Effective date: 5/1/2021
Reviewed: 2/2021, 2/2022, 3/2023, 3/2024
Scope: Medicaid

SPECIALTY GUIDELINE MANAGEMENT

ORLADEYO (berotralstat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Orladeyo is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adults and pediatric patients 12 years and older.

Limitations of Use
Orladeyo should not be used for treatment of acute HAE attacks

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. For initial authorization, the following should be documented:
   1. C1 inhibitor functional and antigenic protein levels
   2. F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) gene mutation testing, if applicable
   3. Chart notes confirming family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine therapy, if applicable
B. For continuation of therapy, chart notes demonstrating a reduction in frequency of attacks

III. CRITERIA FOR INITIAL APPROVAL

Authorization for 6 months may be granted for prevention of hereditary angioedema attacks in members 12 years of age or older when the following criteria is met:
   A. Medication is prescribed by, or in consultation with allergist/immunologist or a physician who specializes in the treatment of HAE or related disorders.
   B. Patient has documented diagnosis of HAE type I or type II and meets one of the following:
      1. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets one of the following criteria:
         i. C1 inhibitor (C1-INH) antigenic level is below the lower limit of normal as defined by the laboratory performing the test; OR

ii. 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); OR

2. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   a) Member has an F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1) gene, heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) mutation as confirmed by genetic testing, OR
   b) Member has a family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

C. Dose does not exceed one Orladeyo 150mg capsule a day
D. Will not be used in combination with Cinryze, Takhzyro or Haegarda

IV. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continuation of therapy when all of the following criteria are met:

A. Member meets the criteria for initial approval.
B. Patient has had a favorable clinical response (i.e., decrease in HAE acute attack frequency, decrease in HAE attack severity, or decrease in duration of HAE attacks) since initiating Orladeyo prophylactic therapy compared with baseline (i.e., prior to initiating prophylactic therapy).

V. QUANTITY LIMIT

Orladeyo 110mg & 150mg: 1 capsule per day

VI. REFERENCES

1. Orladeyo [package insert]. Durham, NC: BioCryst Pharmaceuticals, Inc.; November 2023.Accessed February 2024.
2. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2021 revision and update. *Allergy*. 2022 Jan 10. doi: 10.1111/all. 15214. Online ahead of print.
3. Henao MP, Kraschnewski J, Kelbel T, Craig T. Diagnosis and screening of patients with hereditary angioedema in primary care. *Therapeutics and Clin Risk Management*. 2016; 12: 701-711.
4. Zuraw B, Lumry WR, Johnston DT, et al. Oral once-daily berotralstat for the prevention of hereditary angioedema attacks: A randomized, double-blind, placebo-controlled phase 3 trial. *J Allergy Clin Immunol*. 2020;S0091-6749(20)31484-6.
5. 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: In Practice*. 2021 Jan;9(1):132-150.e3.
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7. Kanani, A., Schellenberg, R. & Warrington, R. Urticaria and angioedema. *All Asth Clin Immun* 7, S9 (2011), Table 2.