VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Hereditary Angioedema – Orladeyo Prior Authorization Policy
- Orladeyo® (berotralstat capsules – Biocryst)

REVIEW DATE: 01/04/2023

OVERVIEW

Orladeyo, an inhibitor of plasma kallikrein, is indicated for **prophylaxis to prevent attacks of hereditary angioedema (HAE)** in patients ≥ 12 years of age.[1]

Guidelines

According to US HAE Association Medical Advisory Board Guidelines (2020), when HAE is suspected based on clinical presentation, appropriate testing includes measurement of the serum C4 level, C1 esterase inhibitor (C1-INH) antigenic level, and C1-INH functional level.[2] Low C4 plus low C1-INH antigenic or functional level is consistent with a diagnosis of HAE types I/II. The decision on when to use long-term prophylaxis cannot be made on rigid criteria but should reflect the needs of the individual patient. First-line medications for HAE I/II include intravenous C1-INH, Haegarda® (C1-INH [human] subcutaneous injection), or Takhzyro® (lanadelumab-flyo subcutaneous injection). The guideline was written prior to approval of Orladeyo.

According to World Allergy Organization/European Academy of Allergy and Clinical Immunology guidelines (2021), it is recommended to evaluate for long-term prophylaxis at every visit, taking disease activity, burden, and control as well as patient preference into consideration.[3] The following therapies are supported as first-line options for long-term prophylaxis: plasma-derived C1-INH (87% agreement), Takhzyro (89% agreement), and Orladeyo (81% agreement). With regard to plasma-derived C1-INH, it is noted that Haegarda provided very good and dose-dependent preventative effects on the occurrence of HAE attacks; the subcutaneous route may provide more convenient administration and maintain improved steady-state plasma concentrations compared with the intravenous route. Of note, androgens are not recommended in the first-line setting for long-term prophylaxis. Recommendations are not made regarding long-term prophylaxis in HAE with normal C1-INH.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Orladeyo. Because of the specialized skills required for evaluation and diagnosis of patients with this condition, approval requires Orladeyo to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below.

Documentation: Documentation will be required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory records, and prescription claims records.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indication

1. **Hereditary Angioedema (HAE) Due to C1 Inhibitor (C1-INH) Deficiency [Type I or Type II] – Prophylaxis.** Approve Orladeyo for 1 year if the patient meets one the following criteria (A or B):
   - **A)** Initial therapy. Approve if the patient meets all of the following criteria (i, ii, and iii):
     - **i.** Patient is ≥ 12 years of age; AND
     - **ii.** Patient has HAE type I or type II as confirmed by the following diagnostic criteria (a and b):
       Note: A diagnosis of HAE with normal C1-INH (also referred to as HAE type III) does NOT satisfy this requirement.
       - **a)** Patient has low levels of functional C1-INH protein (< 50% of normal) at baseline, as defined by the laboratory reference values **[documentation required]**; AND
       - **b)** Patient has lower than normal serum C4 levels at baseline, as defined by the laboratory reference values **[documentation required]**; AND
     - **iii.** The medication is prescribed by or in consultation with an allergist/immunologist or a physician who specializes in the treatment of HAE or related disorders.
   - **B)** Patient is currently receiving Orladeyo. Approve if the patient meets all of the following criteria (i, ii, iii, and iv):
     - **i.** Patient is ≥ 12 years of age; AND
     - **ii.** Patient has a diagnosis of HAE type I or II **[documentation required]**; AND
       Note: A diagnosis of HAE with normal C1-INH (also referred to as HAE type III) does NOT satisfy this requirement.
     - **iii.** According to the prescriber, the patient has had a favorable clinical response since initiating Orladeyo prophylactic therapy compared with baseline (i.e., prior to initiating prophylactic therapy); AND
       Note: Examples of favorable clinical response include decrease in HAE acute attack frequency, decrease in HAE attack severity, or decrease in duration of HAE attacks.
     - **iv.** The medication is prescribed by or in consultation with an allergist/immunologist or a physician who specializes in the treatment of HAE or related disorders.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Orladeyo is not recommended in the following situations:

1. **Concomitant Use with Other Hereditary Angioedema (HAE) Prophylactic Therapies.** Note: Examples of other HAE prophylactic therapies include Cinryze (C1 esterase inhibitor [human] intravenous infusion), Haegarda (C1 esterase inhibitor [human] subcutaneous injection), and Takhzyro (lanadelumab-flyo subcutaneous injection).
   Orladeyo has not been studied in combination with other prophylactic therapies for HAE, and combination therapy for long-term prophylactic use is not recommended. Patients may use other medications, including Cinryze, for on-demand treatment of acute HAE attacks, and for short-term (procedural) prophylaxis.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Orladeyo® capsules [prescribing information]. Durham, NC: Biocryst; December 2020.
2. Busse PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 guidelines for the management of hereditary angioedema. *J Allergy Clin Immunol Pract*. 2021;9(1):132-150.e3.
3. Maurer M, Magerl M, Betschel S, et al. The international WAO/EAACI guideline for the management of hereditary angioedema: the 2021 revision and update. *Allergy*. 2022;77(7):1961-1990.