MEDICAL MUTUAL®

Drug Policy

Policy:	**201823**	**Initial Effective Date: 10/20/2018**
Code(s):	**HCPCS J0593**	**Annual Review Date: 09/21/2023**
SUBJECT:	**Takhzyro (Lanadelumab-flyo)**	**Last Revised Date: 09/21/2023**

☒Subject to Site of Care

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

Initial and renewal requests for the medication(s) listed in this policy are subject to site of care management. When billed under the medical benefit, administration of the medication will be restricted to a non-hospital facility-based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless the member meets the site of care exception criteria. To view the exception criteria and a list of medications subject to site of care management please click here.

OVERVIEW

Takhzyro is indicated as prophylaxis treatment for hereditary angioedema. Takhzyro is a fully human monoclonal antibody that binds plasma kallikrein and inhibits its proteolytic activity. Takhzyro is dosed every 2 to 4 weeks dependent on patient's control while taking Takhzyro. Takhzyro can be self-administered via the subcutaneous route.

POLICY STATEMENT

This policy involves the use of Takhzyro. Prior authorization is recommended for pharmacy and medical benefit coverage of Takhzyro. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, and Initial/Extended Approval** for the diagnosis provided. **Waste Management** applies for all covered conditions that are administered by a healthcare professional. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Takhzyro as well as the monitoring required for AEs and long-term efficacy, initial approval requires Takhzyro be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

The Site of Care Medical Necessity Criteria applies to initial therapy and reauthorizations under the medical benefit.

RECOMMENDED AUTHORIZATION CRITERIA

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

1. **Hereditary Angioedema [Type I or Type II]; Prophylaxis**
   Patient must meet the following criteria (a, b, c, d, e, f, AND g):
   - **a)** Patient is 2 years of age or older; AND
   - **b)** The patient has HAE as confirmed by the following criteria (i or ii):
     - i. Patient has low levels of functional C1-INH protein (below 50% of normal) at baseline, as defined by the laboratory reference values [documentation required]; OR
     - ii. Patient has lower than normal serum C4 levels (< 14 mg/dL) at baseline, as defined by the laboratory reference values AND lower than normal C1-INH levels (< 19.9 mg/dL) at baseline, as defined by the laboratory reference values [documentation required]; AND
   - **c)** The medication is prescribed by or in consultation with an allergist, immunologist, hematologist or a physician that specializes in the treatment of HAE or related disorders; AND
   - **d)** All other causes of acquired angioedema (e.g., medications, auto-immune diseases) have been excluded; AND
   - **e)** Patient has at least ONE of the following criteria (i, ii, or iii):
     - i. Patient has a history of one or more severe attack(s) per month (defined as an attack that significantly interrupts daily activities despite short-term treatment)
     - ii. Disabling symptoms for at least 5 days per month
     - iii. Laryngeal edema; AND
   - **f)** Patient has at least ONE of the following criteria (i, ii, or iii)
     - i. Patient must have history of self-limiting, non-inflammatory subcutaneous angioedema, without urticaria, which is recurrent and lasts >12 hours
     - ii. Self-limiting, recurrent abdominal pain without a clear organic cause lasting >6 hours
     - iii. A history of laryngeal edema; AND
   - **g)** Site of care medical necessity is met*.

2. **Patient has been started on Takhzyro.**
   Patient must meet the following criteria (a, b, c, d, e, f, g, h, i, AND j):
   - **a)** The patient has HAE as confirmed by the following criteria (i or ii):
     - i. Patient has low levels of functional C1-INH protein (below 50% of normal) at baseline, as defined by the laboratory reference values [documentation required]; OR
     - ii. Patient has lower than normal serum C4 levels (< 14 mg/dL) at baseline, as defined by the laboratory reference values AND lower than normal C1-INH levels (< 19.9 mg/dL) at baseline, as defined by the laboratory reference values [documentation required]; AND
   - **b)** The medication is prescribed by or in consultation with an allergist, immunologist, hematologist or a physician that specializes in the treatment of HAE or related disorders; AND
   - **c)** All other causes of acquired angioedema (e.g., medications, auto-immune diseases) have been excluded; AND
   - **d)** Patient has at least ONE of the following criteria (i, ii, or iii):
     - i. Patient has a history of one or more severe attack(s) per month (defined as an attack that significantly interrupts daily activities despite short-term treatment)
     - ii. Disabling symptoms for at least 5 days per month

iii. Laryngeal edema; AND

e) Patient has at least ONE of the following criteria (i, ii, or iii)
   i. Patient must have history of self-limiting, non-inflammatory subcutaneous angioedema, without urticaria , which is recurrent and lasts >12 hours
   ii. Self-limiting, recurrent abdominal pain without a clear organic cause lasting >6 hours
   iii. A history of laryngeal edema

f) Patient has at least 1 annual assessment by an HAE specialist if it has been one year since initial approval; AND

g) According to the prescriber, the patient has had a favorable clinical response (e.g., decrease in number of HAE acute attack frequency, decrease in HAE attack severity, decrease in duration of HAE attacks) since initiating Takhzyro prophylactic therapy compared with baseline (i.e., prior to initiating prophylactic therapy); AND

h) 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.

i) If patient is dosing every 2 weeks and has been attack free for 6 months, dosing will be reduced to every 4 weeks; AND

j) Site of care medical necessity is met*.

Dosing in Takhzyro. *Dosing must meet the following (medical benefit only):*

Indication	Dose
Prophylaxis of Hereditary Angioedema (HAE) attacks	Adult and Pediatric Patients ≥12 Years of Age • Administer 300 mg subcutaneously every 2 weeks. • A dosing interval of 300 mg every 4 weeks is also effective and may be considered if the patient is well-controlled (e.g., attack free) for more than 6 months Pediatric Patients 6 to <12 Years of Age • Administer 150 mg subcutaneously every 2 weeks. • A dosing interval of 150 mg every 4 weeks is also effective and may be considered if the patient is well-controlled (e.g., attack free) for more than 6 months Pediatric Patients 2 to <6 Years of Age • Administer 150 mg subcutaneously every 4 weeks. **NOTE: • Adult and pediatric patients ≥12 years of age: Takhzyro may be administered by the patient or caregiver after being instructed trained by a healthcare professional. • Pediatric patients 2 to <12 years of age: Takhzyro should be administered by a healthcare provider or caregiver.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 180 days (6 months)
B) *Extended Approval:* 365 days (1 year)

Waste Management for All Indications.
Takhzyro:

• 150 mg/1 mL (150 mg/mL) solution in a single-dose prefilled syringe.

• 300 mg/2 mL (150 mg/mL) solution in a single-dose prefilled syringe.

• 300 mg/2 mL (150 mg/mL) solution in a single-dose vial.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Takhzyro has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Concomitant Use with Other HAE Prophylactic Therapies (e.g., Cinryze, or Haegarda).** 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, for on-demand treatment of acute HAE attacks, and for short-term (procedural) prophylaxis.

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

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Takhzyro ® [prescribing information]. Lexington, MA:Dyax Corp (Shire). February 2023.
2. Craig TJ, Schneider LC, MacGinnitie AJ.Plasma-derived C1-INH for managing hereditary angioedema in pediatric patients: A systematic review. Pediatr Allergy Immunol. 2015 Sep;26(6):537-44.
3. Agostoni, Angelo, et al.“"Hereditary and acquired angioedema: problems and progress: proceedings of the third C1 esterase inhibitor deficiency workshop and beyond”" Journal of Allergy and Clinical Immunology 114.3 (2004): S51-S131.
4. Weiler CR, van Dellen RG. Genetic test indications and interpretations in patients with hereditary angioedema. Mayo Clin Proc. 2006 Jul;81(7):958-72

5. 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.
6. Prada AE, Zahedi K, Davis AE 3rd. Regulation of C1 inhibitor synthesis. Immunobiology 1998; 199:377.
7. Cladribine. In: DRUGDEX [online database]. Truven Health Analytics. Greenwood Village, CO. Last updated 09 May 2019. Accessed 12 September 2019.
8. Busse PJ, Christiansen SC, Riedl MA, Banerji A, Bernstein JA, Castaldo AJ, Craig T, Davis-Lorton M, Frank MM, Li HH, Lumry WR, Zuraw BL. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. J Allergy Clin Immunol Pract. 2021 Jan;9(1):132-150.e3. doi: 10.1016/j.jaip.2020.08.046. Epub 2020 Sep 6.

Prior approval is required for HCPCS Codes J0593

†When *injection, lanadelumab-flyo* (J0593) is determined to be Takhzyro