

**ORLADEYO
(berotralstat)****RATIONALE FOR INCLUSION IN PA PROGRAM****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).

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



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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.; November 2023.