Harvard Pilgrim Health Care | TUFTS Health Plan

Pharmacy Medical Necessity Guidelines:
Hereditary Angioedema Medications

Effective: May 1, 2026

Guideline Type	☒ Prior Authorization ☐ Non-Formulary ☐ Step-Therapy ☐ Administrative

Applies to:

Commercial Products

☒ Harvard Pilgrim Health Care Commercial products; Fax: 617-673-0988

☒ Tufts Health Plan Commercial products; Fax: 617-673-0988

Public Plans Products

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product); Fax: 617-673-0988

Note: While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to ensure that prior authorization has been obtained.

Overview

Food and Drug Administration – Approved Indications

Andembry (garadacimab-gxii) is an activated Factor XII [FXIIa] inhibitor [monoclonal antibody]) indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients aged 12 years and older.

Dawnzera (donidalorsen) is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older.

Haegarda (C1 Esterase Inhibitor [Human]) is a plasma-derived concentrate of C1 Esterase Inhibitor (Human) indicated for routine prophylaxis to prevent hereditary angioedema (HAE) attacks in patients 6 years of age and older.

Icatibant is a bradykinin B2 receptor antagonist indicated for the treatment of acute attacks of HAE in adults 18 years of age and older.

Orladeyo (berotralstat) is a plasma kallikrein inhibitor indicated for prophylaxis to prevent attacks of HAE in adults and pediatric patients 2 years and older.

Ruconest (C1 esterase inhibitor [recombinant]) is a C1 esterase inhibitor [recombinant] indicated for the treatment of acute attacks in adult and adolescent patients with HAE.

Takhzyro (lanadelumab-flyo) is a plasma kallikrein inhibitor (monoclonal antibody) indicated for prophylaxis to prevent attacks of HAE in adult and pediatric patients 2 years and older.

Clinical Guideline Coverage Criteria

Dawnzera (donidalorsen)

The plan may authorize coverage of Dawnzera for Members when **ALL** of the following criteria are met:

Initial Authorization Criteria

1. Documented diagnosis of hereditary angioedema

AND

2. The patient is at least 12 years of age or older

AND

3. Prescribed by or in consultation with an allergist, hematologist, or immunologist

AND

4. Documentation that “on-demand” therapy (e.g., icatibant, Kalbitor, Ruconest, Berinert) did not provide satisfactory control or access to “on-demand” therapy is limited

Reauthorization Criteria

1. Documented diagnosis of hereditary angioedema

AND

2. The patient is at least 12 years of age or older

AND

3. Prescribed by or in consultation with an allergist, hematologist, or immunologist

AND

4. Documentation of a positive clinical response as evidenced by **one (1)** of the following:
    a. An improvement in severity and duration of attacks has been achieved and sustained
    b. A decrease in attack frequency

AND

5. For patients who have been attack free for 12 months, provider attestation that consideration has been given to changing the patient to a dosing interval of every 8 weeks

Haegarda (C1 Esterase Inhibitor [Human])

The plan may authorize coverage of Haegarda for Members when ALL of the following criteria are met:

Initial Authorization Criteria

1. Documented diagnosis of hereditary angioedema

AND

2. Patient is at least 6 years of age or older

AND

3. Prescribed by or in consultation with an allergist, hematologist, or immunologist

AND

4. Documentation that “on-demand” therapy (e.g., icatibant, Kalbitor, Ruconest, Berinert) did not provide satisfactory control or access to “on-demand” therapy is limited

Reauthorization Criteria

1. Documented diagnosis of hereditary angioedema

AND

2. Patient is at least 6 years of age or older

AND

3. Prescribed by or in consultation with an allergist, hematologist, or immunologist

AND

4. Documentation of a positive clinical response as evidenced by **one (1)** of the following:
    a. An improvement in severity and duration of attacks has been achieved and sustained
    b. A decrease in attack frequency

Orladeyo (berotralstat)

The plan may authorize coverage of Oradeyo for Members when **ALL** of the following criteria are met:

Initial Authorization Criteria

1. Documented diagnosis of hereditary angioedema

AND

2. Patient is at least 2 years of age or older

AND

3. Prescribed by or in consultation with an allergist, hematologist, or immunologist

AND

4. Documentation that “on-demand” therapy (e.g., icatibant, Kalbitor, Ruconest, Berinert) did not provide satisfactory control or access to “on-demand” therapy is limited

Reauthorization Criteria

1. Documented diagnosis of hereditary angioedema

AND

2. Patient is at least 2 years of age or older

AND

3. Prescribed by or in consultation with an allergist, hematologist, or immunologist

AND

4. Documentation of a positive clinical response as evidenced by **one (1)** of the following:
    a. An improvement in severity and duration of attacks has been achieved and sustained
    b. A decrease in attack frequency

Andembry (garadacimab-gxii)

The plan may authorize coverage of Andembry for Members when **ALL** of the following criteria are met:

Initial Authorization Criteria

1. Documented diagnosis of hereditary angioedema

AND

2. Patient is at least 12 years of age or older

AND

3. Prescribed by or in consultation with an allergist, hematologist, or immunologist

AND

4. Documentation that “on-demand” therapy (e.g., icatibant, Kalbitor, Ruconest, Berinert) did not provide satisfactory control or access to “on-demand” therapy is limited

Reauthorization Criteria

1. Documented diagnosis of hereditary angioedema

AND

2. Patient is at least 12 years of age or older

AND

3. Prescribed by or in consultation with an allergist, hematologist, or immunologist

AND

4. Documentation of a positive clinical response as evidenced by **one (1)** of the following:
    a. An improvement in severity and duration of attacks has been achieved and sustained
    b. A decrease in attack frequency

Takhzyro (lanadelumab-flyo)

The plan may authorize coverage of Takhzyro for Members when **ALL** of the following criteria are met:

Initial Authorization Criteria

1. Documented diagnosis of hereditary angioedema

AND

2. The patient is at least 2 years of age or older

AND

3. Prescribed by or in consultation with an allergist, hematologist, or immunologist

AND

4. Documentation that “on-demand” therapy (e.g., icatibant, Kalbitor, Ruconest, Berinert) did not provide satisfactory control or access to “on-demand” therapy is limited

Reauthorization Criteria

1. Documented diagnosis of hereditary angioedema

AND

2. The patient is at least 2 years of age or older

AND

3. Prescribed by or in consultation with an allergist, hematologist, or immunologist

AND

4. Documentation of a positive clinical response as evidenced by **one (1)** of the following:
    a. An improvement in severity and duration of attacks has been achieved and sustained
    b. A decrease in attack frequency

AND

5. For patients who have been attack free for 12 months, provider attestation that consideration has been given to changing the patient to a dosing interval of 300 mg every four (4) weeks

Icatibant (C1 esterase inhibitor [recombinant])

The plan may authorize coverage of icatibant for Members when **ALL** of the following criteria are met:

1. Documented diagnosis of hereditary angioedema

AND

2. The patient is at least 18 years of age or older

AND

3. Prescribed by or in consultation with an allergist, hematologist, or immunologist

Ruconest (C1 esterase inhibitor [recombinant])

The plan may authorize coverage Ruconest for Members when **ALL** of the following criteria are met:

1. Documented diagnosis of hereditary angioedema

AND

2. The patient is at least 13 years of age or older

AND

3. Prescribed by or in consultation with an allergist, hematologist, or immunologist

Limitations

1. Andembry, Haegarda and Orladeyo will be authorized for 12 months.
2. Takhzyro and Dawnzera will be authorized for 6 months.
3. Patients new to the plan stable on Andembry, Dawnzera, Haegarda, Orladyo, or Takhzyro should be reviewed against Initial Therapy.
4. For a non-formulary medication request, please refer to the Pharmacy Medical Necessity Guidelines for Formulary Exceptions and submit a formulary exception request to the plan as indicated.

Codes

None

References

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Approval And Revision History

September 13, 2022: Reviewed by the Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:

- May 9, 2023: Updated approval duration and age requirements of Takhzyro to 6 months (effective August 1, 2023)
- March 12, 2024: No changes
- October 8, 2024: Removed Sajazir from the Medical Necessity Guideline. Sajazir will be moved to non-formulary status (eff 1/1/25).
- November 12, 2024: Added Ruconest to the Medical Necessity Guideline. Removed the requirement of documentation the patient has a history of at least one (1) severe attack within the past 6 months for acute treatments (eff 1/1/25).
- August 12, 2025: Updated age requirements of Ruconest to at least 13 years of age (eff 9/1/25).
- October 14, 2025: Added Andembry (garadacimab-gxii) to the Medical Necessity Guideline (eff 11/1/25).
- April 14, 2026: Effective May 1, 2026, added Dawnzera criteria and updated Orladeyo indication for patients 2 years of age and older. Removed Carelink from covered business lines.

Background, Product and Disclaimer Information

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. The plan makes coverage decisions on a case-by-case basis considering the individual member's health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member’s benefit document, the provisions of the benefit document will govern.

Treating providers are solely responsible for the medical advice and treatment of members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.