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Section:	Prescription Drugs	Effective Date:	April 1, 2021
Subsection:	Hematological Agents	Original Policy Date:	September 14, 2018
Subject:	Takhzyro	Page:	1 of 4

Last Review Date: March 12, 2021

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 patients 12 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 12 years of age have not been established (1).

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Related policies

Berinert, Cinryze, Firazyf, Haegarda, 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** in patients 12 years of age and older for the routine prevention of hereditary angioedema (HAE) attacks and if the conditions indicated below are met.

Takhzyro may be considered **investigational** in patients less than 12 years of age and for all other indications.

Prior-Approval Requirements

Age 12 years of age and older

Diagnosis

The patient must have the following:

Hereditary Angioedema (HAE)

AND the following:

1. Routine prevention of angioedema attacks
2. **NO** dual therapy with other agents for the prevention of hereditary angioedema attacks
3. Inadequate treatment response or intolerance to a short-term course (5-days or less) of an androgen such as danazol, or a contraindication to one such as:
 - a. Undiagnosed abnormal genital bleeding
 - b. Markedly impaired hepatic, renal, or cardiac function
 - c. Pregnancy (member is currently pregnant or may become pregnant)
 - d. Breast feeding
 - e. Porphyria
 - f. Androgen-dependent tumor
 - g. Active thrombosis or history of thromboembolic disease

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h. Prepubertal child

Prior – Approval *Renewal* Requirements

Age 12 years of age and older

Diagnosis

The patient must have the following:

Hereditary Angioedema (HAE)

AND the following:

1. Routine prevention of angioedema attacks
2. **NO** dual therapy with other agents for the prevention of hereditary angioedema attacks

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

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decreases plasma kallikrein activity to control excess bradykinin generation in patients with HAE. The safety and effectiveness of Takhzyro in pediatric patients less than 12 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]. Lexington, MA: Dyax Corp.; November 2018.

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

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.