Mass General Brigham
Health Plan

Hereditary Angioedema Agents
Berinert (c1 esterase inhibitor)
Cinryze (c1 esterase inhibitor)
Firazyr (icatibant)
Haegarda (c1 esterase inhibitor)
Kalbitor (ecallantide)
Ruconest (c1 esterase inhibitor)
Effective 06/01/2025

Plan	☒ MassHealth UPPL ☐Commercial/Exchange	**Program Type**	☒ Prior Authorization ☐ Quantity Limit ☐ Step Therapy
Benefit	☐ Pharmacy Benefit ☒ Medical Benefit		
Specialty Limitations	N/A		
Contact Information	**Medical and Specialty Medications** All Plans | Phone: 877-519-1908 | Fax: 855-540-3693		
	Non-Specialty Medications All Plans | Phone: 800-711-4555 | Fax: 844-403-1029		
Notes	Berinert, Cinryze, and Ruconest are also available on the pharmacy benefit. Please see the MassHealth Drug List for coverage and criteria. Additional agents from this class are available through the pharmacy benefit. Please see the MassHealth Drug List for coverage and criteria.		

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

- Cinryze (c1 esterase inhibitor)
- Haegarda (c1 esterase inhibitor)

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)

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)

1. Diagnosis of hereditary angioedema acute attack treatment
2. Prescriber is an allergist or immunologist consultation notes from an allergist or immunologist regarding the diagnosis are provided
3. Appropriate dosing

Cinryze (c1 esterase inhibitor, human)
Haegarda (c1 esterase inhibitor, human)

1. Diagnosis of hereditary angioedema prophylaxis
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 attack per month
    b. Member has a history of recurrent laryngeal attacks
4. Appropriate dosing

Continuation of Therapy

Berinert, Firazyr, 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 and Haegarda:
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, Firazyr, Kalbitor, and Ruconest: **1 year**
    b. Cinryze and Haegarda: **6 months**

References

1. Berinert [package insert]. King of Prussia (PA): CSL Behring GmbH; 2021 Sep.
2. Cinryze [package insert]. Deerfield (IL): Takeda Pharmaceuticals America, Inc.; 2024 Dec.
3. Firazyr [package insert]. Deerfield (IL): Takeda Pharmaceuticals America, Inc.; 2024 Jan.
4. Haegarda [package insert]. King of Prussia (PA): CSL Behring GmbH; 2022 Feb.
5. Kalbitor [package insert]. Deerfield (IL): Takeda Pharmaceuticals America, Inc.; 2023 Dec.
6. Ruconest [package insert]. Warren (NJ): Pharming Healthcare Inc.; 2020 Apr.
7. Zuraw BL. Hereditary Angioedema. NEJM 2008;359(10):1027-1036.
8. Tse K, Zuraw BL, Recognizing and managing hereditary angioedema. Cleveland Clinic Journal of Medicine 2013;80(5):297-308.
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10. 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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15. 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
16. 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.
17. 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.
18. 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.
19. 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.
05/15/25 Reviewed and updated for P&T. Performed annual medical criteria review. Policy has been updated to better reflect agents with prior authorization on medical benefit. Orladeyo and Takhzyro were pharmacy benefit only and thus have been removed. Firazyr and Haegarda will be managed through the medical benefit only. Updated formatting & references accordingly. Removed required trial of generic icatibant per Brand Name guideline as its not applicable to medical benefit. Effective 6/1/25