

**Hereditary Angioedema Agents:**  
**Berinert (c1 esterase inhibitor)**  
**Cinryze (c1 esterase inhibitor)**  
**Firazyr (icatibant)**  
**Haegarda (c1 esterase inhibitor)**  
**Kalbitor (ecallantide)**  
**Orladeyo (berotralstat)**  
**Ruconest (c1 esterase inhibitor)**  
**Takhzyro (lanadelumab-flyo)**  
**Effective 10/02/2023**

|                              |   |                     |  |
|------------------------------|---|---------------------|--|
| <b>Plan</b>                  | <input checked="" type="checkbox"/> MassHealth<br><input type="checkbox"/> Commercial/Exchange  | <b>Program Type</b> | <input checked="" type="checkbox"/> Prior Authorization<br><input checked="" type="checkbox"/> Quantity Limit<br><input type="checkbox"/> Step Therapy |
| <b>Benefit</b>               | <input checked="" type="checkbox"/> Pharmacy Benefit<br><input checked="" type="checkbox"/> Medical Benefit (NLX)   |                     |  |
| <b>Specialty Limitations</b> | These medications have been designated specialty and must be filled at a contracted specialty pharmacy.   |                     |  |
| <b>Contact Information</b>   | <b>Specialty Medications</b>  |                     |  |
|                              | All Plans   | Phone: 866-814-5506 | Fax: 866-249-6155  |
|                              | <b>Non-Specialty Medications</b>  |                     |  |
|                              | MassHealth  | Phone: 877-433-7643 | Fax: 866-255-7569  |
|                              | Commercial  | Phone: 800-294-5979 | Fax: 888-836-0730  |
|                              | Exchange  | Phone: 855-582-2022 | Fax: 855-245-2134  |
|                              | <b>Medical Specialty Medications (NLX)</b>  |                     |  |
|                              | All Plans   | Phone: 844-345-2803 | Fax: 844-851-0882  |
| <b>Exceptions</b>            | Kalbitor is only available through the medical benefit.<br>Berinert, Cinryze, Firazyr, Haegarda, Ruconest are available through both pharmacy and medical benefits. |                     |  |

### Overview

The following medications are indicated for prophylaxis to prevent attack of hereditary angioedema (HAE):

- Cinryze (c1 esterase inhibitor)
- Haegarda (c1 esterase inhibitor)
- Orladeyo (berotralstat)
- Takhzyro (lanadelumab-flyo)

The following medications are indicated for the treatment of acute attacks of HAE:

- Berinert (c1 esterase inhibitor)
- Firazyr (icatibant)\* ‡
- Kalbitor (ecallantide) ^
- Ruconest (c1 esterase inhibitor)

\*Available as an A-rated generic, both brand and A-rated generic require PA

^This drug is available through the medical benefit only.

‡Branded generic is available.

### Coverage Guidelines

Authorization may be granted for members new to the plan who are currently receiving treatment with requested medication, excluding when the product is obtained as samples or via manufacturer's patient assistance programs.

#### OR

Authorization may be granted for members when ALL the following criteria are met:

**Berinert**® (c1 esterase inhibitor, human)

**Firazyr**® (icatibant)

**Kalbitor**® (ecallantide)

**Ruconest**® (c1 esterase inhibitor, recombinant)

Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of hereditary angioedema
2. Prescriber is an allergist or immunologist consultation notes from an allergist or immunologist regarding the diagnosis are provided
3. If request is for BRAND NAME Firazyr®, prescriber must also provide medical records documenting an inadequate response or adverse reaction to generic icatibant (as per the Brand Name guideline)
4. Appropriate dosing

**Cinryze**® (c1 esterase inhibitor, human)

**Haegarda**® (c1 esterase inhibitor, human)

**Orladeyo**® (berotralstat)

**Takhzyro**® (lanadelumab-flyo)

Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of hereditary angioedema.
2. Prescriber is an allergist or immunologist or consultation notes from an allergist or immunologist regarding the diagnosis are provided
3. Member meets **ONE** of the following:
  - a. Member has more than one HAE event per month
  - b. Member has a history of recurrent laryngeal attacks
4. Appropriate dosing

### Continuation of Therapy

Berinert®, icatibant, Kalbitor®, and Ruconest®:

Reauthorization may be granted with documentation of the use or expiration of previously approved product. Quantity approved may be dependent on documented previous utilization and should not allow for a quantity greater than that required to treat up to two attacks.

Cinryze®, Haegarda®, Orladeyo®, and Takhzyro®:

Reauthorization may be granted for members who experience a positive clinical response to the requested medication.

### Limitations

1. Initial approvals and reauthorizations will be granted for the following:
  - a. Berinert®, icatibant, Kalbitor®, and Ruconest®: **1 year**
  - b. Cinryze®, Haegarda®, Orladeyo®, and Takhzyro®: **6 months**



- The following quantity limits apply:

|                     |                           |
|---------------------|---------------------------|
| Berinert            | 6 vials per 12 months     |
| Cinryze             | 120 vials per 6 months    |
| Firazyr (icatibant) | 6 syringes per 12 months  |
| Haegarda            | 120 vials per 6 months    |
| Oraldeyo            | 180 capsules per 6 months |
| Ruconest            | 8 vials per 12 months     |
| Takhzyro            | 24 mL per 6 months        |

## References

- Zuraw BL. Hereditary Angioedema. *NEJM* 2008;359(10):1027-1036.
- Tse K, Zuraw BL, Recognizing and managing hereditary angioedema. *Cleveland Clinic Journal of Medicine* 2013;80(5):297-308.
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- Xu Y, Buyantseva LV, Agarwal NS, Olivieri K, Zhi YX, Craig TJ. Update on treatment of hereditary angioedema. *Clinical & Experimental Allergy* 2013;43:395-405.
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- The U.S. Hereditary Angioedema Association. HAE Symptoms [webpage on the internet] Honolulu (HI): The U.S. Hereditary Angioedema Association; (2018) [cited 2021 Apr 29]. Available from: <https://www.haea.org/symptoms.php>.
- The U.S. Hereditary Angioedema Association. HAE Attack Triggers [webpage on the internet] Honolulu (HI): The U.S. Hereditary Angioedema Association; (2021) [cited 2021 Apr 29]. Available from: <https://www.haea.org/Triggers.php>.
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20. Zuraw BL, Bernstein JA, Lang DM, Craig T, Dreyfus D, Hsieh F, et al. A focused parameter update: hereditary angioedema, acquired C1 inhibitor deficiency, and angiotensin-converting enzyme inhibitor-associated angioedema. *J Allergy Clin Immunol* 2013;131(6):1491-3.
21. Bowen T, Cicardi M, Farkas H, Bork K, Longhurst HJ, Zuraw B, et al. 2010 International consensus algorithm for the diagnosis, therapy and management of hereditary angioedema. *Allergy, Asthma & Clinical Immunology* 2010; 6:24-36.
22. Busse PJ, Christiansen SC, Riedl MA, Banerji A, Bernstein JA, Castaldo AJ, et al. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. 2021 Jan;9(1):132-150.e3.



**Review History**

05/19/2021 – Created and Reviewed May P&T. Effective 07/01/2021.

9/21/2022 – Reviewed and Updated for Sept P&T; Separated out MH vs. Comm/Exch. Effective 1/1/2023

02/08/2023 - Reviewed and updated for Feb P&T. Matched MH UPPL criteria. Updated references and quantity limits. Added requirement of appropriate dosing to criteria. Renamed criteria to HAE agents and added the following: Berinert, Cinryze, Firazyr, Haegarda, Kalbitor, Ruconest, Takhzyro. Clarified that Kalbitor is only available under medical benefit. Effective 4/1/23.

09/13/23 – Reviewed and updated for P&T. Clarified benefit coverage. No clinical changes. Effective 10/2/23.

