UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2024 P 2232-6
Program	Prior Authorization/Medical Necessity
Medication	Orladeyo® (berotralstat)*
P&T Approval Date	3/2021, 8/2021, 10/2021, 10/2022, 10/2023, 3/2024
Effective Date	6/1/2024

1. Background:
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. Orladeyo should not be used for the treatment of acute HAE attacks.[1]

2. Coverage Criteria[a]:

A. Orladeyo* will be approved based on **all** of the following criteria:

1. Diagnosis of hereditary angioedema (HAE) as confirmed by **one** of the following:

   a. C1 inhibitor (C1-INH) deficiency or dysfunction (Type I or II HAE) as documented by **one** of the following (per laboratory standard):

      (1) C1-INH antigenic level below the lower limit of normal
      (2) C1-INH functional level below the lower limit of normal

-OR-

   b. HAE with normal C1 inhibitor levels and **one** of the following:

      (1) Confirmed presence of variant(s) in the gene(s) for factor XII, angiopoietin-1, plasminogen-1, kininogen-1, myoferlin, and heparan sulfate-glucosamine 3-O-sulfotransferase 6
      (2) Recurring angioedema attacks that are refractory to high-dose antihistamines with confirmed family history of angioedema
      (3) Recurring angioedema attacks that are refractory to high-dose antihistamines with unknown background de-novo mutation(s) (i.e., no family history) (HAE-unknown)

-AND-

2. **All** of the following:

   a. Prescribed for the prophylaxis of HAE attacks

-AND-

   b. Not used in combination with other approved products indicated for prophylaxis against HAE attacks (i.e., Cinryze, Haegarda, Takhzyro)

-AND-

c. Prescriber attests that patient has experienced attacks of a severity and/or frequency such that they would clinically benefit from prophylactic therapy with Orladeyo

-AND-

d. History of failure to **both** of the following (document date of trial and list reason for therapeutic failure):

(1) Haegarda (C1 esterase inhibitor, human)
(2) Takhzyro(lanadelumab)

-AND-

3. Prescribed by **one** of the following:

a. Immunologist
b. Allergist

Authorization of therapy will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

* Orladeyo is typically excluded from coverage. Coverage reviews may be in place if required by law or the benefit plan.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. Orladeyo [package insert]. Durham, NC: BioCryst Pharmaceuticals Inc.; March 2022
2. Busse, P., Christiansen, S., Riedl, M., et. al. "US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema." *The Journal of Allergy and Clinical Immunology.* 2020 September 05.
3. Maurer, M., Magerl, M., et. al. "The international WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update." *World Allergy Organization Journal.* 2018 February 27.

Program	Prior Authorization/Medical Necessity – Orladeyo (berotralstat)
Change Control	
3/2021	New program.
8/2021	Criteria updated to include failure of both Haegarda and Takhzyro. Reauthorization criteria removed. Exclusion statement added.

10/2021	Removed Initial Authorization verbiage and updated formatting with no change to clinical criteria.
10/2022	Annual review with no changes to clinical criteria. Updated reference.
10/2023	Annual review with no changes to clinical criteria.
3/2024	Annual review with update to diagnostic criteria for HAE with normal C1 inhibitor levels.