Idaho Medicaid's Therapeutic Criteria for

Medications Used for Prophylaxis and Acute Attack Treatment for Hereditary Angioedema (HAE)

Updated May 2020

Confirmation of Diagnosis

1. Type 1 – Deficiency (85% of patients)
   (a) Normal C1 level and a low C4 level (< 14 mg/dl) or
   (b) Low C4 level (< 14 mg/dl) and low C1 inhibitor level (C1-INH < 19 mg/dl)
2. Type 2 – Dysfunctional (15% of patients)
   (a) Normal C1-INH level (≥ 19mg/dl) and low C1-INH functional level (< 50%)
3. Type 3 – Mutation in Factor XII gene (OMIM610618)

Clinical Features of Hereditary Angioedema

Recurrent episodes of angioedema and/or abdominal pain including:

1. Laryngeal angioedema and/or
2. Localized subcutaneous swelling without urticaria lasting more than 12 hours and/or
3. Abdominal symptoms including abdominal pain lasting more than 6 hours

Short-term Prophylaxis Criteria - Prior to elective dental and surgical procedures

1. Minor dental and medical procedures:
   Danazol given five days prior to procedure and for 2 days after procedure. Contra-indicated in pregnancy.
   a. If already on danazol, double the dose
   b. If not already on danazol, dose is 600mg/day (adults) or 100-300mg/day (children).
2. Major dental procedures and intubation:
   Cinryze (C1 inhibitor concentrate) 20 units/kg given 1-6 hours prior to procedure.
   Note – this medication should be given in the medical facility that is performing the procedure. Prior authorization is required.

Long-term Prophylaxis Criteria for Initiation of Therapy (initial approval will be for a three month trial period)

1. Minimize or eliminate trigger factors if possible (e.g. discontinue ACE-inhibitors, estrogen containing birth control pills)
2. ≥ 2 HAE attacks monthly or patient is disabled for more than 5 days per month or history of an airway compromising event
3. First line agent – oral danazol (prior authorization not required)
4. Second line agents (if therapy with danazol has been tried and failed or is contra-indicated)
   (a) oral tranexamic acid – prior authorization is not required OR

(b) Intravenous **Cinryze (C1 Esterase Inhibitor, Human)** – preferred agent. Prior authorization required regardless of whether it is billed as a medical claim (J0598) or as a prescription claim
(c) Subcutaneous **Haegarda (C1 Esterase Inhibitor, Human)** – preferred agent. Prior authorization is required regardless of whether it is billed as a medical claim (J0599) or as a prescription claim.
(d) Subcutaneous **Takhzyro (lanadelumab-flyo)** – non-preferred agent. Therefore it requires trial and failure of a preferred agent or medical necessity documentation why none of the preferred agents are clinically appropriate. Prior authorization is required regardless of whether it is billed as a medical claim (J0593) or as a prescription claim.

Long-term Prophylaxis Criteria for Continuation of Therapy

1. Documentation that patient has been adherent to prophylactic therapy.
2. Improvement documented in frequency, severity, and duration of HAE attacks from baseline.
3. Continue to minimize or eliminate trigger factors if possible.

Therapeutic Criteria for Treatment of Acute Attacks

Patient must be experiencing at least one symptom of a moderate or severe attack – laryngeal swelling, facial swelling, severe abdominal pain, and/or abdominal attack with obstruction.

1. **Firazyr (icatibant)** is a preferred agent. Prior authorization is required for both medical claims (J1744) and prescription claims to verify that the patient has a confirmed diagnosis of HAE and is experiencing acute attacks.
    - Mechanism of action: Bradykynin B2 receptor antagonist. HAE patients have an absence or dysfunction of C1-esterase inhibitor which leads to excess bradykinin production.
    - Dosage Form/Route of Administration: Prefilled syringe administered subcutaneously in the abdominal area. May be self-administered.
    - Type of attack: Approved for all types of attacks. Given the potential for airway obstruction during acute laryngeal HAE attacks, patients are advised to seek medical attention in an appropriate healthcare facility immediately in addition to treatment with Firazyr (icatibant).
2. **Kalbitor (ecallantide)** is also a preferred agent. Prior authorization is required for both medical claims (J1290) and prescription claims to verify that the patient has a confirmed diagnosis of HAE and is experiencing acute attacks.
    - Mechanism of action: Selective and reversible inhibitor of plasma kallikrein which reduces the conversion of kininogen to bradykinin thereby treating the symptoms of the disease during acute episodic attacks of HAE.
    - Dosage Form/Route of Administration: Each dose is comprised of three 10mg/ml 1ml vials administered subcutaneously as three 10mg injections in the abdominal area, thigh, or upper arm. Must be administered by a healthcare professional with appropriate medical support to manage anaphylaxis. It may be administered at home through Kalbitor Home Infusion Services who provides a trained infusion

nurse to come to the patient's house on-demand to administer the medication subcutaneously.
    - Type of attack: Approved for all types of attacks.
3. **Berinert (C1 Esterase Inhibitor, human)** is a non-preferred agent and requires trial and failure of a preferred agent or medical necessity documentation why none of the preferred agents are clinically appropriate. Prior authorization is required for both medical claims (J0597) and prescription claims to verify that the patient has a confirmed diagnosis of HAE and is experiencing acute attacks.
    - Mechanism of action: C1 Esterase Inhibitor that is either lacking or non-functioning in HAE patients.
    - Dosage Form/Route of Administration: Single use vials each containing 500 International Units (IU) as a freeze dried powder that needs to be reconstituted with sterile water. Dose is 20 IU per kg of body weight administered intravenously at a rate of 4ml/min (takes approximately 7 minutes to administer). It is FDA approved for self-administration after proper training from a healthcare professional.
    - Type of attack: Approved for all types of attacks. Given the potential for airway obstruction during acute laryngeal HAE attacks, patients self-administering Berinert should be advised to immediately seek medical attention in an appropriate healthcare facility after treatment with Berinert.
4. **Ruconest (plasma-free C1 Esterase Inhibitor, recombinant)** is a non-preferred agent agent and requires trial and failure of a preferred agent or medical necessity documentation why none of the preferred agents are clinically appropriate. Prior authorization is required for both medical claims (J0596) and prescription claims to verify that the patient has a confirmed diagnosis of HAE and is experiencing acute attacks.
    - Mechanism of action: C1 Esterase Inhibitor that is either lacking or non-functioning in HAE patients.
    - Dosage Form/Route of Administration: Single use vials each containing 2100 International Units (IU) as a freeze dried powder that needs to be reconstituted with sterile water. Dose is 50 IU per kg of body weight up to a maximum of 4200 IU (2 vials) administered intravenously over approximately 5 minutes. It is FDA approved for self-administration after proper training from a healthcare professional.
    - Type of attack: Approved for acute attacks. Effectiveness in clinical studies was not established in HAE patients with laryngeal attacks.

Initially written: October 2011

Revised: January 2013
Reviewed by Idaho Medicaid's Medical Director.

Revised: May 2014
Approved by Idaho Medicaid's Pharmacy & Therapeutics Committee 5-18-2014

Revised: May 2015
Approved by Idaho Medicaid's Pharmacy & Therapeutics Committee 5-24-2015

Revised: August 2016
Approved by Idaho Medicaid's Pharmacy & Therapeutics Committee 5-20-2016

Revised: May 2017
Approved by Idaho Medicaid's Pharmacy & Therapeutics Committee 5-19-2017

Revised May 2018
Approved by Idaho Medicaid's Pharmacy & Therapeutics Committee 5-18-2018

Revised June 2019
Approved by Idaho Medicaid's Pharmacy & Therapeutics Committee 5-17-2019

Revised May 2020
Approved by Idaho Medicaid's Pharmacy & Therapeutics Committee 5-15-2020