**Drug/Drug Class:** Hereditary Angioedema Treatment Agents PDL Edit  
**First Implementation Date:** May 9, 2019  
**Revised Date:** April 2, 2020  
**Prepared For:** MO HealthNet  
**Prepared By:** MO HealthNet/Conduent  
**Criteria Status:** ☒ Revision of Existing 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®), and lanadelumab-flyo (Takhzyro™). 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 (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 <12 years old, 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 patients with severely symptomatic disease. The preferred option for both adult and pediatric patients is plasma-derived C1 esterase inhibitors. In adults, attenuated androgens (e.g., danazol) are considered the second-line option. In pediatric patients, antifibrinolytics (e.g., tranexamic acid) are recommended as a second-line option, but data supporting their use are limited. The 2013 American Academy of Allergy, Asthma, and Immunology (AAAAI) guideline that covers hereditary angioedema provides similar recommendations as the WAO/EAACI guidance. Lanadelumab-flyo was not mentioned in either guideline as it was not approved at the time of publication.
Total program savings for the PDL classes will be regularly reviewed.

### Program-Specific Information:

<table>
<thead>
<tr>
<th>Preferred Agents for Prophylaxis of Hereditary Angioedema</th>
<th>Non-Preferred Agents for Prophylaxis of Hereditary Angioedema</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Haegarda®</td>
<td>• Cinryze®</td>
</tr>
<tr>
<td>• Takhzyro™</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Preferred Agents for Treating Acute Hereditary Angioedema Attack</th>
<th>Non-Preferred Agents for Treating Acute Hereditary Angioedema Attack</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Berinert®</td>
<td>• Firazyr®</td>
</tr>
<tr>
<td>• Icatibant</td>
<td>• Kalbitor®</td>
</tr>
<tr>
<td></td>
<td>• Ruconest®</td>
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</tbody>
</table>

### Type of Criteria:

- [ ] Increased risk of ADE
- [x] Preferred Drug List
- [ ] Appropriate Indications
- [ ] Clinical Edit

### Data Sources:

- [ ] Only Administrative Databases
- [x] Databases + Prescriber-Supplied

### Setting & Population

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

### Approval Criteria

- Documented diagnosis of hereditary angioedema in the last year with confirmed lack of or non-functioning C1 esterase inhibitors
- 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
- Documented compliance on current therapy regimen

### Denial Criteria

- Lack of adequate trial on required preferred agents
- Therapy will be denied if no approval criteria are met

### 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

1 year

References

4. USPDI, Micromedex; 2019.
5. Drug Facts and Comparisons On-line; 2019