of acute treatment

**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.

For additional safety information, please click [here](#) for Full Prescribing Information and discuss with your doctor.
HOW IS CINRYZE® MADE?

CINRYZE® (C1 esterase inhibitor [human]) is made from purified human blood that is collected from US plasma donors at US-licensed collection centers. Products made from human blood may contain infectious agents. CINRYZE goes through a complex purification process designed to help reduce the risk of transmitting infectious disease. The specific steps to minimize the risk of transmitting an infectious agent include careful donor screening, testing for the presence of viruses, and pasteurization and nanofiltration.

Shire is committed to the HAE community and is dedicated to helping patients with HAE.

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.

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For additional safety information, please click here for Full Prescribing Information and discuss with your doctor.
I refuse to let HAE limit my life; instead, I’m going to chase after my dreams. This is my life, and HAE’s just along for the ride.
HOW IS CINRYZE® ADMINISTERED?

The administration of CINRYZE® (C1 esterase inhibitor [human]) requires a needle to be placed in a vein in the arm. CINRYZE should be prepared and administered at room temperature. 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.

### DOING OF CINRYZE®

<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>1,000 U intravenous</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>500 U intravenous</td>
</tr>
<tr>
<td>DOSING REGIMEN</td>
<td>Single dose can be administered every 3 or 4 days</td>
<td>The dose may be adjusted according to individual response, up to 1,000 U every 3 to 4 days</td>
</tr>
<tr>
<td>INFUSION RATE</td>
<td>1 mL/min (10 minutes)</td>
<td>1 mL/min (5 minutes)</td>
</tr>
</tbody>
</table>

**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

For additional safety information, please click [here](#) for Full Prescribing Information and discuss with your doctor.
FLEXIBLE ADMINISTRATION

There are several options for administering CINRYZE® (C1 esterase inhibitor [human]). Talk to your healthcare provider about which option is best for you and your lifestyle.

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

STORING CINRYZE®

- CINRYZE should be stored at 2°C to 25°C (36°F to 77°F)
- CINRYZE should be protected from light
- Once CINRYZE is prepared, it must be used within 3 hours

Patients should only self-administer after being trained by a healthcare provider.

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
- 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

Path to Independence™ is a free training program designed to help teach patients and/or their caregivers how to self-administer or administer CINRYZE. For more information, contact your OnePath® Patient Support Manager at 1-866-888-0660.
ADDITIONAL RESOURCES

The US Hereditary Angioedema Association (HAEA) is a great resource for people living with HAE—and for their families. Visit the HAEA website at www.haea.org to learn about the wide variety of services offered by the organization.

You, Me & HAE, a mentor program, can pair you with a mentor who also has HAE and is currently on therapy with CINRYZE® (C1 esterase inhibitor [human]). Contact your OnePath® Patient Support Manager to request a mentor.

The Shire Speaker Program Series offers educational events for you and your loved ones to learn more about living with HAE and preventive treatment with CINRYZE.

For additional safety information, please click here for Full Prescribing Information and discuss with your doctor.
ONEPATH® PRODUCT SUPPORT SERVICES

OnePath is your dedicated and experienced team to help ensure you can access your treatment. You will receive a Patient Support Manager (PSM) who will work with you one-on-one to help you access your prescribed Shire therapy.

Your OnePath Patient Support Manager can help by:

- Navigating insurance coverage and payment issues
- Working with specialty pharmacies to facilitate access to therapy
- Providing information about financial assistance options
- Connecting patients and caregivers with educational resources and more!

Plus, when you are enrolled in OnePath, you can download and use the OnePath Mobile App to track your health in a personal eDiary.* Additionally, you can call or text your dedicated Patient Support Manager right from the app, update personal or insurance information, and more!

*OnePath will not have access to this data.

Call your OnePath Patient Support Manager at 1-866-888-0660, Monday through Friday, 8:30 AM–8:00 PM ET, for more information.
Indication
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