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| **Department:** | Pharmacy | **Original Approval:** | 10/19/2018 |
| **Policy #:** | PM567 | **Last Approval:** | 10/19/2018 |
| **Title:** | Hereditary Angioedema (HAE) Agents | | |
| **Approved By:** | MMLT | | |

## REQUIRED CLINICAL DOCUMENTATION FOR REVIEW

Documentation required to determine medical necessity for Lanadelumab-flyo (Takhzyro) for subcutaneous use: History and/or physical examination notes and relevant specialty consultation notes that address the problem and need for the service: -Diagnosis -Age -Prescribed by or in consultation with an allergist, immunologist, dermatologist, hematologist, pulmonologist, or medical geneticist -Labs/diagnostics - Medication list (current and past) to include start and end dates of previous trials for hereditary angioedema.

BACKGROUND
Hereditary Angioedema (HAE) is a very rare and potentially life-threatening defect in the gene that controls a blood protein called C1 Inhibitor. Symptoms include edema (swelling) in various parts of the body, including the hands, feet, face and airway (throat). Swelling of the airway or throat is particularly dangerous, because it can cause death by asphyxiations. The absence of a family history does not rule out the diagnosis of HAE, as many as 25% of HAE cases result from a spontaneous mutation of the C1-inhibitor gene at conception.

## DEFINITIONS

None

## INDICATIONS/CRITERIA

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| **Medicaid Members** | ***Continue to criteria for approval below.*** |
| **Medicare Members** | ***Step-utilization of Part D drugs not required.*** |

| ***Drug*** | ***Medical Necessity*** |
|---|---|
| ecallantide (**KALBITOR®**)<br>icatibant (**FIRAZYR®**)<br>human C1 esterase inhibitor (**BERINERT®**) | For the treatment for **acute attacks of hereditary angioedema (HAE)**. |

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| recombinant C1 esterase inhibitor (**RUCONEST®**) | |
| human C1 esterase inhibitor (**CINRYZE®**, **HAEGARDA®**) lanadelumab-flyo (**TAKHZYRO™**) | For routine **prophylaxis of hereditary angioedema (HAE)** with a history of moderate or severe attacks. |

**FDA-Approved Indications**

1. For the treatment for **acute attacks of hereditary angioedema (HAE).**

**Criteria.** Approve if **ALL** of the following are met:

A. Diagnosis of hereditary angioedema (HAE) confirmed by documentation of serum C4 **AND** C1-INH (antigenic or functional level) that are below the lower limits of normal
B. History of moderate or severe HAE attacks (i.e. airway swelling, severe abdominal pain, facial swelling, nausea and vomiting, painful facial distortion)
C. **BOTH** of the following:
    a. For the treatment of acute HAE attacks
    b. Not used in combination with other approved treatments for acute HAE attacks (e.g. **Firazyr**, **Kalbitor** or **Ruconest**)
D. Medications known to cause angioedema (e.g. ACE inhibitors, ARBs, estrogen products) have been evaluated and discontinued when appropriate
E. Prescribed by or in consultation with a specialist in **ONE** of the following:
    a. Allergy
    b. Immunology
    c. Dermatology
    d. Hematology
    e. Pulmonology
    f. Medical Genetics

**Dosing.**[1] *Dosing must meet the following:*

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| recombinant C1 esterase inhibitor (**RUCONEST®**) | 12 vials (2100 units each) per 30 days |
| icatibant (**FIRAZYR®**) | 9 injections (30 mg each) per 30 days |
| ecallantide (**KALBITOR®**) | 18 injections (10 mg each) per 30 days |
| human C1 esterase inhibitor **(BERINERT®)** | quantity sufficient to treat four attacks per 30 days based on a dose of 20 IU per kg of body weight per dose |

**Approval**

*Initial Approval- 3 months*

*Extended Approval*. 12 months with documented clinical improvement in severity/duration of attacks and functional improvement or stability with the medication.

**Duration of therapy.** Indefinite.

**Labs/Diagnostics.** Functional C1-INH protein and serum C4 levels must be performed at baseline, as outlined in above criteria.

**2.** For routine **prophylaxis of hereditary angioedema (HAE)** with a history of moderate or severe attacks.

**Criteria.** Approve if **ALL** of the following are met:

A. Diagnosis of hereditary angioedema (HAE) confirmed by documentation of serum C4 AND C1-INH (antigenic or functional level) that are below the lower limit of normal
B. History of moderate or severe HAE attacks (e.g. airway swelling, severe abdominal pain, facial swelling, nausea and vomiting, painful facial distortion)
C. **BOTH** of the following:
    a. For prophylaxis against HAE attacks
    b. Not used in combination with other approved C1 esterase inhibitors indicated for prophylaxis against HAE attacks
D. History of failure, contraindication, or intolerance of **ONE** of the following for HAE prophylaxis:
    a. 17-alpha alkylated androgen (e.g., danazol and stanozolol)
    b. Antifibrinolytics (e.g., aminocaproic acid (Amikar), tranexamic acid (Cyklokapron))
E. Medications known to cause angioedema (i.e. ACE-Inhibitors, estrogens, angiotensin II receptor blockers) have been evaluated and discontinued when appropriate
F. Prescribed by or in consultation with a specialist in **ONE** of the following:
    a. Allergy
    b. Immunology
    c. Dermatology
    d. Hematology
    e. Pulmonology
    f. Medical Genetics

**Dosing-** Dosing must meet the following:

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| human C1 esterase inhibitor (**CINRYZE®**) | 10,000 units (20 vials) per 30 days |
| human C1 esterase inhibitor (**HAEGARDA®**) | 60IU per kg body weight twice weekly |
| lanadelumab-flyo **(TAKHZYRO™)** | 2 vials per 28-days |

**Approval**

*Initial Approval- 3 month*

*Extended Approval*. 12 months with documented clinical improvement in severity/duration of attacks and functional improvement or stability with the medication.

**Duration of therapy.** Indefinite.

**Labs/Diagnostics.** Functional C1-INH protein and serum C4 levels must be performed at baseline, as outlined in above criteria.

## SPECIAL CONSIDERATIONS

None

## LIMITATIONS/EXCLUSIONS

Please refer to a product line's certificate of coverage for benefit limitations and exclusions for these services:

| PRODUCT LINE | LINK TO CERTIFICATE OF COVERAGE |
|---|---|
| MEDICARE ADVANTAGE | http://healthfirst.chpw.org/for-members/resource-library/handbooks-and-guides |
| WASHINGTON APPLE HEALTH | http://chpw.org/our-plans/apple-health/ |
| INTEGRATED MANAGED CARE | http://chpw.org/our-plans/apple-health/ |

## Citations & References

| | | |
|---|---|---|
| **CFR** | | |
| **WAC** | WAC 284-43-2050 | |
| **RCW** | | |
| **Contract Citation** | ☒ WAH | |
| | ☒ IMC | |
| | ☒ MA | |
| **Other Requirements** | | |
| **NCQA Elements** | | |
| **References** | 1. Firazyr [Prescribing Information]. Lexington, MA. Shire Orphan Therapies, LLC. November 2015.<br>2. Product Information: KALBITOR® subcutaneous injection, ecallantide subcutaneous injection. Dyax Corp. (per FDA), Burlington, MA, 2014.<br>3. Ruconest [Prescribing Information]. Raleigh, NC. Santarus, Inc. February 2015. | |

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| | 4. Product Information: HAEGARDA® subcutaneous injection, C1 esterase inhibitor (human) subcutaneous injection. CSL Behring LLC (per FDA), Kankakee, IL, 2017.<br>5. Product Information: Berinert® intravenous injection, C1 esterase inhibitor (human) intravenous injection. CSL Behring LLC (per manufacturer), Kankakee, IL, 2016.<br>6. Product Information: Cinryze® IV injection, C1 esterase inhibitor (human) IV injection. Shire ViroPharma Incorporated (per DailyMed), Lexington, MA, 2016<br>7. Micromedex® 2.0, (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.micromedexsolutions.com/ (cited: 01/31/2018).<br>8. Washington State HCA Medical Policy No.85.80.00 HAE Agents |

## Revision History

| Revision Date | Revision Description | Revision Made By |
|---|---|---|
| 10/16/18 | NEW | Jennifer Farley, PharmD |
| 10/19/2018 | Approval | MMLT |