UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2024 P 2031-14
Program	Prior Authorization/Medical Necessity
Medication	Cinryze® (C1 esterase inhibitor, human)* * Cinryze is excluded from coverage for the majority of our benefits
P&T Approval Date	8/2014, 8/2015, 7/2016, 7/2017, 7/2018, 7/2019, 6/2020, 3/2021, 3/2022, 3/2023, 3/2024
Effective Date	6/1/2024

1. Background:
Cinryze is a plasma-derived C1 esterase inhibitor (human) indicated for routine prophylaxis against angioedema attacks in adolescent, adult, and pediatric (6 years of age and above) patients with hereditary angioedema (HAE).[1]

2. Coverage Criteria [a]:

A. Initial Authorization

1. **Cinryze** will be approved based on **all** of the following criteria:

   a. Diagnosis of hereditary angioedema (HAE) as confirmed by **one** of the following:

      (1) C1 inhibitor (C1-INH) deficiency or dysfunction (Type I or II HAE) as documented by **one** of the following (per laboratory standard):

         (a) C1-INH antigenic level below the lower limit of normal
         (b) C1-INH functional level below the lower limit of normal

-OR-

      (2) HAE with normal C1 inhibitor levels and **one** of the following:

         (a) Confirmed presence of variant(s) in the gene(s) for factor XII, angiopoietin-1, plasminogen-1, kininogen-1, myoferlin, and heparan sulfate-glucosamine 3-O-sulfotransferase 6
         (b) Recurring angioedema attacks that are refractory to high-dose antihistamines with confirmed family history of angioedema
         (c) Recurring angioedema attacks that are refractory to high-dose antihistamines with unknown background de-novo mutation(s) (i.e., no family history) (HAE-unknown)

-AND-

   b. **All** of the following**:**

      (1) Prescribed for the prophylaxis of HAE attacks

-AND-

(2) Not used in combination with other products indicated for prophylaxis against HAE attacks (e.g., Haegarda, Orladeyo, Takhzyro)

-AND-

(3) Prescriber attests that patient has experienced attacks of a severity and/or frequency such that they would clinically benefit from prophylactic therapy with Cinryze

-AND-

c. Submission of medical records documenting a history of failure, contraindication, or intolerance to Haegarda (C1 esterase inhibitor, human)

-AND-

d. Prescribed by **one** of the following:

(1) Immunologist
(2) Allergist

Authorization of therapy will be issued for 12 months.

B. Reauthorization

1. **Cinryze** will be approved based on **all** of the following criteria:

a. Documentation of positive clinical response to Cinryze therapy.

-AND-

b. Reduction in the utilization of on-demand therapies used for acute attacks (e.g., Berinert, Firazyr, Ruconest) as determined by claims information, while on Cinryze therapy

-AND-

c. **Both** of the following:

(1) Prescribed for the prophylaxis of HAE attacks

-AND-

(2) Not used in combination with other products indicated for prophylaxis against HAE attacks (e.g., Haegarda, Orladeyo, Takhzyro)

-AND-

d. Prescribed by **one** of the following:

(1) Immunologist
(2) Allergist

Authorization of therapy will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Programs:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. Cinryze [package insert]. Lexington, MA: ViroPharma Biologics LLC ; February 2023.
2. Maurer M, Magerl 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.
3. Wu, E. Hereditary angioedema with normal C1 inhibitor. In: UpToDate, Saini, S (Ed), UpToDate, Waltham, MA, 2023.
4. Busse, P., Christiansen, S., Riedl, M., et. al. "US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema." *The Journal of Allergy and Clinical Immunology.* 2020 September 05.
5. 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(7):1961-1990. doi:10.1111/all.15214

Program	Prior Authorization/Medical Necessity - Cinryze (C1 esterase inhibitor, human)
Change Control	
8/2014	New program.
9/2014	Administrative change - Tried/Failed exemption for State of New Jersey removed.
8/2015	Annual review. No change.
7/2016	Annual review with no changes to the coverage criteria. Updated background and references. Added Maryland, Indiana and West Virginia coverage information.
11/2016	Administrative change. Added California coverage information.
2/2017	Administrative change. Correct Oxford effective date.
7/2017	Annual review. No change to criteria. Updated reference.
7/2018	Annual review. Updated coverage criteria. Updated references.
7/2019	Annual review. Updated background and references.
6/2020	Annual review. Aligned criteria with acute and prophylactic therapies. Removed off-label use for acute attacks. Added notation that Cinryze is

	excluded for most plans.
3/2021	Added diagnosis criteria and aligned combination use language with prophylactic therapies. Updated references.
3/2022	Annual review. Updated references.
3/2023	Annual review. Updated references.
3/2024	Annual review with update to diagnostic criteria for HAE with normal C1 inhibitor levels. Simplified reauthorization criteria. Updated reference.