MEDICAL MUTUAL®

Drug Policy

Policy:	**201021-MRX (10-23)**	**Initial Effective Date:** **12/21/2010** **Annual Review Date:** **08/21/2025** **Last Revised Date:** **08/21/2025**
Code(s):	**HCPCS J1290**	
SUBJECT:	**Kalbitor (ecallantide)**	

Subject to: ☒Site of Care
☒Medication Sourcing

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

Initial and renewal requests for the medication(s) listed in this policy are subject to site of care management. When billed under the medical benefit, administration of the medication will be restricted to a non-hospital facility-based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless the member meets the site of care exception criteria. To view the exception criteria and a list of medications subject to site of care management please click here.

I. Length of Authorization

- Initial*: Prior authorization validity will be provided initially for 12 weeks.
- Renewal*: Prior authorization validity may be renewed every 12 weeks thereafter.

*The cumulative amount of medication(s) the patient has on-hand, indicated for the acute treatment of HAE, will be taken into account when authorizing. The authorization will provide a sufficient quantity in order for the patient to have a cumulative amount of HAE medication on-hand in order to treat up to 4 acute attacks per 4 weeks for the duration of the authorization.

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- 240 billable units per 28 days

III. Initial Approval Criteria [1]

Submission of supporting clinical documentation (including but not limited to medical records, chart notes, lab results, and confirmatory diagnostics) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission as part of the evaluation of this request. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e., genetic, and mutational testing)

supporting initiation when applicable. Please provide documentation via direct upload through the PA web portal or by fax. Failure to submit the medical records may result in the denial of the request due to inability to establish medical necessity in accordance with policy guidelines.

Coverage is provided in the following conditions:

- Patient is at least 12 years of age; **AND**

Universal Criteria [1,13,18]

- Must be prescribed by, or in consultation with, a specialist in allergy, immunology, hematology, pulmonology, or medical genetics; **AND**
- Will not be used in combination with another agent indicated for the treatment of acute attacks (i.e., Berinert [C1 esterase inhibitor, human], Firazyr [icatibant], Ruconest [C1 esterase inhibitor, recombinant]); ***NOTE****: Requests for combination duplicate therapy may be appropriate in some situations and will be reviewed on a case-by-case basis*; **AND**
- Confirmation the patient is avoiding the following possible triggers for HAE attacks:
  - Estrogen-containing oral contraceptive agents AND hormone replacement therapy; **AND**
  - Antihypertensive agents containing ACE inhibitors or angiotensin II receptor blockers (ARBs); **AND**
  - Dipeptidyl peptidase IV (DPP-IV) inhibitors (e.g., sitagliptin); **AND**
  - Neprilysin inhibitors (e.g., sacubitril); **AND**

Treatment of acute attacks of Hereditary Angioedema (HAE) † Φ [1,13,18,19,21]

- Patient has a history of moderate to severe cutaneous attacks (without concomitant hives) OR abdominal attacks OR mild to severe airway swelling attacks of HAE (i.e., debilitating cutaneous/gastrointestinal symptoms OR laryngeal/pharyngeal/tongue swelling); **AND**
- Patient has one of the following clinical presentations consistent with a HAE subtype§, which must be confirmed by repeat blood testing (treatment for acute attack should not be delayed for confirmatory testing):

HAE I (C1-Inhibitor deficiency) § [13,18,19,21]

• Low C1 inhibitor (C1-INH) antigenic level (C1-INH antigenic level below the lower limit of normal as defined by the laboratory performing the test); **AND** • Low C4 level (C4 below the lower limit of normal as defined by the laboratory performing the test); **AND** • Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test); **AND** ○ Patient has a family history of HAE; **OR** ○ Acquired angioedema has been ruled out (i.e., patient onset of symptoms occurs prior to 30 years of age, normal C1q levels, patient does not have underlying disease such as lymphoma or benign monoclonal gammopathy [MGUS], etc.)
HAE II (C1-Inhibitor dysfunction) § [18,21]
• Normal to elevated C1-INH antigenic level; **AND** • Low C4 level (C4 below the lower limit of normal as defined by the laboratory performing the test); **AND** • Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)
HAE with normal C1INH (formerly known as HAE III) § [18,19,21]
• Normal to near normal C1-INH antigenic level; **AND** • Normal to near normal C4 level; **AND** • Normal to near normal C1-INH functional level; **AND** • Repeat blood testing during an attack has confirmed the patient does not have abnormal lab values indicative of HAE I or HAE II; **AND** • Either of the following: ○ Patient has a known HAE-causing mutation (e.g., mutation of coagulation factor XII gene [F12 mutation], mutation in the angiopoietin-1 gene, mutation in the plasminogen gene, mutation in the kininogen 1 gene, mutation in the myoferlin gene, mutation in the heparan sulfate- glucosamine 3-O-sulfotransferase 6 gene, etc.); **OR** ○ Patient has a family history of HAE and documented lack of efficacy of chronic high-dose antihistamine therapy (*e.g. cetirizine standard dosing at up to four times daily or an alternative equivalent, given for at least one month or an interval long enough to expect three or more angioedema attacks*)

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); **Φ** Orphan Drug

IV. Renewal Criteria [1]

Coverage can be renewed based upon the following criteria:

- Patient must continue to meet the universal and other indication-specific relevant criteria identified in section III; **AND**
- Significant improvement in severity and duration of attacks has been achieved and sustained; **AND**

- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include serious hypersensitivity reactions, including anaphylaxis, etc.; **AND**
- The cumulative amount of medication(s) the patient has on-hand, indicated for the acute treatment of HAE, will be taken into account when authorizing. The authorization will provide a sufficient quantity in order for the patient to have a cumulative amount of HAE medication(s) on-hand in order to treat up to 4 acute attacks per 4 weeks for the duration of the authorization.

V. Dosage/Administration [1]

Indication	Dose
Treatment of Acute Hereditary Angioedema (HAE) attack	Administer 30 mg subcutaneously by a healthcare professional in three 10 mg injections. An additional dose of 30 mg may be administered if the attack persists. Not to exceed a total of two 30 mg doses (60 mg) in 24 hours. ***Note:** Kalbitor should ONLY be administered by a healthcare professional.*

VI. Billing Code/Availability Information

HCPCS Code:

- J1290 – Injection, ecallantide, 1 mg; 1 billable unit = 1 mg

NDC:

- Kalbitor 10 mg/mL; carton of 3 single-use vials: 47783-0101-xx

VII. References

1. Kalbitor [package insert]. Lexington, MA; Takeda Pharmaceuticals U.S.A., Inc.; November 2021. Accessed June 2025.
2. Cicardi M, Levy RJ, McNeil DL, et al. Ecallantide for the treatment of acute attacks in hereditary angioedema. N Engl J Med. 2010 Aug 5;363(6):523-31. doi: 10.1056/NEJMoa0905079.
3. Bowen T, Cicardi M, Farkas H, et al. Canadian 2003 International Consensus Algorithm For the Diagnosis, Therapy, and Management of Hereditary Angioedema. J Allergy Clin Immunol. 2004 Sep;114(3):629-37.
4. Bygum A, Andersen KE, Mikkelsen CS. Self-administration of intravenous C1-inhibitor therapy for hereditary angioedema and associated quality of life benefits. Eur J Dermatol. Mar-Apr 2009;19(2):147-151.
5. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy and management of hereditary angioedema. Allergy Asthma Clin Immunol. 2010;6(1):24.
6. Craig T, Aygören-Pürsün E, Bork K, et al. WAO Guideline for the Management of Hereditary Angioedema. World Allergy Organ J. 2012 Dec;5(12):182-99.

7. Gompels MM, Lock RJ, Abinun M, et al. C1 inhibitor deficiency: consensus document. Clin Exp Immunol. 2005;139(3):379.
8. Betschel S, Badiou J, Binkley K, et al. Canadian hereditary angioedema guideline. Asthma Clin Immunol. 2014 Oct 24;10(1):50. doi: 10.1186/1710-1492-10-50.
9. Zuraw BL, Bernstein JA, Lang DM, et al. A focused parameter update: hereditary angioedema, acquired C1 inhibitor deficiency, and angiotensin-converting enzyme inhibitor-associated angioedema. J Allergy Clin Immunol. 2013 Jun;131(6):1491-3. doi: 10.1016/j.jaci.2013.03.034.
10. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. J Allergy Clin Immunol Pract. 2013 Sep-Oct;1(5):458-67.
11. Frank MM, Zuraw B, Banerji A, et al. Management of children with Hereditary Angioedema due to C1 Inhibitor deficiency. Pediatrics. 2016 Nov. 135(5)
12. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: Consensus of an international expert panel. Allergy Asthma Proc. 2012;33 Suppl 1:145-156.
13. Maurer M, Mager M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema-The 2017 revision and update. Allergy. 2018 Jan 10. doi: 10.1111/all.13384.
14. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. Ann Allergy Asthma Immunol. 2012;109:395-402.
15. Wintenberger C, Boccon-Gibod I, Launay D, et al. Tranexamic acid as maintenance treatment for non-histaminergic angioedema: analysis of efficacy and safety in 37 patients. Clin Exp Immunol. 2014 Oct; 178(1): 112–117.
16. Saule C, Boccon-Gibod I, Fain O, et al. Benefits of progestin contraception in non-allergic angioedema. Clin Exp Allergy. 2013 Apr;43(4):475-82.
17. Frank MM, Sergent JS, Kane MA, et al. Epsilon aminocaproic acid therapy of hereditary angioneurotic edema; a double-blind study. N Engl J Med. 1972:286:808-812.
18. Betschel S, Badiou J, Binkley K, et al. The International/Canadian Hereditary Angioedema Guideline. Allergy Asthma Clin Immunol. 2019; 15: 72. Published online 2019 Nov 25. doi: 10.1186/s13223-019-0376-8.
19. Busse PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. J Allergy Clin Immunol Pract. 2021 Jan;9(1):132-150.e3. doi: 10.1016/j.jaip.2020.08.046.
20. Riedl M, Campion M, Horn PT, et al. Response time for ecallantide treatment of acute hereditary angioedema attacks. Ann Allergy Asthma Immunol. 2010 Dec;105(6):430-436.e2. doi: 10.1016/j.anai.2010.09.005.

21. Maurer M, Magerl M, Betschel S, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – The 2021 revision and update. Allergy. 2021 Nov 22. doi: 10.1111/all.15214

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D84.1	Defects in the complement system

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA

MEDICAL MUTUAL®

Drug Policy

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

Prior approval is required for HCPCS Codes J1290