Orladeyo (berotralstat)

Override(s)	Approval Duration
Prior Authorization Quantity Limit	Initial Authorization: 6 months Continuation Authorization: 1 year

Medications	Quantity Limit
Orladeyo (berotralstat) capsules	May be subject to quantity limit

APPROVAL CRITERIA

Initial requests for Orladeyo (berotralstat) may be approved if the following criteria are met:

I. Individual has a diagnosis of hereditary angioedema; **AND**
II. Individual is using for prophylaxis against acute attacks of hereditary angioedema for either of the following:
    A. Short-term prophylaxis prior to surgery, dental procedures or intubation; **OR**
    B. Long-term prophylaxis to minimize the frequency and/or severity of recurrent attacks;

AND

III. Individual is 12 years of age or older;

AND

IV. Documentation is provided that diagnosis is confirmed by a C4 level below the lower limit of normal as defined by laboratory test AND any of the following:
    A. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by lab test with documentation provided; **OR**
    B. C1-INH functional level below the lower limit of normal as defined by lab test with documentation provided; **OR**
    C. Presence of a known HAE-causing C1-INH mutation;

AND

V. Individual has a history of moderate or severe attacks such as airway swelling, severe abdominal pain, facial swelling, nausea and vomiting, or painful facial distortion.

Requests for Orladeyo may be approved for continuation of use in prophylactic care if the following criteria are met:

I. Confirmation of a positive clinical response defined as a clinically significant reduction in the number and/or frequency of HAE attacks occurred.

Requests for Orladeyo (berotralstat) may not be approved for the following:

I. In combination with other HAE agents for prophylaxis of acute attacks (including but not limited to Cinryze, Haegarda, or Takhzyro)
II. For the treatment of acute HAE attacks; **OR**
III. May not be approved when the above criteria are not met and for all other indications.

Key References:

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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;9:132-50.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2022. URL: http://www.clinicalpharmacology.com. Updated periodically.
4. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: July 9, 2022.
5. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
6. Efficacy ans Safety Study of DX-2930 to Prevent Acute Angioedema Attacks in Patients with Type I and Type II HAE. NCT02586805 (HELP Study). Available at https://www.clinicaltrials.gov/ct2/show/study/NCT02586805.
7. Haegarda [Package Insert]. Marburg, Germany. CSL Behring, GmbH.; 2017.
8. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.
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10. Riedl MA, Bernstein JA, Craig T, et al. An open-label study to evaluate the long-term safety and efficacy of lanadelumab for prevention of attacks in hereditary angioedema: design of the HELP study extension. *Clin Transl Allergy*. 2017;7:36.
11. Riedl MA. Creating a Comprehensive Treatment Plan for Hereditary Angioedema. *Immunol Allergy Clin N Am*. 2013; 33 (4): 471-485. doi:10.1016/j.iac.2013.07.003.
12. Takhzyro [Package Insert]. Lexington, MA. Dyax Corp, Shire; 2018.
13. Zuraw B, 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.
14. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 Recommendations for the Management of Hereditary Angioedema Due to C1 Inhibitor Deficiency. *J Allergy Clin Immunol: In Practice*. 2013; 1:458-67. doi:10.1016/j.jaip.2013.07.002.
15. Zuraw BL, Bernstein JA, Lang DM, et al. A focused parameter update: Hereditary angioedema, acquired C1 inhibitor deficiency, and angiotensin-converting enzyme inhibitor–associated angioedema. *J Allergy Clin Immunol*. 2013; 131(6):1491-1493.e1-e25. Available from: http://www.jacionline.org/article/S0091-6749(13)00523-X/pdf.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.