UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2024 P 2153-7
Program	Prior Authorization/Medical Necessity
Medication	Takhzyro® (lanadelumab-flyo)
P&T Approval Date	11/2018, 11/2019, 6/2020, 3/2021, 3/2022, 3/2023, 3/2024
Effective Date	6/1/2024

1. Background:
Takhzyro is a plasma kallikrein inhibitor (monoclonal antibody) indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 2 years and older.[1]

2. Coverage Criteria [a]:

A. Initial Authorization

1. **Takhzyro** will be approved based on **all** of the following criteria:

   a. Diagnosis of hereditary angioedema (HAE) as confirmed by **one** of the following:

      (1) C1 inhibitor (C1-INH) deficiency or dysfunction (Type I or II HAE) as documented by **one** of the following (per laboratory standard):

         (a) C1-INH antigenic level below the lower limit of normal
         (b) C1-INH functional level below the lower limit of normal

-OR-

      (2) HAE with normal C1 inhibitor levels and **one** of the following:

         (a) Confirmed presence of variant(s) in the gene(s) for factor XII, angiopoietin-1, plasminogen-1, kininogen-1, myoferlin, and heparan sulfate-glucosamine 3-O-sulfotransferase 6
         (b) Recurring angioedema attacks that are refractory to high-dose antihistamines with confirmed family history of angioedema
         (c) Recurring angioedema attacks that are refractory to high-dose antihistamines with unknown background de-novo mutation(s) (i.e., no family history) (HAE-unknown)

-AND-

   b. **Both** of the following:

      (1) For prophylaxis against HAE attacks

-AND-

      (2) Not used in combination with other products indicated for prophylaxis against HAE attacks (e.g., Cinryze, Haegarda, Orladeyo)

-AND-

c. **Both** of the following:

(1) Prescriber attests that patient has experienced attacks of a severity and/or frequency such that they would clinically benefit from prophylactic therapy with Takhzyro.

-AND-

(2) Documentation of baseline HAE attack rate is greater than or equal to one attack per 4 weeks.

-AND-

d. Prescribed by **one** of the following:

(1) Immunologist
(2) Allergist

Adult and pediatric patients 12 years of age and older: Authorization of Takhzyro 300mg given every 2 weeks will be issued for 8 months.
Pediatric patients 6 to less than 12 years of age: Authorization of Takhzyro 150 mg given every 2 weeks will be issued for 8 months.
Pediatric patients less than 6 years of age: Authorization of Takhzyro 150 mg given every 4 weeks will be issued for 12 months.

B. Reauthorization

1. **Takhzyro** will be approved based on **all** of the following criteria:

a. Documentation of positive clinical response while on Takhzyro therapy

-AND-

b. Reduction in the utilization of on-demand therapies used for acute attacks (e.g., Berinert, Ruconest, Firazyr, Kalbitor) as determined by claims information, while on Takhzyro therapy.

-AND-

c. Prescribed by **one** of the following:

(1) Immunologist
(2) Allergist

-AND-

d. **All** of the following:

(1) For prophylaxis against HAE attacks

-AND-

(2) Not used in combination with other products indicated for prophylaxis against HAE attacks (e.g., Cinryze, Haegarda, Orladeyo)

-AND-

e. **One** of the following:

(1) Patient is less than 6 years of age
(Pediatric patients less than 6 years of age: Authorization of Takhzyro 150 mg given every 4 weeks for 12 months).

-OR-

(2) Documentation of the number of acute HAE attacks in the previous 6 months, while on Takhzyro therapy, therefore:

(a) Patient experienced no (zero) acute HAE attacks in the previous 6 months:
(Adult and pediatric patients 12 years of age and older: Authorization of Takhzyro 300mg given every 4 weeks for 12 months)*
(Pediatric patients 6 to less than 12 years of age: Authorization of Takhzyro 150 mg given every 4 weeks for 12 months)*

(b) Patient experienced one or more acute HAE attacks in the previous 6 months:
(Adult and pediatric patients 12 years of age and older: Authorization of Takhzyro 300 mg given every 2 weeks for 6 months)
(Pediatric patients 6 to less than 12 years of age: Authorization of Takhzyro 150 mg given every 2 weeks for 6 months)

* Patients experiencing unexpected breakthrough HAE attacks once switched to every 4 week dosing will require additional review to allow for 2 weeks dosing.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Programs:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. Takhzyro [package insert]. Lexington, MA: Dyax Corp; February 2023.
2. Riedl MA, Bernstein JA, Craig T, et al. An open-label study to evaluate the long-term safety and efficacy of lanadelumab for prevention of attacks in hereditary angioedema: design of the HELP study extension. Clin Transl Allergy. 2017 Oct 6;7:36.
3. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema-The 2017 revision and update. Allergy. 2018 Jan 10.
4. Wu, E. Hereditary angioedema with normal C1 inhibitor. In: UpToDate, Saini, S (Ed), UpToDate, Waltham, MA, 2023.
5. Busse, P., Christiansen, S., Riedl, M., et. al. "US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema." *The Journal of Allergy and Clinical Immunology.* 2020 September 05.
6. 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. doi:10.1111/all.15214

Program	Prior Authorization/Medical Necessity - Takhzyro® (lanadelumab-flyo)
Change Control	
11/2018	New program.
11/2019	Annual review. Updated references.
6/2020	Align criteria with acute and prophylactic therapies.
3/2021	Added diagnosis criteria and aligned combination use language with prophylactic therapies. Updated references.
3/2022	Annual review. No changes.
3/2023	Annual review. Updated background with expanded FDA indication in patients aged 2 years and older. Updated criteria to reflect recommended dosage for pediatric patients less than 12 years of age. Updated references.
3/2024	Annual review. Update to diagnostic criteria for HAE with normal C1 inhibitor levels. Updated and simplified reauthorization criteria.