

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

Plan	<input checked="" type="checkbox"/> MassHealth UPPL <input type="checkbox"/> Commercial/Exchange	Program Type	<input checked="" type="checkbox"/> Prior Authorization <input checked="" type="checkbox"/> Quantity Limit <input type="checkbox"/> Step Therapy
Benefit	<input checked="" type="checkbox"/> Pharmacy Benefit <input checked="" type="checkbox"/> Medical Benefit		
Specialty Limitations	These medications have been designated specialty and must be filled at a contracted specialty pharmacy.		
Contact Information	Medical and Specialty Medications		
	All Plans	Phone: 877-519-1908	Fax: 855-540-3693
Exceptions	Non-Specialty Medications		
	All Plans	Phone: 800-711-4555	Fax: 844-403-1029
Exceptions	Kalbitor is only available through the medical benefit. Berinert, Cinryze, Firazyr, Haegarda, Ruconest are available through both pharmacy and medical benefits.		

Overview

The following medications are indicated for prophylaxis to prevent attacks 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

Mass General Brigham Health Plan includes Mass General Brigham Health Plan, Inc. and Mass General Brigham Health Insurance Company.

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:

Beriner[®] (c1 esterase inhibitor, human)

Firazy[®] (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 Firazy[®], 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

Beriner[®], 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. Beriner[®], icatibant, Kalbitor[®], and Ruconest[®]: **1 year**
 - b. Cinryze[®], Haegarda[®], Orladeyo[®], and Takhzyro[®]: **6 months**
2. The following quantity limits apply:

Beriner [®]	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

1. Zuraw BL. Hereditary Angioedema. *NEJM* 2008;359(10):1027-1036.
2. Tse K, Zuraw BL, Recognizing and managing hereditary angioedema. *Cleveland Clinic Journal of Medicine* 2013;80(5):297-308.
3. Zuraw B, Farkas H. Hereditary angioedema: Epidemiology, clinical manifestations, exacerbating factors, and prognosis. In Saini S (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2022 [cited 2022 Feb]. Available from: <http://www.uptodate.com/utd/index.do>.
4. 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.
5. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema-The 2017 revision and update. *Allergy*. 2018 Aug;73(8):1575-1596.
6. 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>.
7. 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>.
8. Zuraw B, Farkas H. Hereditary angioedema (due to C1 inhibitor deficiency): General Care and long-term prophylaxis. In Saini S (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2022 [cited 2022 Feb]. Available from: <http://www.uptodate.com/utd/index.do>.
9. Orladeyo® [package insert]. Durham (NC): BioCryst Pharmaceuticals, Inc.; 2020 Dec.
10. Cicardi M, Bork K, Caballero T, Craig T, Li HH, Longhurst H, et al. Evidence-based recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: consensus report of an International Working Group. *European Journal of Allergy and Clinical Immunology*. 2012; 67:147-157
11. 19. Gompels MM, Lock RJ, Abinum M, Bethune CA, Davies G, Grattan C, et al. C1 inhibitor deficiency: consensus document. *Clin Exp Immunol* 2005; 141 (1):189-90.
12. 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.
13. 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.
14. 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.

