# SmartPA Criteria Proposal

| | |
|---|---|
| **Drug/Drug Class:** | Hereditary Angioedema Agents PDL Edit |
| **First Implementation Date:** | May 9, 2019 |
| **Proposed Date:** | December 16, 2021 |
| **Prepared For:** | MO HealthNet |
| **Prepared By:** | MO HealthNet/Conduent |
| **Criteria Status:** | ☐Existing Criteria<br>☒Revision of Existing Criteria<br>☐New Criteria |

## Executive Summary

**Purpose:** The MO HealthNet Pharmacy Program will implement a state-specific preferred drug list.

**Why Issue Selected:** Hereditary angioedema is a rare disease, occurring in an estimated 1 in 50,000 people. The disease is characterized by recurrent attacks of angioedema, without urticaria or pruritis, that occur due to C1-inhibitor deficiency (type I) or dysfunction (type II). The agents for hereditary angioedema include C1 esterase inhibitors (Berinert®, Cinryze®, Haegarda®, Ruconest®), ecallantide (Kalbitor®), icatibant (Firazyr®), lanadelumab-flyo (Takhzyro®), and berotralstat (Orladeyo®). The primary mediator of the swelling with hereditary angioedema is bradykinin, which is present in excess amounts during attacks. These agents aim to address the underlying pathophysiology by either working as a replacement for missing or malfunctioning C1 inhibitor, targeting kallikrein (berotralstat, ecallantide, and lanadelumab-flyo) to prevent excess bradykinin generation or inhibiting the binding of bradykinin through inhibition of its receptors (icatibant).

The International World Allergy Organization/European Academy of Allergy and Clinical Immunology (WAO/EAACI) guidelines provide the most current recommendations for both acute attacks and long-term management. Early treatment with C1 esterase inhibitors (plasma-derived or recombinant), ecallantide, or icatibant should be considered for all attacks, with definitive treatment strongly recommended for any attack affecting or potentially affecting the upper airway. For pediatric patients aged less than 12 years, plasma-derived C1 esterase inhibitors are recommended for treatment. Early treatment is associated with a quicker resolution of symptoms and attack duration. In order to facilitate early treatment, it is also recommended that patients have an agent available to them in the home. The second-line treatment option for acute attacks is plasma.

Long-term prophylaxis is appropriate for all patients regardless of disease severity. The preferred option for both adult and pediatric patients is plasma-derived C1 esterase inhibitors. However, the first oral prophylactic therapy, Orladeyo, was approved in December 2020 for use in patients aged 12 years and older and may prove to be a viable option for those patients currently untreated or with an aversion to injections.

Total program savings for the PDL classes will be regularly reviewed.

| Program-Specific Information: | Preferred Agents for Prophylaxis of Hereditary Angioedema | Non-Preferred Agents for Prophylaxis of Hereditary Angioedema |
|---|---|---|
| | • Haegarda®<br>• Takhzyro® | • Cinryze®<br>• Orladeyo® |
| | **Preferred Agents for Treating Acute Hereditary Angioedema Attack** | **Non-Preferred Agents for Treating Acute Hereditary Angioedema Attack** |
| | • Berinert®<br>• Icatibant<br>• Sajazir™ | • Firazyr®<br>• Kalbitor®<br>• Ruconest® |

**Type of Criteria:** ☐ **Increased risk of ADE** ☒ **Preferred Drug List**
☒ **Appropriate Indications** ☐ **Clinical Edit**

**Data Sources:** ☐ **Only Administrative Databases** ☒ **Databases + Prescriber-Supplied**

## Setting & Population

- Drug class for review: Hereditary Angioedema Treatment Agents
- Age range: All appropriate MO HealthNet participants

## Approval Criteria

- Documented compliance on current therapy regimen **AND**
- Prescribed by or in consultation with an allergy-immunologist, maternal-fetal medicine specialist (for pregnant individuals), or other specialist in the treated disease state **AND**
- Documented diagnosis of hereditary angioedema in the last year **AND**
- Documentation of the following:
  - Low (<50% of normal) C1INH antigenic or functional level **AND**
  - Low C4 level (either at baseline or during an attack) **AND**
- Failure to achieve desired therapeutic outcomes with trial on 2 preferred agents
  - Documented trial period for preferred agents **OR**
  - Documented ADE/ADR to preferred agents
- For Orladeyo
  - Initial approval of prior authorization is for 6 months. Renewal of prior authorization may be given for an additional 12 months following documentation of the following:
    - Documented compliance on current therapy regimen **AND**
    - Documentation of benefit of therapy based on goals of therapy

## Denial Criteria

- Lack of adequate trial on required preferred agents
- Therapy will be denied if all approval criteria are not met
- Claim exceeds maximum dosing limitation for the following:

| Drug Description | Generic Equivalent | Max Dosing Limitation |
|---|---|---|
| ORLADEYO 110 MG CAPSULE | BEROTRALSTAT | 1 capsule per day |
| ORLADEYO 150 MG CAPSULE | BEROTRALSTAT | 1 capsule per day |

## Required Documentation

| | | | |
|---|---|---|---|
| Laboratory Results: | ☐ | Progress Notes: | ☐ |
| MedWatch Form: | ☐ | Other: | ☐ |

## Disposition of Edit

Denial: Exception "0160" (Preferred Drug List Edit)
Rule Type: PDL

## Default Approval Period

6 months

## References


- Evidence-Based Medicine and Fiscal Analysis: "Agents for Hereditary Angioedema (HAE)", Conduent, L.L.C., Richmond, VA; November 2021.
- Evidence-Based Medicine Analysis: "Hereditary Angioedema Treatment Agents", UMKC-DIC; September 2021.
- Busse PJ, Christinasen SC, Riedl MA, et. al. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. https://www.haea.org/assets/img/TreatmentGuidelines040321.pdf. J Allergy clin Immunol Pract 2021 Jan; 9(1): 132-150.
- Tarzi M, Hickey A, Forster T, et. al. An evaluation of tests used for the diagnosis and monitoring of C1 inhibitor deficiency: normal serum C4 does not exclude hereditary angio-oedema. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2219337/pdf/cei0149-0513.pdf. Clin Exp Immunol. 2007 Sept; 149(3): 513-516.
- USPDI, Micromedex; 2021.
- Drug Facts and Comparisons On-line; 2021.