CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Hereditary Angioedema – Takhzyro Utilization Management Medical Policy
- Takhzyro® (lanadelumab-flyo subcutaneous injection – Shire/Takeda)

REVIEW DATE: 10/15/2025

OVERVIEW

Takhzyro, a human monoclonal antibody inhibitor of plasma kallikrein, is indicated for **prophylaxis to prevent attacks of hereditary angioedema (HAE)** in patients ≥ 2 years of age.[1]

Guidelines

According to US HAE Association Medical Advisory Board Guidelines (2020), when HAE is suspected based on clinical presentation, appropriate testing includes measurement of the serum C4 level, C1 esterase inhibitor (C1-INH) antigenic level, and C1-INH functional level.[2] Low C4 plus low C1-INH antigenic or functional level is consistent with a diagnosis of HAE types I/II. The decision on when to use long-term prophylaxis cannot be made on rigid criteria but should reflect the needs of the individual patient. First-line medications for HAE I/II include intravenous C1-INH, Haegarda® (C1-INH [human] subcutaneous injection), or Takhzyro. The guideline was written prior to approval of Orladeyo® (berotralstat capsules).

According to World Allergy Organization/European Academy of Allergy and Clinical Immunology guidelines (2021), it is recommended to evaluate for long-term prophylaxis at every visit, taking disease activity, burden, and control as well as patient preference into consideration.[3] The following therapies are supported as first-line options for long-term prophylaxis: plasma-derived C1-INH (87% agreement), Takhzyro (89% agreement), and Orladeyo (81% agreement). With regard to plasma-derived C1-INH, it is noted that Haegarda provided very good and dose-dependent preventative effects on the occurrence of HAE attacks; the subcutaneous route may provide more convenient administration and maintain improved steady-state plasma concentrations compared with the intravenous route. Of note, androgens are not recommended in the first-line setting for long-term prophylaxis. Recommendations are not made regarding long-term prophylaxis in HAE with normal C1-INH.

A Phase III trial comparing Takhzyro with placebo for prophylactic use in HAE with normal C1-INH failed to demonstrate a statistically significant difference in reducing the number of attacks.[4]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Takhzyro. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Takhzyro as well as the monitoring required for adverse events and long-term efficacy, approval requires Takhzyro to be prescribed by or in consultation with a physician who specializes in the condition being treated. A patient who has previously met initial therapy criteria for Takhzyro for the requested indication under the Coverage Review Department and is currently receiving the requested therapy is only required to meet the continuation therapy criteria (i.e., currently receiving Takhzyro). If past criteria have not been met under the Coverage Review Department and the patient is currently receiving Takhzyro, initial therapy criteria must be met.

Documentation: Documentation will be required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory records, and prescription claims records. All documentation must include patient-specific identifying information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Takhzyro is recommended in those who meet the following criteria:

FDA-Approved Indication

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1. **Hereditary Angioedema (HAE) Due to C1 Inhibitor (C1-INH) Deficiency – Prophylaxis**. Approve Takhzyro for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial therapy. Approve if the patient meets BOTH of the following (i and ii):
     - **i.** Patient has HAE type I or type II as confirmed by the following diagnostic criteria (a and b):
       Note: A diagnosis of HAE with normal C1-INH (also known as HAE type III) does NOT satisfy this requirement.
       - **a)** Patient has low levels of functional C1-INH protein (< 50% of normal) at baseline, as defined by the laboratory reference values **[documentation required]**; AND
       - **b)** Patient has lower than normal serum C4 levels at baseline, as defined by the laboratory reference values **[documentation required]**; AND
     - **ii.** The medication is prescribed by or in consultation with an allergist/immunologist or a physician who specializes in the treatment of HAE or related disorders; OR
   - **B)** Patient is currently receiving Takhzyro prophylaxis. Approve if the patient meets ALL of the following (i, ii, and iii):
     Note: If the patient is currently receiving the requested therapy, but has not previously received approval of Takhzyro for this indication through the Coverage Review Department, review under criteria for Initial Therapy.
     - **i.** Patient has a diagnosis of HAE type I or type II **[documentation required]**; AND
       Note: A diagnosis of HAE with normal C1-INH (also known as HAE type III) does NOT satisfy this requirement.
     - **ii.** According to the prescriber, the patient has had a favorable clinical response since initiating Takhzyro prophylactic therapy compared with baseline (i.e., prior to initiating prophylactic therapy); AND
       Note: Examples of a favorable clinical response include decrease in HAE acute attack frequency, decrease in HAE attack severity, or decrease in duration of HAE attacks.
     - **iii.** The medication is prescribed by or in consultation with an allergist/immunologist or a physician who specializes in the treatment of HAE or related disorders.

   Dosing. Approve ONE of the following dosing regimens (A, B, or C):
   - **A)** For patients who are ≥ 12 years of age: Approve a dose of 300 mg per injection, administered subcutaneously no more frequently than once every 2 weeks; OR
   - **B)** For patients who are 6 to < 12 years of age: Approve a dose of 150 mg per injection, administered subcutaneously no more frequently than once every 2 weeks; OR
   - **C)** For patients who are < 6 years of age: Approve a dose up to 150 mg per injection, administered subcutaneously no more frequently than once every 4 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Takhzyro is not recommended in the following situations:

1. **Concomitant Use with Other Hereditary Angioedema (HAE) Prophylactic Therapies.** Takhzyro has not been studied in combination with other prophylactic therapies for HAE, and combination therapy for long-term prophylactic use is not recommended. Patients may use other medications, including Cinryze® (C1 esterase inhibitor [human] intravenous infusion), for on-demand treatment of acute HAE attacks, and for short-term (procedural) prophylaxis.
   Note: Examples of other HAE prophylactic therapies include Cinryze (C1 esterase inhibitor [human] intravenous infusion), Haegarda (C1 esterase inhibitor [human] subcutaneous injection), and Orladeyo (berotralstat capsules).

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Takhzyro® subcutaneous injection [prescribing information]. Lexington, MA: Takeda; February 2023.
2. Busse PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 guidelines for the management of hereditary angioedema. *J Allergy Clin Immunol Pract*. 2021;9(1):132-150.e3.
3. 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(7):1961-1990.
4. Riedl MA, Staubach P, Farkas H, et al. Lanadelumab for prevention of attacks of non-histaminergic normal C1 inhibitor angioedema: results from the randomized, double-blind CASPIAN study and CASPIAN open-label extension. *Front. Immunol*. 2025 May 21;16:1502325.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	It was added to the Policy Statement that a person who has previously met initial therapy criteria for Takhzyro for the requested indication under the Coverage Review Department and is currently receiving Takhzyro, is only required to meet continuation of therapy criteria (i.e., patient is currently receiving Takhzyro). If past criteria have not been met under the Coverage Review Department and the patient is currently receiving Takhzyro, initial criteria must be met. In addition, the following changes were made: **Hereditary Angioedema (HAE) Due to C1 Inhibitor (C1-INH) Deficiency – Prophylaxis:** Deleted [Type I or Type II] from indication heading. Under criteria for "Patient is currently receiving Takhzyro prophylaxis", added a Note that patient has to meet initial therapy criteria and approval through the Coverage Review Department if they had previously received initial therapy approval through another entity. Also added the word "type" before II while referring to diagnosis of HAE types.	09/20/2023
Annual Revision	No criteria changes.	10/09/2024
Annual Revision	No criteria changes.	10/15/2025