Clinical Policy: Lanadelumab-fylo (Takhzyro)

Reference Number: ERX.SPA.293
Effective Date: 12.01.18
Last Review Date: 02.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Lanadelumab-fylo (Takhzyro™) is a human monoclonal antibody that inhibits the proteolytic activity of kallikrein to reduce the generation of bradykinin.

FDA Approved Indication(s)
Takhzyro is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients 12 years and older.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Takhzyro is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Hereditary Angioedema (must meet all)**:**

1. Diagnosis of HAE confirmed by one of the following (a or b):
   a. Low C4 level and low C1-INH antigenic or functional level (*see Appendix D)*;
   b. Normal C4 level and normal C1-INH level, and both of the following (i and ii):
      i. History of recurrent angioedema;
      ii. Family history of angioedema;
2. Prescribed by or in consultation with an allergist, hematologist, or immunologist;
3. Age ≥ 12 years;
4. Member meets one of the following (a, b, or c):
   a. Member experiences more than one severe event per month;
   b. Member is disabled more than five days per month;
   c. Member has a history of previous airway compromise;
5. Member is not using Takhzyro in combination with another FDA-approved product for long-term prophylaxis of HAE attacks (e.g., Cinryze®, Haegarda®, Orladeyo™);
6. Dose does not exceed 300 mg every 2 weeks.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Hereditary Angioedema (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by reduction in attacks from baseline;

3. Member is not using Takhzyro in combination with another FDA-approved product for long-term prophylaxis of HAE attacks (e.g., Cinryze, Haegarda, Orladeyo);
4. Request is for 300 mg every 4 weeks, unless documentation supports member is not well-controlled (e.g., attack(s) within the last 6 months);
5. If request is for a dose increase, new dose does not exceed 300 mg every 2 weeks.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CI-INH: C1 esterase inhibitor
C4: complement component 4
FDA: Food and Drug Administration
HAE: hereditary angioedema

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- Diagnosis of HAE:
  - There are two classifications of HAE: HAE with C1-INH deficiency (further broken down into Type I and Type II) and HAE of unknown origin (also known as Type III).
  - In both Type I (~85% of cases) and Type II (~15% of cases), C4 levels are low. C1-INH antigenic levels are low in Type I while C1-INH functional levels are low in Type II. Diagnosis of Type I and II can be confirmed with laboratory tests. Reference ranges for C4 and C1-INH levels can vary across laboratories (see below for examples); low values confirming diagnosis are those which are below the lower end of normal.

Laboratory Test & Reference Range	Mayo Clinic	Quest Diagnostics	Lab Corp
C4	14 – 40 mg/dL	16 – 47 mg/dL	13 – 44 mg/dL
C1-INH, antigenic	19 – 37 mg/dL	21 – 39 mg/dL	21 – 39 mg/dL
C1-INH, functional	Normal: > 67% Equivocal: 41 – 67% Abnormal: < 41%	Normal: ≥ 68% Equivocal: 41 – 67% Abnormal: ≤ 40%	Normal: > 67% Equivocal: 41 – 67% Abnormal: < 41%

  - Type III, on the other hand, presents with normal C4 and C1-INH levels. Some patients have an associated mutation in the FXII gene, while others have no identified genetic indicators. Type III is very rare (number of cases unknown), and there are no laboratory tests to confirm the diagnosis. Instead the diagnosis is clinical and supported by recurrent episodes of angioedema with a strong family history of angioedema.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
HAE attack prophylaxis	300 mg SC every 2 weeks A dosing interval of 300 mg every 4 weeks may be considered if the patient is well-controlled (e.g., attack free) for more than 6 months	300 mg SC every 2 weeks

VI. Product Availability

Injection: 300 mg/2 mL (150 mg/mL) solution in single dose vial

VII. References

1. Takhzyro Prescribing Information. Lexington, MA: Shire ViroPharma Incorporated; November 2018. Available at: https://www.takhzyro.com/. Accessed October 8, 2020.
2. Maurer M, Mager M, Ansotegui I, et al. The International WAO/ESSCI guideline for the management of hereditary angioedema – the 2017 revision and update. *World Allergy Organ J.* 2018; 11:5
3. Cicardi M, Aberer W, Banerji A, et al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. *Allergy.* 2014; 69(5): 602-616.
4. Zuraw B, Bernstein J, Lang D. 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.
5. Mayo Clinic Laboratories [internet database]. Rochester, Minnesota: Mayo Foundation for Medical Education and Research. Updated periodically. Accessed November 4, 2019.
6. Quest Diagnostics ® [internet database]. Updated periodically. Accessed November 4, 2019.
7. LabCorp [internet database]. Burlington, North Carolina: Laboratory Corporation of America. Updated periodically. Accessed November 4, 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	09.25.18	11.18
1Q 2019 annual review: removed rheumatologist as a prescriber specialist option; added requirement that member is not using requested product in combination with other approved products for the long-term prophylaxis of HAE attacks; references reviewed and updated.	11.19.18	02.19
1Q 2020 annual review: HAE lab reference range updated; revised dosing criteria for dose reduction if member is well-controlled per PI; references reviewed and updated.	11.04.19	02.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	10.08.20	02.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.