

## Hereditary Angioedema Prophylaxis

**Cinryze (C1 esterase inhibitor [human]), Haegarda (C1 esterase inhibitor [human]), Orladeyo (Berotralstat), Takhzyro (lanadelumab-flyo), and Andembry (garadacimab-gxii), Dawnzera (donidalorsen)**

### Products for prophylaxis against attacks of hereditary angioedema (HAE):

- **Cinryze** (C1 esterase inhibitor [human])
- **Haegarda** (C1 esterase inhibitor [human])
- **Orladeyo** (berotralstat)
- **Takhzyro** (lanadelumab-flyo)
- **Andembry** (garadacimab-gxii)
- **Dawnzera** (donidalorsen)

### Coverage Criteria:

1. Prescribed by a hematologist, allergist or immunologist; **and**,
2. Patient has a diagnosis of hereditary angioedema (HAE) as confirmed by one of the following (Note: lab reference values and documentation confirming diagnosis required):
  - a. A C1 inhibitor deficiency or dysfunction (HAE-C1INH [Type I or Type II]) as documented by both of the following:
    - i. A C4 level below the lower limit of normal; **and**,
    - ii. One of the following:
      1. C1 inhibitor (C1INH) antigenic level below the lower limit of normal; **or**,
      2. C1 inhibitor (C1INH) functional level below the lower limit of normal; **or**,
  - b. Normal C1 inhibitor (HAE-nl-C1INH [previously Type III]) as documented by both of the following:
    - i. Confirmed mutation in one of the following genes as confirmed by genetic testing: coagulation factor XII (F12), plasminogen (PLG), angiopoietin-1 (ANGPT1), kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), myoferlin (MYOF)); **and**,
    - ii. All other causes of angioedema have been ruled out; **and**,
3. Requested medication is used to prevent future attacks when there is a history of at least 2 attacks per month, with at least one symptom of a moderate or severe attack including one of the following:
  - a. Airway swelling; **or**,
  - b. Nausea and vomiting or severe abdominal pain; **or**,
  - c. Facial swelling or painful distortion of the face; **and**,
4. Patient is not prescribed more than one therapy (e.g., Cinryze, Haegarda, Takhzyro, Orladeyo, Andembry, Dawnzera) for prophylaxis; **and**,
5. For Cinryze, Orladeyo, Andembry, or Dawnzera, patient has tried and failed, or has a contraindication to the use of both of the following:
  - a. Takhzyro; **and**,
  - b. Haegarda; **and**,

6. Documentation of a hereditary angioedema management plan and use of the requested therapy is in accordance with that plan (Note: submission of plan is required); **and**,
7. Prescribed within FDA approved dosing regimen, including appropriate age (Note: a recent weight within the past 30 days must be provided for weight-based regimens per medical documentation).

**Renewal Criteria:**

1. Medical chart documentation of the number and severity of the HAE attacks occurring in the previous 6 months; **and**,
2. Patient has experienced a reduction in the number of HAE attacks; **and**,
3. For patients prescribed Takhzyro, dosing frequency has been changed to one injection per month if the patient has been attack-free for 6 months.

**Coverage Duration:**

Initial authorization will be provided for 6 months.

Reauthorization will be provided for 6 months.

**Other Criteria:**

Cinryze: For patients at least 6 years of age: initial maximum dose of 1,000 units every 3 to 4 days.

Patients requiring doses exceeding this limit will require a trial with another alternative (in addition to Takhzyro and Haegarda) for HAE prophylaxis therapy and allowed up to a maximum of 25,000 units per 30 days if approved.

Haegarda: For patients at least 6 years of age: maximum of 60,000 units per 30 days.

Takhzyro:

- For patients 2 years to 6 years of age: maximum of one 150 mg dose per 28 days.
- For patients 6 years to 12 years of age: maximum of two 150 mg doses per 28 days for initial 6 months.
- For patients 12 years or older: maximum of two 300 mg doses per 28 days for initial 6 months.

Orladeyo: For patients at least 12 years of age: maximum of one capsule per day.

Andembry: For patients at least 12 years of age: maximum of one 200 mg autoinjector per 30 days.

Dawnzera: For patients at least 12 years of age: maximum of one 80 mg autoinjector per 28 days