RX.PA.001.CCH ACUTE HEREDITARY ANGIOEDEMA PRODUCTS: Berinert (C1 Esterase Inhibitor, Human), Kalbitor® (Ecallantide), Firazyr® (Icatibant), and Ruconest® (C1 Esterase Inhibitor, Recombinant)

The purpose of this policy is to define the prior authorization process for Acute Hereditary Angioedema (HAE) Products: Berinert® (C1 esterase inhibitor [human]), Kalbitor® (ecallantide), Firazyr® (icatibant), and Ruconest® (C1 esterase inhibitor, [recombinant]).

- Berinert® (C1 esterase inhibitor [human]) is indicated for the treatment of acute abdominal, facial, or laryngeal attacks of HAE in adult and pediatric patients.
- Kalbitor® (ecallantide) is approved for the treatment of acute attacks of HAE in patients aged 12 years or older.
- Firazyr® (icatibant) is indicated for the treatment of acute attacks of HAE in adults aged 18 years or older.
- Ruconest® (C1 esterase inhibitor, [recombinant]) is indicated for the treatment of acute attacks in adult and adolescent patients with HAE.

DEFINITIONS

Hereditary Angioedema (HAE) – a rare disorder characterized by recurrent attacks of swelling that may involve the peripheral extremities, abdomen, genitalia, face, oropharynx, or larynx due to low levels of endogenous or functional C1 inhibitor.

POLICY

It is the policy of the Health Plan to maintain a prior authorization process that promotes appropriate utilization of specific drugs with potential for misuse or limited indications. This process involves a review using Food and Drug Administration (FDA) criteria to make a determination of Medical Necessity, and approval by the Medical Policy Committee.

The drugs, Berinert® (C1 esterase inhibitor [human]), Kalbitor® (ecallantide), Firazyr® (icatibant), and Ruconest® (C1 esterase inhibitor, [recombinant]) are subject to the prior authorization process.

PROCEDURE

Initial Authorization Criteria:

Must meet all the criteria listed below:

- Must be prescribed for the treatment of acute HAE attacks
- Must be prescribed by or under the direction of a HAE specialist. A HAE specialist is defined as an allergist/immunologist who demonstrates clinical expertise in HAE through research, publication, referrals/consults.
- Must have a diagnosis of HAE confirmed by ALL the following laboratory values on two separate instances (copy of laboratory reports required, must include reference ranges):
    - Low C4 complement level (mg/dL)
    - Normal C1q complement component level (mg/dL)
        - C1q complement component level is not required for patients under the age of 18 OR patients whose symptoms began before age 18
    - Either of the following:
        - Low C1 esterase inhibitor antigenic level (mg/dL)
        - Low C1 esterase inhibitor functional level (percent)
- Must have received at least one dose of requested product as treatment for acute HAE attack in the past. Chart documentation indicating patient response and ability to tolerate medication is required.
- Must meet the following age requirements:
    - Berinert – 2 years or older
    - Kalbitor – 12 years or older
    - Firazyr – 18 years or older
    - Ruconest – 13 years or older

Reauthorization Criteria:

All prior authorization renewals are reviewed on an annual basis to determine the Medical Necessity for continuation of therapy. Authorization may be extended at 1-year intervals based upon chart documentation from the prescriber that the member's condition has improved based upon the prescriber's assessment while on therapy.

Limitations:

Length of Authorization (if above criteria met)	
Initial Authorization	1 fill
Reauthorization	Up to 1 year
Quantity Level Limit	
Firazyr	3 syringes per fill
Kalbitor	4 vials per fill
Ruconest	4 vials per fill

If the established criteria are not met, the request is referred to a Medical Director for review, if required for the plan and level of request.

HCPCS Codes:

HPCPS Code	Brand	Description
J0596	RUCONEST	INJ C1 ESTERASE INHIBITOR (RECOMBINANT), 10 UNITS
J0597	BERINERT	INJ C-1 ESTERASE INHIB HUMAN, 10 UNITS
J1290	KALBITOR	INJECTION ECALLANTIDE, 1 MG
J1744	FIRAZYR	INJECTION ICATIBANT, 1 MG

REFERENCES

1. Berinert [Package Insert]. Kankakee, IL: CSL Behring LLC; July 2016.
2. Kalbitor [Package Insert]. Cambridge, MA: Dyax Corp.; March 2015.
3. Firazyr [Package Insert]. Lexington, MA: Shire Orphan Therapies, Inc.; August 2011
4. Ruconest [prescribing information]. Raleigh, NC: Sakix Pharmaceutical, Inc.; July 2014
5. Gompels MM, Lock RJ, Abinun M et al. C1 inhibitor deficiency: consensus document. *Clinical and Experimental Immunology* 2005; 139:379-394
6. Zuraw BL. Hereditary angioedema. *N Engl J Med* 2008;359:1027-36
7. Epstein TG, Bernstein JA. Current and emerging management options for hereditary angioedema in the US. *Drugs* 2008;68(18):2561-2573
8. Bowen T, Cicardi M, Bork K et al. Hereditary angioedema: a current state-of-the-art review, VII: Canadian Hungarian 2007 international consensus algorithm for the diagnosis, therapy, and management of hereditary angioedema. *Ann Allergy Asthma Immunol* 2008;100(Suppl 2):S30-S40
9. Farkas H, Varga L, Szeplaki G et al. Management of hereditary angioedema in pediatric patients. *Pediatrics* 2007;120:e713-e722
10. Agostoni A, Aygoren-Pursun E, Binkley KE et al. Hereditary and acquired angioedema: problems and progress – proceedings of the third C1 esterase inhibitor deficiency workshop and beyond. *J Allergy Clin Immunol* 2004;114(3 suppl):S51-S131
11. Craig T, Reidl M, Dykewicz MS, et al. When is prophylaxis for hereditary angioedema necessary? *Ann Allergy Asthma Immunol* 2009;102:366-372
12. Cicardi M, Banerji F, Bracho A, et al. Icatibant, a new bradykinin-receptor antagonist, in hereditary angioedema. *N Engl J Med* 2010;363:532-41
13. 13. Riedl MA, Bernstein JA, Li H, et al. Recombinant human C1-esterase inhibitor relieves symptoms of hereditary angioedema attacks: phase 3, randomized, placebo-controlled trial. Ann Allergy Immunol 2014;112:163-169
14. Riedl MA, Levy RJ, Suez D, et al. Efficacy and safety of recombinant C1 inhibitor for the treatment of hereditary angioedema attacks: a North American open-label study. Ann Allergy Immunol 2013;110:295-299
15. Cicardi M, Craig TJ, Martinez-Saguer I, Hebert j, Longhurst HJ, Review of Recent Guidelines and Consensus Statements on Hereditary Angioedema Therapy with Focus on Self-Administration Int Arch Allergy Immunol 2013;161(suppl 1):3–9.
16. Kreuz W, Rusicke E, Martinez-Saguer I, Aygoren-Pursun E, Heller C, Klingbeil T (2012) Home Therapy with intravenous human C1 inhibitor in children and adolescents with hereditary angioedema. Transfusion 52:100-107.
17. Farkas H, Pediatric hereditary angioedema due to C1-inhibitor deficiency Allergy, Asthma & Clinical Immunology 2010, 6:18.

RECORD RETENTION

Records Retention for Evolent Health documents, regardless of medium, are provided within the Evolent Health records retention policy and as indicated in CORP.028.E Records Retention Policy and Procedure.

REVIEW HISTORY

DESCRIPTION OF REVIEW / REVISION	DATE APPROVED
Initial review	3/22