Lanadelumab-flyo (Takhzyro®)	Place of Service **Self-Administration** – *May be covered under the pharmacy benefit* **HCPCS: J0593** per 1 mg

Condition(s) listed in policy *(see criteria for details)*:

- Hereditary Angioedema (HAE), prophylaxis

AHFS therapeutic class: Complement inhibitor

Mechanism of action: Plasma kallikrein inhibitor (monoclonal antibody)

(1) Special Instructions and Pertinent Information

Takhzyro® is managed under the Outpatient Pharmacy Benefit. If the patient has a prescription drug benefit, please contact Blue Shield Pharmacy Services to obtain a prior authorization.

To submit a request to the medical benefit, please submit clinical information for prior authorization review, including medical rationale why the patient cannot self-administer Takhzyro® in the home.

(2) Prior Authorization/Medical Review is required for the following condition(s)

All requests for lanadelumab-flyo (Takhzyro®) must be sent for clinical review and receive authorization prior to drug administration or claim payment.

Hereditary Angioedema (HAE), prophylaxis

1. Chart documentation for the clinical diagnosis of Type I or Type II Hereditary Angioedema (HAE), including serum C4 and C1-INH (antigenic or functional level) that are below the limits of the laboratory's normal reference range, **AND**
2. Patient has a history of frequent or severe attacks (i.e., an HAE attack at least once per month, a history of serious attacks with laryngeal/ upper airway involvement or attacks resulting in impaired daily living), **AND**
3. Not used in the combination with other HAE therapies for the prophylaxis of HAE attacks (e.g., Berinert, Cinryze, Haegarda, Orladeyo)

Covered Doses
Up to 300 mg SC every 2 weeks

Coverage Period
Indefinite

ICD-10:
D84.1

(3) The following condition(s) DO NOT require Prior Authorization/Preservice

All requests for lanadelumab-flyo (Takhzyro®) must be sent for clinical review and receive authorization prior to drug administration or claim payment.

(4) This Medication is NOT medically necessary for the following condition(s):

Coverage for a Non-FDA approved indication, requires that criteria outlined in Health and Safety Code § 1367.21, including objective evidence of efficacy and safety are met for the proposed indication.

Please refer to the Provider Manual and User Guide for more information.

(5) Additional Information

How supplied:

300 mg/2 mL single-dose vial or prefilled syringe

HAE Diagnosis[1]:

- Suspicion of HAE-1/2 should prompt laboratory investigations to support a diagnosis
  - Measurements of serum/plasma levels of C1-INH function, C1- INH protein, and C4 are used to diagnose HAE-1/2
  - HAE-1: Both concentration and function of C1-INH are low (<50% of normal).
  - HAE-2:
    - C1-INH concentrations are normal or elevated
    - C1-INH function is low (<50% of normal)
  - C4 levels are usually low in HAE-1/2 patients, but the sensitivity and specificity of C4 as a marker for HAE are limited.
  - Sequencing of the SERPING1 gene can be supportive in the diagnostic workup of some HAE-1/2 patients (including prenatal diagnosis); however, bio-chemical C1-INH testing is effective and less expensive than genetic testing
- HAE with normal C1 inhibitor (HAE-nC1-INH)
  - The different forms of HAE share some clinical features and, possibly, therapeutic options with HAE-1/2
  - Can only be diagnosed by genetic testing, which is becoming increasingly available
  - Genetic testing should be performed and include testing for the 6 recognized HAE types:
    - HAE with mutation in the factor XII gene (HAE-FXII)
    - HAE with mutation in the angiopoietin-1 gene (HAE-ANGPT1)
    - HAE with mutation in the plasminogen gene (HAE-PLG)
    - HAE with mutation in the kininogen 1 gene (HAE-KNG1)
    - HAE with mutation in the myoferlin gene (HAE-MYOF)
    - HAE with mutation in the heparan sulfate 3-O- sulfotransferase 6 gene (HAE-HS3ST6).
  - Additional mutations are likely to be identified in the future and should be included in the genetic diagnostic workup for HAE.

Type of Angioedema	Laboratory Findings		
	C4 Level	C1 INH Level	Functional C1 INH Level
HAE – Type I	↓	↓	↓
HAE – Type II	↓	↔ or ↑	↓

Key: ↓ - decreased, ↑ - increased, ↔ - normal

(6) References

- AHFS®. Available by subscription at http://www.lexi.com
- 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. 2020;S2213-2198(20)30878-3. doi:10.1016/j.jaip.2020.08.046
- DrugDex®. Available by subscription at http://www.micromedexsolutions.com/home/dispatch

- 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.
- Takhzyro® (lanadelumab-flyo) [Prescribing information]. Lexington, MA: Dyax Corp; 2/2022.
- Zuraw BL, Bernstein JA, Lang DM, et al. A focused parameter update: Hereditary angioedema, acquired C1 inhibitor deficiency, and angiotensin-converting enzyme inhibitor–associated angioedema. J Allergy Clin Immunol. 2013 Jun;131(6):1491 – 3. DOI: https://doi.org/10.1016/j.jaci.2013.03.034

1. 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.

(7) Policy Update

Date of last review: 1Q2023
Date of next review: 1Q2024
Changes from previous policy version:

- No clinical change to policy following routine annual review.

BSC Drug Coverage Criteria to Determine Medical Necessity
Reviewed by P&T Committee