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Section:	Prescription Drugs	**Effective Date:**	April 1, 2021
Subsection:	Hematological Agents	**Original Policy Date:**	January 22, 2021
Subject:	Orladeyo	**Page:**	1 of 4

Last Review Date: March 12, 2021

Orladeyo

Description

Orladeyo (berotralstat)

Background

Orladeyo (berotralstat) is a plasma kallikrein inhibitor 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. Orladeyo decreases plasma kallikrein activity to control excess bradykinin generation in patients with HAE (1).

Regulatory Status

FDA-approved indication: Orladeyo is a plasma kallikrein inhibitor indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adults and pediatric patients 12 years and older (1).

Limitations of use: Orladeyo should not be used for treatment of acute HAE attacks (1).

Additional doses or doses of Orladeyo higher than 150 mg once daily are not recommended. An increase in QT was observed at dosages higher than the recommended 150 mg once daily dosage and was concentration dependent (1).

The safety and effectiveness of Orladeyo in pediatric patients less than 12 years of age have not been established (1).

Related policies
Berinert, Cinryze, Firazyr, Haegarda, Kalbitor, Ruconest, Takhzyro

Policy

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

Orladeyo 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.

Orladeyo is 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 ALL of the following:

1. Used for the 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
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. Used for the 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

Quantity 84 capsules per 84 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Orladeyo (berotralstat) is a plasma kallikrein inhibitor 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. Orladeyo decreases plasma kallikrein activity to control excess bradykinin generation in patients with HAE (1).

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

References

1. Orladeyo [package insert]. Durham, NC: BioCryst Pharmaceuticals, Inc.; December 2020.

Policy History

Date	Action
January 2021	Addition to PA
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.