

Orladeyo® (berotralstat) (Oral)

Document Number: IH-0582

Last Review Date: 10/03/2022

Date of Origin: 01/05/2021

Dates Reviewed: 01/2021, 10/2021, 10/2022

I. Length of Authorization

Coverage will be provided for 6 months and may be renewed annually thereafter.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Orladeyo 110 mg capsules: 1 capsule per day
- Orladeyo 150 mg capsules: 1 capsule per day

B. Max Units (per dose and over time) [HCPCS Unit]:

- 150 mg per day

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

- Patient has tried and failed, is intolerant, or has a contraindication to lanadelumab (Takhzyro™); **AND**
- Patient is at least 12 years of age; **AND**

Universal Criteria ^{1,13,18}

- Must be prescribed by, or in consultation with, a specialist in: allergy, immunology, hematology, pulmonology, or medical genetics; **AND**
- Not used in combination with other prophylactic therapies targeting C1 inhibitor (i.e., Cinryze, Haegarda, etc.) or kallikrein (i.e., Takhzyro, etc.); **AND**
- Confirmation the patient is avoiding the following possible triggers for HAE attacks:
 - Estrogen-containing oral contraceptive agents **AND** hormone replacement therapy; **AND**
 - Antihypertensive agents containing ACE inhibitors; **AND**
 - Dipeptidyl peptidase IV (DPP-IV) inhibitors (e.g., sitagliptin); **AND**
 - Neprilysin inhibitors (e.g., sacubitril); **AND**
- Patient will avoid concomitant therapy with all of the following:

- Coadministration with P-gp or BCRP-inhibitors (e.g., cyclosporine, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**
- Coadministration with P-gp inducers (e.g., rifampin, St. John’s Wort, etc.); **AND**

Prophylaxis to prevent Hereditary Angioedema (HAE) attacks † Φ 1,13,18,19,20

- Patient has a history of one of the following criteria for long-term HAE prophylaxis:
 - History of two (2) or more severe HAE attacks per month (i.e., airway swelling, debilitating cutaneous or gastrointestinal episodes)
 - Patient is disabled more than 5 days per month by HAE
 - History of at least one laryngeal attack caused by HAE; **AND**
- Treatment of patient with “on-demand” therapy (i.e., Kalbitor, Firazyr, Ruconest, or Berinert) did not provide satisfactory control or access to “on-demand therapy” is limited; **AND**
- Patient has one of the following clinical presentations consistent with a HAE subtype, which must be confirmed by repeat blood testing (treatment for acute attack should not be delayed for confirmatory testing):

| HAE I (C1-Inhibitor deficiency) 13,18,19,20 |
|--|
| <ul style="list-style-type: none"> • Low C1 inhibitor (C1-INH) antigenic level (C1-INH antigenic level below the lower limit of normal as defined by the laboratory performing the test); AND • Low C4 level (C4 below the lower limit of normal as defined by the laboratory performing the test); AND • Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test); AND <ul style="list-style-type: none"> ○ Patient has a family history of HAE; OR ○ Acquired angioedema has been ruled out (i.e., patient onset of symptoms occur prior to 30 years old, normal C1q levels, patient does not have underlying disease such as lymphoma or benign monoclonal gammopathy [MGUS], etc.) |
| HAE II (C1-Inhibitor dysfunction) 18,20 |
| <ul style="list-style-type: none"> • Normal to elevated C1-INH antigenic level; AND • Low C4 level (C4 below the lower limit of normal as defined by the laboratory performing the test); AND • Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test) |
| HAE with normal C1INH (formerly known as HAE III) 18,19,20 |
| <ul style="list-style-type: none"> • Prophylaxis for HAE with normal C1-INH is not routinely recommended and will be evaluated on a case-by-case basis <ul style="list-style-type: none"> ○ Prior to consideration of long-term prophylaxis, the patient must have demonstrated: <ul style="list-style-type: none"> ▪ An inadequate response or intolerance to an adequate trial of prophylactic therapy with an antifibrinolytic agent (e.g., tranexamic acid (TXA) or aminocaproic acid) and/or a 17α-alkylated androgen (e.g., danazol) unless contraindicated. Female patients may derive additional benefit from progestins^{15,16,17}; AND ▪ Response to therapy from an agent indicated for the treatment of acute attacks (i.e., C1 esterase inhibitor, icatibant, ecallantide, etc.) |

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Ⓢ Orphan Drug

IV. Renewal Criteria ^{1,13,18,19,20}

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: severe QT prolongation, etc.; **AND**
- Significant improvement in severity, frequency, and/or duration of attacks have been achieved and sustained

V. Dosage/Administration ¹

| Indication | Dose |
|--|---|
| Prophylaxis of Hereditary Angioedema (HAE) attacks | Administer 150 mg orally once daily, with food.. – <i>Refer to the package insert for dosing in patients with hepatic impairment, when used concomitantly with P-gp or BCRP inhibitors, or in patients with persistent GI reactions.</i> |

VI. Billing Code/Availability Information

HCPCS Code:

- J8499 – Prescription drug, oral, non-chemotherapeutic, nos

NDC:

- Orladeyo 110 mg oral capsules: 72769-0102-xx
- Orladeyo 150 mg oral capsules: 72769-0101-xx

VII. References

1. Orladeyo [package insert]. Durham, NC; BioCryst Pharmaceuticals.; March 2022. Accessed August 2022.
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Appendix 1 – Covered Diagnosis Codes

| ICD-10 | ICD-10 Description |
|--------|----------------------------------|
| D84.1 | Defects in the complement system |

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Articles (LCAs), and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at:

<https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

| Medicare Part B Administrative Contractor (MAC) Jurisdictions | | |
|---|---|---|
| Jurisdiction | Applicable State/US Territory | Contractor |
| E (1) | CA, HI, NV, AS, GU, CNMI | Noridian Healthcare Solutions, LLC |
| F (2 & 3) | AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ | Noridian Healthcare Solutions, LLC |
| 5 | KS, NE, IA, MO | Wisconsin Physicians Service Insurance Corp |
| 6 | MN, WI, IL | National Government Services, Inc. (NGS) |
| H (4 & 7) | LA, AR, MS, TX, OK, CO, NM | Novitas Solutions, Inc. |
| 8 | MI, IN | Wisconsin Physicians Service Insurance Corp |
| N (9) | FL, PR, VI | First Coast Service Options, Inc. |
| J (10) | TN, GA, AL | Palmetto GBA, LLC |
| M (11) | NC, SC, WV, VA (excluding below) | Palmetto GBA, LLC |
| L (12) | DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA) | Novitas Solutions, Inc. |
| K (13 & 14) | NY, CT, MA, RI, VT, ME, NH | National Government Services, Inc. (NGS) |
| 15 | KY, OH | CGS Administrators, LLC |