Clinical Policy: Hereditary Angioedema Treatments

Reference Number: PHW.PDL.501
Effective Date: 01/01/2020
Last Review Date: 11/2023

Revision Log

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health and Wellness® that Hereditary Angioedema Treatments are **medically necessary** when the following criteria are met:

I. Requirements for Prior Authorization of Hereditary Angioedema (HAE) Agents

A. Prescriptions That Require Prior Authorization

All prescriptions for Hereditary Angioedema (HAE) Agents must be prior authorized.

B. Review of Documentation for Medical Necessity

In evaluating a request for prior authorization of a prescription for an HAE Agent, the determination of whether the requested prescription is medically necessary will take into account whether the member:

1. Is prescribed the HAE Agent for an indication that is included in the U.S. Food and Drug Administration (FDA)-approved package labeling OR a medically accepted indication; **AND**

2. Is age-appropriate according to FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature; **AND**

3. Is prescribed a dose that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature; **AND**

4. Is prescribed the HAE Agent by or in consultation with an appropriate specialist (i.e., an allergist/immunologist, hematologist, or dermatologist); **AND**

5. Does not have a contraindication to the prescribed medication; **AND**

6. With the exception of requests for short-term prophylaxis (e.g., surgical or dental procedure), will not be using the requested HAE Agent with another HAE Agent for the same indication (i.e., more than one HAE Agent for acute treatment or more than one HAE Agent for long-term prophylaxis); **AND**

7. For a diagnosis of HAE Type I or II (with C1 inhibitor deficiency/dysfunction), has **both** of the following lab values obtained on two separate instances:

a. Low C4 complement level (mg/dL)
b. At least **one** of the following:

    i. Low C1 esterase inhibitor antigenic level (mg/dL)
    ii. Low C1 esterase inhibitor functional level [(<65%) unless already using an androgen or C1 esterase inhibitor];

AND

8. For a diagnosis of HAE Type III (with normal C1 inhibitor), **all** of the following:

    a. Has **all** of the following lab values:

        i. Normal C4 complement level (mg/dL),
        ii. Normal C1 esterase inhibitor antigenic level (mg/dL),
        iii. Normal C1 esterase inhibitor functional level,

    b. Has a history of recurrent angioedema without urticaria,

    c. **One** of the following:

        i. **Both** of the following:

            a) Has documentation of a family history of HAE
            b) Failed to respond to maximum recommended doses of antihistamines (e.g., cetirizine 20 mg twice daily)

        ii. Has a HAE-causing genetic mutation;

    AND

9. Is not taking an estrogen-containing medication unless medically necessary or an ACE inhibitor; **AND**

10. If prescribed the HAE Agent for long-term prophylaxis, has poorly controlled HAE based on the prescriber's assessment despite use of an HAE Agent for on demand/acute treatment; **AND**

11. For a non-preferred HAE Agent, **one** of the following:

    a. Has a history of therapeutic failure, contraindication, or intolerance to the preferred HAE Agents approved or medically accepted for the member's indication
    b. Has a current history (within the past 90 days) of being prescribed the same non-preferred HAE Agent (does not apply to non-preferred brands when the

therapeutically equivalent generic, interchangeable biosimilar, or unbranded biologic is preferred or to non-preferred generics, interchangeable biosimilars, or unbranded biologics when the therapeutically equivalent brand, interchangeable brand, or brand biologic product is preferred)

See the Preferred Drug List (PDL) for the list of preferred HAE Agents at https://papdl.com/preferred-drug-list;

AND

12. If a prescription for an HAE Agent is for a quantity that exceeds the quantity limit, the determination of whether the prescription is medically necessary will also take into account the guidelines set forth in PA.CP.PMN.59 Quantity Limit Override

    NOTE: If the member does not meet the clinical review guidelines listed above but, in the professional judgment of the physician reviewer, the services are medically necessary to meet the medical needs of the member, the request for prior authorization will be approved.

FOR RENEWALS OF PRIOR AUTHORIZATION FOR AN HAE AGENT: The determination of medical necessity of a request for renewal of a prior authorization for an HAE agent that was previously approved will take into account whether the member:

1. Is prescribed a dose that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature; **AND**

2. Is prescribed the HAE Agent by or in consultation with an appropriate specialist (i.e., an allergist/immunologist, hematologist, or dermatologist); **AND**

3. With the exception of requests for short-term prophylaxis, will not be using the requested HAE Agent with another HAE Agent for the same indication (i.e., more than one HAE Agent for acute treatment or more than one HAE Agent for long-term prophylaxis); **AND**

4. If prescribed the HAE Agent for acute treatment, has documentation of a positive clinical response to the requested medication; **AND**

5. If prescribed the HAE Agent for long-term prophylaxis, has a documented reduction in the number of HAE attacks; **AND**

6. If a prescription for an HAE Agent is for a quantity that exceeds the quantity limit, the determination of whether the prescription is medically necessary will also take into account the guidelines set forth in PA.CP.PMN.59 Quantity Limit Override

    NOTE: If the member does not meet the clinical review guidelines listed above but, in the professional judgment of the physician reviewer, the services are medically

necessary to meet the medical needs of the member, the request for prior authorization will be approved.

C. Clinical Review Process

Prior authorization personnel will review the request for prior authorization and apply the clinical guidelines in Section B. above, to assess the medical necessity of a prescription for an HAE Agent. If the guidelines in Section B are met, the reviewer will prior authorize the prescription. If the guidelines are not met, the prior authorization request will be referred to a physician reviewer for a medical necessity determination. Such a request for prior authorization will be approved when, in the professional judgment of the physician reviewer, the services are medically necessary to meet the medical needs of the member.

D. **Approval Duration**

Berinert, Ruconest, Firazyr, Kalbitor	**Acute attacks**	**6 months**
Cinryze, Haegarda	**Long-term prophylaxis**	**12 months**
	Short-term prophylaxis	**2 doses per procedure**
Takhzyro	**Long-term prophylaxis**	**New request: 6 months** **Renewal request: 12 months**

E. References

1. Berinert Package Insert. Kankakee, Il: CSL Behring LLC; September 2021.
2. Busse PJ, Christiansen SC, Riedl MA, Banerji A, Bernstein JA, Castaldo AJ, Craig T, Davis-Lorton M, Frank MM, Li HH, Lumry WR, Zuraw BL. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. J Allergy Clin Immunol Pract. 2021 Jan;9(1):132-150.e3. doi: 10.1016/j.jaip.2020.08.046. Epub 2020 Sep 6. PMID: 32898710.
3. Cinryze Package Insert. Lexington, MA:Takeda Pharmaceuticals U.S.A., Inc.; February 2023.
4. Firazyr Package Insert. Lexington, MA: Takeda Pharmaceuticals America, Inc.; October 2021.
5. Frank MM, Zuraw B, Banerji A, et al. Management of Children With Hereditary Angioedema Due to C1 Inhibitor Deficiency. Pediatrics. 2016;138(5):e20160575
6. Haegarda Package Insert. Kankakee, Il: CSL Behring LLC; January 2022.
7. Kalbitor Package Insert. Lexington, MA: Takeda Pharmaceuticals U.S.A., Inc.; November 2021.
8. Maurer, M, Magerl, M, Betschel, S, et al. The international WAO/EAACI guideline for the management of hereditary angioedema—The 2021 revision and update. Allergy. 2022; 77: 1961–1990. doi:10.1111/all.15214
9. Orladeyo Package Insert. Durham, NC: BioCryst Pharmaceuticals, Inc.; March 2022.
10. Ruconest Package Insert. Warren, NJ: Pharming Healthcare Inc.; April 2020.

11. Sajazir Package Insert. Cambridge, United Kingdom: Cycle Pharmaceuticals Ltd; May 2022.
12. Takhzyro Package Insert. Lexington, MA: Takeda Pharmaceuticals U.S.A., February 2023.
13. Zuraw B, Bork K. Hereditary angioedema with normal C1 inhibitor. Saini S, Felweg AM, eds. Waltham, MA: UpToDate Inc. Updated October 11, 2021. Accessed August 08, 2023.
14. Zuraw B, Farkas H. Hereditary angioedema: Acute treatment of angioedema attacks. Saini S, Felweg AM, eds. Waltham, MA: UpToDate Inc. Updated March 23, 2020 May 09. 2023. Accessed July 28, 2020 August 08, 2023.
15. Zuraw B, Farkas H. Hereditary angioedema (due to C1 inhibitor deficiency): Pathogenesis and diagnosis. Saini S, Felweg AM, eds. Waltham, MA: UpToDate Inc. Updated February 08, 2022. Accessed August 08, 2023.
16. Zuraw B, Farkas H. Hereditary angioedema (due to C1 inhibitor deficiency): General care and long-term prophylaxis. Saini S, Felweg AM, eds. Waltham, MA; UpToDate Inc. Updated June 29, 2023. Accessed August 8, 2023.

Reviews, Revisions, and Approvals	Date
Policy created	01/01/2020
Q3 2020 annual review: no changes.	07/2020
Q1 2021: policy revised according to DHS revisions effective 01/05/2021	11/2020
Q1 2022 annual review: no changes.	11/2021
Q1 2023 annual review: no changes.	11/2022
Q1 2024: policy revised according to DHS revisions effective 01/08/2024	11/2023