

donidalorsen (Dawnzera™)

Policy # 00968

Original Effective Date: 06/01/2026

Current Effective Date: 06/01/2026

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider donidalorsen (Dawnzera™)† for routine prophylaxis against hereditary angioedema (HAE) attacks to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility will be considered for the use of donidalorsen (Dawnzera) for routine prophylaxis against HAE attacks when the following criteria are met:

- **Initial:**
 - Patient is greater than or equal to 12 years of age; AND
 - Patient has a diagnosis of HAE confirmed by appropriate laboratory test(s); AND
 - Patient has a history of laryngeal edema or airway compromise with an episode of HAE OR a history of at least 2 HAE attacks per month; AND
 - Dawnzera will not be used in combination with another agent for the prevention of HAE attacks. Other agents for the prevention of HAE attacks include C1-INH (Cinryze®, Haegarda®)†, lanadelumab-flyo (Takhzyro™)†, berotralstat (Orladeyo™)†, and garadacimab (Andembry®)†
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- **Continuation**
 - Patient has received an initial authorization for Dawnzera; AND
 - Prescriber attests that the patient has responded to Dawnzera as evidenced by a decrease in HAE attacks from baseline; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
 - Dawnzera will not be used in combination with another agent for the prevention of HAE attacks. Other agents for the prevention of HAE attacks include C1-INH (Cinryze, Haegarda), lanadelumab-flyo (Takhzyro), berotralstat (Orladeyo), and garadacimab (Andembry).
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of donidalorsen (Dawnzera) when Dawnzera will be used in combination with another agent for the prevention of HAE attacks to be **not medically necessary**.**

Based on review of available data, the Company considers the continued use of donidalorsen (Dawnzera) when the patient has not responded to Dawnzera or when Dawnzera will be used in combination with another agent for the prevention of HAE attacks to be **not medically necessary**.**

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of donidalorsen (Dawnzera) when patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational**.*

Policy Guidelines

Diagnosis of HAE can be confirmed by any of the following:

- 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 (i.e., 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); OR
- Normal C1-INH as confirmed by laboratory testing AND at least one of the following:
 - Presence of a genetic mutation associated with type 3 HAE (e.g., F12, angiotensinogenase-1, plasminogen, or kininogen-1 mutations); OR
 - Documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine for at least one month

Background/Overview

Dawnzera is an antisense oligonucleotide approved as prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients greater than or equal to 12 years of age. It is designed to reduce the production of plasma prekallikrein, a key protein that activates inflammatory mediators associated with acute HAE attacks. A dose of 80 mg should be administered subcutaneously every 4 weeks or every 8 weeks for eligible patients.

HAE is a rare genetic disease with an estimated prevalence historically reported as 1:10,000-1:50,000; however, more recent U.S. data suggest the true prevalence may be higher due to underdiagnosis. It is a potentially life-threatening disease in which there is a deficiency of or lack of functionally active complement-1 esterase inhibitor (C1-INH) in the blood. HAE is characterized by recurrent episodes of sudden attacks of non-pruritic, non-pitting, localized edema. The swelling can occur almost anywhere, but is commonly found in the following body parts: extremities, intestines

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(abdomen), face, larynx, and genitals. Swelling attacks can occur unpredictably and vary in severity and frequency. HAE is inherited in an autosomal dominant manner, and family history is a strong predictor of the disease. However, spontaneous mutation accounts for up to 25% of newly diagnosed cases.

There are three types of HAE. Type I HAE accounts for 80-85% of all cases and results in both decreased antigenic and functional levels of C1-INH. Type II HAE accounts for about 15% of all cases and results in normal antigenic C1-INH levels but decreased functional C1-INH levels. The third variant of HAE is known as HAE with normal C1-INH (previously referred to as HAE type III or estrogen-dependent HAE) and is found predominantly in women. It has been suggested that HAE with normal C1-INH is caused by activating mutations in the gene for coagulation factor XII. It should be noted that there are no randomized or controlled clinical trial data available with any therapy for use in HAE with normal C1-INH.

HAE is diagnosed by clinical history, diagnostic tests, and exclusion of other causes of angioedema. The specific tests required to make the diagnosis include C4, C1q, and C1-INH (antigenic and functional level). Genetic testing is not necessary to confirm the diagnosis of HAE, but may be helpful in selected patients.

Treatment of HAE is divided into prophylactic and on-demand treatment. Current guidelines recommend that all HAE attacks be considered for on-demand treatment. Options for on-demand treatment include C1-INH (Ruconest®, Berinert®)‡, ecallantide (Kalbitor®)‡, icatibant (Firazyr®)‡, and sebetralstat (Ekterly®)‡. The decision to begin long-term prophylaxis should be individualized and considered in all severely symptomatic patients with HAE type I or type II. Approved treatments for long term prophylaxis include C1-INH (Cinryze, Haegarda), lanadelumab-flyo (Takhzyro), berotralstat (Orladeyo), garadacimab (Andembry), and donidalorsen (Dawnzera).

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Dawnzera was approved in August 2025 to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients aged 12 years and older.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Dawnzera for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older was evaluated in a 24-week multicenter, randomized, double-blind, placebo-controlled trial (OASIS-HAE).

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OASIS-HAE included 90 adult and pediatric patients 12 years of age and older with Type I and Type II HAE who had at least 2 investigator-confirmed attacks during the 8-week run-in period. Patients were randomized to receive Dawnzera 80 mg once every 4 weeks, Dawnzera 80 mg once every 8 weeks, or matching placebo. Patients were required to discontinue other prophylactic HAE medications, except androgens and tranexamic acid, prior to entering the trial; all patients were allowed to use rescue medications for treatment of breakthrough HAE attacks.

The primary endpoint for OASIS-HAE was the HAE attack rate (number of investigator-confirmed HAE attacks per 4 weeks) from Week 0 to Week 24. Dawnzera administered subcutaneously every 4 or 8 weeks demonstrated statistically significant reductions in the HAE attack rate compared to placebo. The least squares mean attack rate in the placebo group was 2.26 (95% CI 1.66, 3.09). The least squares mean attack rate in the Dawnzera 80 mg Q4 week group was 0.44 (95% CI 0.21, 0.73) which represented an 81% reduction compared to placebo ($p < 0.001$). The least squares mean attack rate in the Dawnzera 80 mg Q8 week group was 1.02 which represented a 55% reduction compared to placebo ($p = 0.004$).

References

1. Dawnzera [package insert]. Ionis Pharmaceuticals, Inc. Carlsbad, CA. Updated September 2025.
2. Dawnzera New Drug Review. IPD Analytics. Updated September 2025.

Policy History

Original Effective Date: 06/01/2026

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05/07/2026 Medical Policy Committee review

05/13/2026 Medical Policy Implementation Committee approval. New policy.

Next Scheduled Review Date: 05/2027

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

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****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan’s authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan’s pharmacy benefit.