Reference number(s)
7145-A

Standard Medicare Part B Management Dawnzera

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Dawnzera	donidalorsen

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications[1]

Dawnzera is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older.

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

Documentation

The following documentation must be available, upon request, for all submissions:

- For initial authorization:
  - C1 inhibitor functional and antigenic protein levels
  - F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) pathogenic variant testing, if applicable

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  - Chart notes confirming family history of angioedema and the member's angioedema was refractory to a trial of high-dose antihistamine therapy, if applicable
- For continuation of therapy, chart notes demonstrating a reduction in frequency of attacks

Coverage Criteria

Hereditary Angioedema (HAE)[1-4]

Authorization of 12 months may be granted for prevention of HAE attacks when either of the following criteria is met at the time of diagnosis:

- Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing and meets one of the following criteria:
  - C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test, or
  - Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test).
- Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
  - Member has an F12, angiopoietin-1, plasminogen, kininogen-1 (KNG1), heparan sulfate-glucosamine 3-O-sulfotransferase 6 (HS3ST6), or myoferlin (MYOF) pathogenic variant as confirmed by genetic testing, or
  - Member has a documented family history of angioedema and the member's angioedema was refractory to a trial of high-dose antihistamine therapy (i.e., cetirizine at 40 mg per day or the equivalent) for at least one month.

Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization of 12 months may be granted for prevention of HAE attacks when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The member is receiving benefit from therapy. Benefit is defined as:
  - A significant reduction in frequency of attacks (e.g., ≥ 50%) since starting prophylactic treatment, and
  - A reduction in the use of medications to treat acute attacks since starting prophylactic treatment.

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Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Dawnzera.
- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex
    - American Hospital Formulary Service- Drug Information (AHFS-DI)
    - Lexi-Drugs
    - Clinical Pharmacology
- US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema.
- Hereditary Angioedema with Normal C1 Inhibitor: an Updated International Consensus Paper on Diagnosis, Pathophysiology, and Treatment

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Dawnzera are covered.

Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for the above diagnostic criteria can be found in the US HAEA Medical Advisory Board Guidelines for the Management of Hereditary Angioedema. When HAE is suspected based on the clinical presentation, the provider should test serum C4, C1INH antigenic level, and C1INH functional level. Low C4 and low C1INH antigenic or functional levels are consistent with a diagnosis of HAE with an abnormal C1INH.

When a diagnosis of HAE with normal C1INH is suspected, additional genetic tests for factor XII, plasminogen, angiopoietin-1, and kininogen pathogenic variants should be performed. If the genetic testing is unable to be performed or a known pathogenic variant is not found, the US HAEA guidelines indicate a positive family history of recurrent angioedema and a documented lack of efficacy of high-dose antihistamine therapy for at least 1 month or an interval expected to be associated with three or more attacks of angioedema, whichever is longer, can be used as clinical criteria to support the diagnosis. The understanding of the genetic pathogenic variants associated with HAE is evolving. Veronez et al have identified additional genetic pathogenic variants not mentioned in the US HAEA guidelines. There are five new genes associated with HAE and a normal C1-INH: ANGPT1 (angiopoietin-1), PLG (plasminogen), KNG1 (kininogen), MYOF (myoferlin), and HS3ST6 (heparan sulfate-glucosamine 3-O-sulfotransferase 6).

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References

1. Dawnzera [package insert]. Carlsbad, CA: Ionis Pharmaceuticals, Inc.; August 2025.
2. Zuraw BL, Bork K, Bouillet L, et al. Hereditary Angioedema with Normal C1 Inhibitor: an Updated International Consensus Paper on Diagnosis, Pathophysiology, and Treatment. Clin Rev Allergy Immunol. 2025;68(1):24. Published 2025 Mar 7. doi:10.1007/s12016-025-09027
3. 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;9(1):132-150.e3.
4. Veronez CL, Csuka D, Sheik FR, et al. The expanding spectrum of mutations in hereditary angioedema. J Allergy Clin Immunol Pract. 2021;S2213-2198(21)00312-3.

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