Pharmacy Drug Policy & Procedure

Policy Name:	Hereditary Angioedema	Policy #:	2608P

Purpose of the Policy

The purpose of this policy is to establish the criteria for coverage of drug products intended for the treatment and prophylaxis of hereditary angioedema (HAE).

Statement of the Policy

Health Alliance Medical Plans and Health Alliance Northwest will approve the use of the following Hereditary Angioedema treatments under the Specialty benefit when the criteria below have been met.

- Berinert (human C1 esterase inhibitor) covered under Specialty Medical benefit
- Cinryze (human C1 esterase inhibitor) covered under Specialty Medical benefit
- Firazyr (icatibant) covered under Specialty Pharmacy benefit
- Haegarda (human C1 esterase inhibitor) covered under Specialty Pharmacy benefit
- Kalbitor (ecallantide) covered under Specialty Pharmacy benefit
- Orladeyo (berotralstat) covered under Specialty Pharmacy benefit
- Ruconest (recombinant C1 esterase inhibitor) covered under Specialty Medical benefit
- Sajazir (icatibant) covered under Specialty Pharmacy benefit
- Takhzyro (lanadelumab) covered under Specialty Pharmacy benefit

Definitions

Diagnosis of C1INH-HAE requires the following	Two complement sets of test results both of which indicate low complement factor 4 (C4) level (<14 mg/dl or below the testing laboratory's lower limit of normal) plus two complement sets of test results both of which indicate one of the following: • Low C1 inhibitor (C1INH) antigenic level (<19 mg/dl or below the testing laboratory's lower limit of normal), OR • Low C1INH functional level (<50% or below the testing laboratory's lower limit of normal) and presence of normal C1INH antigenic level (19 mg/dl)
Diagnosis of HAE with normal C1INH (formerly Type III)+	Testing indicates a near-normal C4, normal C1INH antigen, and normal C1INH function and one of the following: • Factor XII mutation (FXII-HAE), OR • Family history of angioedema and failure to respond to chronic, high-dose antihistamine therapy (total daily dose: cetirizine 40 mg, desloratadine 20 mg, fexofenadine 480 mg, levocetirizine 20 mg, loratadine 40 mg) for one month or an interval long enough to expect three or more angioedema attacks • **+This is for informational purposes only and not part of any criteria for approval of any drug in this policy**

Treatment of Acute Attacks	Prevention of Attacks
Berinert (C1 Esterase Inhibitor, Human)	Cinryze (C1 Esterase Inhibitor, Human)
Firazyr (Icatibant Acetate)	Haegarda (C1 Esterase Inhibitor, Human)
Icatibant Acetate	Orladeyo (Berotralstat)
Kalbitor (Ecallantide)	Takhzyro (Lanadelumab-flyo)
Ruconest (C1 Esterase Inhibitor Recombinant)	
Sajazir (Icatibant Acetate)	

Criteria

1. Coverage Criteria for Acute Attacks (Berinert, Firazyr, icatibant, Sajazir, Kalbitor, Ruconest)

1.1 Diagnosis of C1INH-HAE (formerly types I/II)
- Evidence of low C4 level (<14 mg/dL AND evidence of low C1 inhibitor (C1INH <19.9 mg/dL) OR low C1INH functional level (functional C1INH < 72%)

1.2 Prescribed by a(n) allergist (allergy doctor), immunologist (immune system doctor), or rheumatologist (musculoskeletal doctor)

1.3 Appropriate age per approved FDA labeling

1.4 Presence of acute hereditary angioedema (HAE) attack confirmed by one or more symptoms (airway swelling, severe abdominal pain, facial swelling, throat swelling, nausea and vomiting, painful face distortion)

1.5 Medications associated with angioedema (e.g., ACE inhibitors, ARBs, NSAIDs, estrogens) have been evaluated and, if appropriate, discontinued

1.6 Request for coverage is reviewed by both a pharmacist and a medical director

1.7 Initial Approval: 12 months, Reapproval: 12 months with documented clinical benefit

2. Coverage Criteria for Prophylaxis (Cinryze, Haegarda, Orladeyo, Takhzyro)

2.1 Diagnosis of C1INH-HAE (formerly types I/II)

2.2 Appropriate age per approved FDA labeling

2.3 History of at least one HAE attack, without the presence of urticaria (raised, itchy rash), per month

2.4 Prescribed by a(n) allergist (allergy doctor), immunologist (immune system doctor), or rheumatologist (musculoskeletal doctor)

2.5 Medications associated with angioedema (e.g., ACE inhibitors, ARBs, NSAIDs, estrogens) have been evaluated and, if appropriate, discontinued

2.6 Trial and failure, intolerance, or contraindication to any one of the following:
- 17 alpha-alkylated androgens (stanozolol, danazol), OR
- Anti-fibrinolytic agents (aminocaproic acid, tranexamic acid)

2.7 Request for coverage is reviewed by both a pharmacist and a medical director

2.8 Initial Approval: 12 months, Reapproval: 12 months with documented clinical benefit

3. Exclusions

3.1 Treatment of any other form of chronic, recurrent angioedema, such as: hereditary angioedema with normal C1 inhibitor (formerly Type III HAE), acquired angioedema, idiopathic angioedema, or recurrent angioedema associated with urticaria and all other indications because its effectiveness has not been established

3.2 Medications for acute attacks will not be approved if being used in combination with another medication used for the treatment of acute attacks because this combination lacks strong evidence for use

3.3 Medications for prophylaxis will not be approved if being used in combination with another medication used for the prevention of attacks because this combination lacks strong evidence for use

Drug	FDA Approved Dose	MDL
Berinert (human C1 esterase inhibitor) ≥5 y/o	20 units/kg IV	500 unit vial is limited to 10 vials per 30 days
Cinryze (human C1 esterase inhibitor) ≥6 y/o	1000 units every 3 to 4 days	500 unit vial is limited to 20 vials per 30 days
Haegarda (human C1 esterase inhibitor) ≥6 y/o	60 units/kg every 3 to 4 days	2000 unit vial is limited to 30 vials per 30 days 3000 unit vial is limited to 20 vials per 30 days
Firazyr and Sajazir (icatibant) ≥18 y/o	30 mg subq; may repeat every 6 hours if response is inadequate or symptoms recur (max 90mg/day)	30 mg/3 mL syringe is limited to 18mL per 30 days
Kalbitor (ecallantide) ≥8 y/o	30 mg subq; may repeat with an additional 30 mg dose within 24 hours if symptoms persist	30-mg kit is limited to 4 kits per 30 days
Ruconest (recombinant C1 esterase inhibitor) ≥13 y/o	<84 kg: 50 units/kg IV as a single dose; administer a 2nd identical dose if symptoms persist. ≥84 kg: 4200 IU administered IV over 5 minutes; administer a 2nd identical dose if symptoms persist. **Max 4200 IU per dose/8400 IU per attack	2100 IU is limited to 8 vials per 30 days
	NOTE: Approvals for 9 to 12 vials per 30 days are reviewed on a case-by-case basis and must include documentation of maximal trigger management as well as documentation that prophylactic medication has been ineffective is contraindicated, or not tolerated	
Orladeyo (berotralstat) ≥12 y/o	150 mg oral once daily	30 capsules per 30 days
Takhzyro (lanadelumab) ≥2 y/o	300 mg subq every 2 weeks	300mg/2mL syringe is limited to 4mL per 28 days

CPT Codes	
96374	Therapeutic, prophylactic or diagnostic injection (specify substance or drug); intravenous push, single or initial substance/drug
96375	Therapeutic, prophylactic or diagnostic injection (specify substance or drug); each additional sequential intravenous push of a new substance/drug
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
96374	Therapeutic, prophylactic or diagnostic injection (specify substance or drug); intravenous push, single or initial substance/drug

HCPCS Codes	
J0597	Injection, C-1 esterase inhibitor (human), Berinert, 10 units
J0598	Injection, C1 esterase inhibitor (human), Cinryze, 10 units

J1744	Injection, icatibant, 1 mg
J0599	Injection, C1 esterase inhibitor (human), (Haegarda), 10 units
J1290	Injection, ecallantide, 1 mg
J0596	Injection, c-1 esterase inhibitor (recombinant), Ruconest, 10 units
J0593	Injection, lanadelumab-flyo, 1 mg

References

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