MEDICAL MUTUAL®

Drug Policy

Policy:	**201823**	**Initial Effective Date: 10/20/2018**
Code(s):	**HCPCS J3590**	**Annual Review Date: 09/20/2018**
SUBJECT:	**Takhzyro (Lanadelumab-flyo)**	**Last Revised Date: 09/20/2018**

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

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

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

1. <u>Hereditary Angioedema [Type I or Type II]; Prophylaxis</u>
Patient must meet the following criteria (a, b, c, d, e, f, g, h, and i)

a) Patient is 12 years of age or older; AND

b) The patient has HAE as confirmed by following criteria (i or ii) [documentation required]:
- i. Patient has low levels of functional C1-INH protein (below 67% or as defined by the laboratory reference values); OR
- ii. Patient has lower than normal serum C4 levels (< 14 mg/dL or as defined by the laboratory reference values) AND lower than normal C1-INH level (< 19.9 mg/dL or as defined by the laboratory reference values); 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) Failure of, intolerance to or unable to receive treatment with attenuated androgens (e.g, danazol, stanozolol); AND
e) All other causes of acquired angioedema (e.g., medications, auto-immune diseases) have been excluded; AND
f) 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

g) 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 uticaria, 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

h) Takhzyro is not used in combination with each other or other approved treatments for prevention of HAE attacks, such as but not limited to Haegarda, Berinert, or Cinryze; AND
i) Site of care medical necessity is met*.

2. Patient has been started on Takhzyro. Approve for, an indication or condition addressed as an approval in the Recommended Authorization Criteria (FDA-Approved Indications), continuation of therapy if the patient meets the following criteria (a, b, c, d, e, f, g, h, i and j)

a) The patient has HAE as confirmed by following criteria (i or ii) [documentation required]:
- i. Patient has low levels of functional C1-INH protein (below 67% or as defined by the laboratory reference values); OR
- ii. Patient has lower than normal serum C4 levels (< 14 mg/dL or as defined by the laboratory reference values) AND lower than normal C1-INH level (< 19.9 mg/dL or as defined by the laboratory reference values); 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) Failure of, intolerance to or unable to receive treatment with attenuated androgens (e.g, danazol, stanozolol); 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 uticaria , 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

g) Takhzyro is not used in combination with each other or other approved treatments for prevention of HAE attacks, such as but not limited to Haegarda, Berinert, or Cinryze; AND
h) Patient has at least 1 annual assessment by an HAE specialist if it has been one year since initial approval; AND
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):*

300 mg every 2 weeks initially and may be reduced to dosing every 4 weeks in patients well-controlled (eg, attack free for >6 months)

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

Waste Management for All Indications.
Solution, Subcutaneous [preservative free]:
Takhzyro: 300 mg/2 mL (2 mL) [contains polysorbate 80]

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. 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.

MEDICAL MUTUAL®

Drug Policy

REFERENCES

- Takhzyro ® [prescribing information]. Lexington, MA:Dyax Corp (Shire). September 2018.
- Craig T, Pursun EA, Bork K, et al. WAO guideline for the management of hereditary angioedema. WAO Journal. 2012;5:182-199.
- 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.
- 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.
- Weiler CR, van Dellen RG. Genetic test indications and interpretations in patients with hereditary angioedema. Mayo Clin Proc. 2006 Jul;81(7):958-72
- Maurer M, Magerl M, Ansotegui I, et al. The International WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update. World Allergy Organization Journal. 2018;11(5).

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

*MMO Site of Care Medical Necessity Criteria:

- Medications in this policy will be administered in a non-hospital facility based location (i.e., home infusion provider, provider’s office, free-standing ambulatory infusion center) unless *at least one* of the following are met[†]:

    1. Age less than 21 years; or
    2. Clinically unstable based upon documented medical history (e.g., patient is hemodynamically unstable); or
    3. History of a severe adverse event from previous administration of the prescribed medication; or
    4. Requested medication is being administered as follows:
        - part of a chemotherapy regimen (e.g., anti-neoplastic agent, colony stimulating factor, erythropoiesis-stimulating agent, anti-emetic) for treatment of cancer; or
        - administered with dialysis; or
    5. Physical or cognitive impairment and caregiver is not available to assist with safe administration of prescribed medication in the home; or
    6. No doses will be allowed in a hospital facility based location; or
    7. Experiencing adverse events that are not managed by premedication or resources available at a non-hospital facility based location.

[†]This criterion does not apply to Medicare or Medicare Advantage members.

MEDICAL MUTUAL®

Drug Policy

Prior approval is required for HCPCS Codes J3590

†When *unclassified biologics* (J3590) is determined to be Takhzyro

HCPCS Code(s):	
J3590	Unclassified biologics