Washington State Health Care Authority

Hematological Agents: Hereditary Angioedema Agents - Prophylaxis

Medical policy no. 85.80.20.AA-1 Effective Date: 4/1/2024

Related medical policies:

Policy Name	Indications
85.82.00.AA – Hematological Agents: Hereditary Angioedema Agents - Acute	Treatment of hereditary angioedema, acute attacks

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the list of the current Apple Health Preferred Drug List (AHPDL), please visit: https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx

Medical necessity

Drug	Medical Necessity
C1 Esterase Inhibitor (Cinryze) C1 Esterase Inhibitor (Haegarda) Berotralstat (Orladeyo) Lanadelumab-FLYO (Takhzyro)	**Hematological Agents: Hereditary Angioedema Agents - Prophylaxis** may be considered medically necessary in patients who meet the criteria described in the clinical policy below. If all criteria are not met, the clinical reviewer may determine there is a medically necessary need and approve on a case-by-case basis. The clinical reviewer may choose to use the reauthorization criteria when a patient has been previously established on therapy and is new to Apple Health.

Clinical policy:

Clinical Criteria	
Hereditary Angioedema, Prophylaxis C1 Esterase Inhibitor (Cinryze)	C1 esterase inhibitor (Cinryze), C1 esterase inhibitor (Haegarda), berotralstat (Orladeyo), or lanadelumab-FLYO (Takhzyro) may be approved when all of the following criteria are met:

C1 Esterase Inhibitor (Haegarda) Berotralstat (Orladeyo) Lanadelumab-FLYO (Takhzyro)	1. Patient meets the following FDA approved age requirements: a. For C1 esterase inhibitor (Cinryze or Haegarda), 6 years or older; **OR** b. For berotralstat, 12 years or older; **OR** c. For lanadelumab, 2 years or older; **AND** 2. Prescribed by, or in consultation with, a specialist (e.g. allergist, immunologist, pulmonologist, hematologist) with expertise in managing hereditary angioedema; **AND** 3. Patient is not prescribed more than one agent that treats hereditary angioedema prophylaxis (e.g. Cinryze, Haegarda, Orladeyo, Takhzyro); **AND** 4. Diagnosis of hereditary angioedema with documentation supporting one of the following: a. For HAE-1: i. C1-INH function - low; **AND** ii. C1-INH protein (antigenic) level - low; **AND** iii. C4 level - low; **OR** b. For HAE-2: i. C1-INH function - low; **AND** ii. C1-INH protein (antigenic) level - normal or elevated; **AND** iii. C4 level - low; **AND** 5. Provider attests that the patient has been evaluated for triggers that may induce attacks and is being counseled to avoid triggers; **AND** 6. Baseline outcomes measures are documented with all the following within the past 6 months: a. Number of hospitalizations b. Number of emergency room visits c. Frequency acute therapies are used for the treatment of hereditary angioedema attacks. If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) C1 esterase inhibitor (Cinryze), C1 esterase inhibitor (Haegarda), berotralstat (Orladeyo), or lanadelumab-FLYO (Takhzyro) may be approved when all of the following criteria are met: 1. Patient is not prescribed more than one agent that treats hereditary angioedema prophylaxis (e.g. Cinryze, Haegarda, Orladeyo, Takhzyro); **AND** 2. Outcomes measures within the past 6 months is submitted with all of the following: a. Number of hospitalizations b. Number of emergency room visits c. Frequency acute therapies are used for the treatment of hereditary angioedema attacks; **AND**

	3. Documentation is submitted demonstrating disease stability or a positive clinical response [e.g. decrease in frequency that acute therapies are used for HAE, decrease in hospitalizations]; **AND** 4. For patients prescribed Takhzyro with every 2 week dosing, documentation is submitted that every 4 week dosing has been considered for patients that have been attack-free for 6 months. If ALL criteria are met, the request will be authorized for **12 months.**

Dosage and quantity limits

Drug	Indication	FDA Approved Dosing	Dosage Form and Quantity Limit
Cinryze	Hereditary angioedema, prophylaxis	-12 years or older: Up to 2000 units, not to exceed 80 units per kg, twice a week -6 to 11 years: Up to 1000 units, twice a week	500 IU Vials • 12 years or older: Up to 32 vials per 28 days • 6 to 11 years: Up to 16 vials per 28 days
Haegarda	Hereditary angioedema, prophylaxis	-6 years or older: 60 units/kg twice a week	2000 IU and 3000 IU vials • 60 international units per kg twice a week; Each dose is rounded to the lowest number of 2000 or 3000 unit vials to minimize waste.
Orladeyo	Hereditary angioedema, prophylaxis	-Up to 150 mg once daily	110 mg and 150 mg capsules • 28 capsules per 28 days
Takhzyro	Hereditary angioedema, prophylaxis	-12 years or older: 300 mg every 2 to 4 weeks -6 years to younger than 12 years: 150 mg every 2 to 4 weeks -2 years to younger than 6 years: 150 mg every 4 weeks	150 mg per 1 ml • 12 years or older: 600 mg per 28 days • 6 years to younger than 12 years: 300 mg per 28 days • 2 years to younger than 6 years: 150 mg per 28 days

Coding:

HCPCS Code	Description
J0593	Injection, lanadelumab-flyo, 1 mg
J0598	Injection, C-1 esterase inhibitor (human), cinryze, 10 units
J0599	Injection, C-1 esterase inhibitor (human), (haegarda), 10 units

Background:

Hereditary Angioedema (HAE) is a rare disease characterized by recurrent attacks of severe swelling of the skin and mucous membranes. Swelling typically occurs in the hands, feet, limbs, face, intestinal tract, or airway. Emotional stress, physical stress, and dental procedures are the most common triggers, however, various triggers of attacks can occur. There are two common forms of HAE, Type I and Type II. Both forms may be managed with acute and prophylaxis treatment depending on severity, attack frequency and drug tolerability. The International World Allergy Organization (WAO)/European Academy of Allergy and Clinical Immunology (EAACI) guidelines recommend the use of plasma-derived C1 inhibitor, lanadelumab or berotralstat as first-line for long-term prophylaxis.

The safety and efficacy of Cinryze for hereditary angioedema (HAE) prophylaxis was demonstrated in two 12-week trials. Study 1 (n=24) was a randomized, double blind, placebo controlled cross-over study. Participants in study 1 had a minimum of 2 hereditary angioedema attacks per month. The mean age was 38.1 years, range 9 to 73. Efficacy was based off number of attacks during the 12-week period. An attack was defined as a participant-reported indication of swelling at any location following a report of no swelling from the previous day. The average number of HAE attacks for Cinryze vs placebo was 6.1 vs 12.7, respectively. However, the effectiveness was variable among the participants. Study 2 (n=12) was a randomized, single-blind, dose-ranging cross-over study consisting of pediatric patients aged 7 to 11 years. Compared to baseline, the mean absolute reduction in the normalized number of HAE attack was 2.6 (71.1%) and 3.0 (84.5%) for Cinryze 500 U and Cinryze 1000 U, respectively. Adverse effects ≥5% include headache, nausea, rash, vomiting and fever.

The safety and efficacy of Haegarda for HAE prophylaxis was demonstrated in two clinical trials. Study 1 (n=90) was a 16-week randomized, open-label, active treatment-controlled study. Participants had HAE type I or II and the median age was 40 (range 12 to 72). For Haegarda vs placebo, time normalized number of HAE attacks per month was 0.52 vs 4.03 at a dose of 60 IU/kg, respectively. Study 2 (n=120) was a randomized, open-label, active treatment-controlled study. Study participants had HAE type I or II and the median age was 41 (range 8 to 72). 93.1% of participants had a ≥50% reduction in time-normalized number of HAE attacks compared to baseline, 86.9% of participants had <1 HAE attack per 4-week period, median annualized attack rates was 1.0 and proportion of HAE attack-free participants was 44.3%. Adverse effects ≥4% include injection site reactions, hypersensitivity, nasopharyngitis and dizziness.

The safety and efficacy of Orladeyo was demonstrated in Part 1 of a randomized, double-blind, placebo-controlled, parallel-group study (n=120). Participants had at least 2 confirmed attacks within the first 8 weeks of the run-in period. The Orladeyo 150 mg group had a 44.2% rate reduction in HAE attack rate compared to placebo, 1.31 vs 2.35, respectively. Adverse effects ≥5% include abdominal pain, vomiting, diarrhea, back pain, gastroesophageal reflux disease headache, fatigue, and flatulence.

The safety and efficacy of Takhzyro was demonstrated in a 26-week randomized, double-blind, placebo-controlled parallel-group study (n=125). Participants had Type I or II HAE and were 12 years of age or older and had at least one confirmed attack per 4 weeks. 52% of participants had ≥3 attacks per month during the run-in period. The mean monthly HAE attack rate after 182 days was 1.92, 0.48, 0.53, and 0.26 for placebo, Takhzyro 150 mg every 4 weeks, Takhzyro 300 mg every 4 weeks, and Takhzyro 300 mg every 2 weeks study groups, respectively. Adverse effects ≥10% include injection site reactions, upper respiratory infection, headache, rash, myalgia, dizziness and diarrhea.

References

1. 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. 2022;77:1961-1990.
2. Cinryze [Prescribing Information]. March 2022. ViroPharma Biologics LLC. March 2022.
3. Haegarda [Prescribing Information]. Marburg, Germany. CSL Behring GmbH. September 2020.
4. Orladeyo [Prescribing Information]. Durham, NC: BioCryst Pharmaceuticals. December 2020.
5. Takhzyro[Prescribing Information]. Lexington, MA. Dyax Corp. November 2018.

History

Approved Date	Effective Date	Version	Action and Summary of Changes
10/18/2023	04/01/2024	85.80.20.AA-1	New Policy