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5.85.032

Section:	Prescription Drugs	**Effective Date:**	January 1, 2026
Subsection:	Hematological Agents	**Original Policy Date:**	September 14, 2018
Subject:	Takhzyro	**Page:**	1 of 5

Last Review Date: December 12, 2025

Takhzyro

Description

Takhzyro (lanadelumab-flyo)

Background

Takhzyro (lanadelumab-flyo) is a fully human monoclonal antibody that binds plasma kallikrein and inhibits its proteolytic activity. Plasma kallikrein is a protease that cleaves high-molecular-weight-kininogen (HMWK) to generate cleaved HMWK (cHMWK) and bradykinin, a potent vasodilator that increases vascular permeability resulting in swelling and pain associated with hereditary angioedema (HAE). In patients with HAE due to C1-inhibitor deficiency or dysfunction, normal regulation of plasma kallikrein activity is not present, which leads to uncontrolled increases in plasma kallikrein activity and results in angioedema attacks. Takhzyro decreases plasma kallikrein activity to control excess bradykinin generation in patients with HAE (1).

Regulatory Status

FDA-approved indication: 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).

Hypersensitivity reactions may occur. In the case of a severe hypersensitivity reaction, Takhzyro should be discontinued, and appropriate treatment should be instituted (1).

The safety and effectiveness of Takhzyro in pediatric patients less than 2 years of age have not been established (1).

Related policies
Berinert, Cinryze, Haegarda, Icatibant, Kalbitor, Orladeyo, Ruconest

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Takhzyro may be considered **medically necessary** if the conditions indicated below are met.

Takhzyro may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 2 years of age and older

Diagnosis

Patient must have the following:

1. Hereditary Angioedema (HAE) with **ONE** of the following:
    a. Patient has a C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing **AND ALL** of the following:
        i. C4 level below the lower limit of normal as defined by the laboratory performing the test
        ii. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test **OR** normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)
    b. Patient has normal C1 inhibitor as confirmed by laboratory testing **AND ONE** of the following:
        i. F12, angiopoietin-1, plasminogen, or kininogen-1 (KNG1) gene mutation as confirmed by genetic testing
        ii. Documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month

AND ALL of the following:

1. Routine prevention of hereditary angioedema attacks
2. **NO** dual therapy with other agents for the prevention of hereditary angioedema attacks (e.g., Cinryze, Haegarda, Orladeyo)

Prior – Approval *Renewal* Requirements

Age 2 years of age and older

Diagnosis

Patient must have the following:

Hereditary Angioedema (HAE)

AND ALL of the following:

1. Routine prevention of hereditary angioedema attacks
2. Patient has experienced a significant reduction in frequency of hereditary angioedema attacks since starting treatment
3. **NO** dual therapy with other agents for the prevention of hereditary angioedema attacks (e.g., Cinryze, Haegarda, Orladeyo)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Takhzyro (lanadelumab-flyo) is a fully human monoclonal antibody that binds plasma kallikrein and inhibits its proteolytic activity. Plasma kallikrein is a protease that cleaves high-molecular-weight-kininogen (HMWK) to generate cleaved HMWK (cHMWK) and bradykinin, a potent

vasodilator that increases vascular permeability resulting in swelling and pain associated with hereditary angioedema (HAE). In patients with HAE due to C1-inhibitor deficiency or dysfunction, normal regulation of plasma kallikrein activity is not present, which leads to uncontrolled increases in plasma kallikrein activity and results in angioedema attacks. Takhzyro decreases plasma kallikrein activity to control excess bradykinin generation in patients with HAE. The safety and effectiveness of Takhzyro in pediatric patients less than 2 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Takhzyro while maintaining optimal therapeutic outcomes.

References

1. Takhzyro [package insert]. Cambridge, MA: Takeda Pharmaceuticals USA, Inc.; January 2025.

Policy History

Date	Action
September 2018	Addition to PA
November 2018	Annual review. Removal of requirement to try and fail tranexamic acid and reworded danazol or androgen trial requirement per SME
September 2019	Annual review and reference update
September 2020	Annual review
March 2021	Annual editorial review
April 2021	Added initiation requirements including C1 inhibitor testing, C4 testing, C1-INH testing, gene mutation testing, or documented family history of refractory angioedema and continuation requirement for significant reduction in frequency of HAE attacks since starting therapy per FEP
June 2021	Annual review
December 2022	Annual review and reference update. Changed policy number to 5.85.032
February 2023	Per PI update, changed age requirement from 12 and older to 2 and older
June 2023	Annual review
December 2023	Annual review
December 2024	Annual review
December 2025	Annual review and reference update. Per SME, removed initiation requirement to t/f a short term course of an androgen

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 12, 2025 and is effective on January 1, 2026.