Medical Policy:

Haegarda® (C1 esterase inhibitor human) and Takhzyro® (lanadelumab-flyo) (Subcutaneous)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.129	January 2, 2024	September 17, 2019

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Length of Authorization

Initial Coverage will be provided for 6 months and may be renewed.

Dosing Limits [Medical Benefit]

Takhzyro:

- 300 mg per 14 days

Haegarda

- 5,600 billable units per 28 days

Guideline

I. Initial Approval Criteria

1. **Prophylaxis against angioedema attacks of Hereditary Angioedema (HAE):**

A. Must be prescribed by, or in consultation with a specialist in: allergy, immunology, hematology, pulmonology, or medical genetics; **AND**
B. The patient has HAE type I or type II as confirmed by the following diagnostic criteria
    i. Patient has low levels of functional C1-INH protein (< 50% of normal) at baseline, as defined by the laboratory reference values; **AND**
    ii. Patient has lower than normal serum C4 levels at baseline, as defined by the laboratory reference values; **AND**
C. Patient must be at least ≥ 2 years of age for Takhzyro and ≥ 6 years of age for Haegarda; **AND**
D. Patient has a history of one of the following criteria for long-term HAE prophylaxis:
    i. History of two (2) or more severe HAE attacks (i.e. airway swelling, debilitating cutaneous or gastrointestinal episodes) per month; **OR**
    ii. Patient is disabled more than 5 days per month by HAE; **OR**
    iii. History of at least one laryngeal attack caused by HAE; **AND**
E. Member has tried and failed treatment with acute therapy (i.e., Kalbitor, Firazyr, Ruconest, or Berinert) and it did not result in meaningful outcomes, such as decreased severity of attacks, avoidance of hospitalization, etc; **AND**
F. Medications known to cause angioedema (i.e. ACE-Inhibitors, estrogens, angiotensin II receptor blockers) have been evaluated and discontinued when appropriate, regardless of HAE type.

II. Renewal Criteria

1. Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: severe hypersensitivity reactions, serious thrombotic events, laryngeal attacks, etc.
2. Significant improvement in severity, duration, and/or frequency of attacks have been achieved and sustained
3. Documentation including frequency of administration will also be required at time of recertification to monitor for appropriate use.

For Takhzyro

1. If 0 attacks have occurred during the prior 6 months while on the medication, a trial with an extended dosing interval of 300mg every four weeks will be required based on package labeling which states that a dose of 300 mg every four weeks is also effective.
2. If documentation is provided that the patient is not attack free (has experienced at least 1 attack), but has had a decrease in severity, duration, and/or frequency of attacks while on the medication compared to baseline, a dosing frequency of 300mg every 2 weeks can be continued.
3. If documentation is provided that the patient has not experienced a decrease in severity, duration, and/or frequency of attacks while on the medication compared to baseline (no benefit from the medication), further treatment will not be authorized.

Dosage/Administration

Drug	Indication	Dose
Takhzyro	Hereditary Angioedema (HAE) prophylaxis	**Adults/adolescents ≥12 years old** **Initial:** 300 mg subQ every 2 weeks; consider dosing once every 4 weeks when patient is attack free for greater than 6 months **Pediatric patients 6 to less than 12 years** 150mg subQ every 2 weeks; consider dosing every 4 weeks if the patient is attack free for more than 6 months **Pediatric patients 2 to less than 6 years** 150mg subQ every 4 weeks
Haegarda	Hereditary Angioedema (HAE) prophylaxis	**Adults/adolescents** 60 International Units (IU)/kg SC injection every 3 or 4 days

Limitations/Exclusions

- Takhzyro and Haegarda (C1 Esterase Inhibitor Human) are not considered medically necessary for indications other than those listed above due to insufficient evidence of therapeutic value.
- Takhzyro and Haegarda must be used as a prophylaxis – not for acute treatment of HAE

Applicable Procedure Codes

Code	Description
J0599	Injection, c-1 esterase inhibitor (human), (Haegarda), 10 units
J0593	Injection, lanadelumab-flyo, (Takhzyro), 1 mg, effective 10/01/19

Applicable NDCs

Code	Description
47783-0644-01	Takhzyro solution single-dose vial 150 mg/1 mL
63833-0829-02	Haegarda powder for solution 3000 IU
63833-0828-02	Haegarda powder for solution 2000 IU

ICD-10 Diagnoses

Code	Description
D84.1	Defects in the complement system

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	1/2/2024	Annual Review: Initial Criteria: HAE: Removed: "Patient has a documented contraindication, severe intolerance, or therapeutic failure to 17 alpha-alkylated androgens (e.g. danazol) for HAE prophylaxis; AND"
EmblemHealth & ConnectiCare	4/10/2023	Updated age for Takhyzro from > 12 years to > 2 years; updated Takhzyro dosing to include ages 2 to 12: **Pediatric patients 6 to less than 12 years** 150mg subQ every 2 weeks; consider dosing every 4 weeks if the patient is attack free for more than 6 months **Pediatric patients 2 to less than 6 years** 150mg subQ every 4 weeks
EmblemHealth & ConnectiCare	1/13/2023	Transfer to New Template
EmblemHealth & ConnectiCare	10/05/20	Updated age criteria for Haegarda from ≥12 years of age to ≥ 6 years of age
EmblemHealth & ConnectiCare	09/17/19	Updated title to reflect brand and generic names, and added age criteria for Haegarda.

EmblemHealth & ConnectiCare	09/17/19	Added J0593, for Takhzyro, effective 10/01/19

References

1. Haegarda® subcutaneous injection [prescribing information]. Kankakee, IL: CSL Behring LLC; June 2017.
2. Bowen T, Cicardi M, Farkas H, et al. 2010 international consensus algorithm for the diagnosis, therapy and management of hereditary angioedema. Ann Allergy Asthma Immunol. 2010;6:24.
3. Craig T, Pursun EA, Bork K, et al. WAO guideline for the management of hereditary angioedema. WAO Journal. 2012;5:182-199.
4. 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: In Practice. 2013;1:458-467. Available at: https://haei.org/wp-content/uploads/2015/04/Zuraw-B-L-US-HAEA-MAB-2013-Recommendations.pdf. Accessed on June 27, 2017.
5. Wagenaar-Bos IGA, Drouet C, Aygoren-Pursun E, et al. Functional C1-inhibitor diagnostics in hereditary angioedema: assay evaluation and recommendations. J Immunol. Methods. 2008;338:14-20.
6. 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:S145-S156.
7. Magerl M, Germenis AE, Maas C, et al. Hereditary angioedema with normal C1 inhibitor. Update on evaluation and treatment. Immunol Allergy Clin N Am. 2017;37:571-584.
8. Takhzyro (lanadelumab-flyo) [prescribing information]. Lexington, MA: Dyax Corp; January 2018.