LOUISIANA BLUE

danicopan (Voydeya™)

Policy # 00902
Original Effective Date: 12/01/2024
Current Effective Date: 12/01/2024

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.

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 danicopan (Voydeya™)‡ for the treatment of paroxysmal nocturnal hemoglobinuria to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for danicopan (Voydeya) for the treatment of paroxysmal nocturnal hemoglobinuria will be considered when the following criteria are met:

- Initial requests (6 months)
  - Patient has a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH) confirmed by documentation of peripheral blood high sensitivity flow cytometry results showing a granulocyte or monocyte clone size of ≥ 5%; AND
  - Patient has been on a stable dose of eculizumab (Soliris®)‡ or ravulizumab (Ultomiris™)‡ for at least 6 months; 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.)*
  - Patient is experiencing clinically significant extravascular hemolysis while receiving Soliris or Ultomiris as evidenced by objective laboratory findings. Examples of objective laboratory findings include reduction in hemoglobin levels, elevated reticulocyte counts, increased transfusion requirements, and transfusion dependence; AND
  - Voydeya will be used in combination with Soliris or Ultomiris; AND
  - Voydeya will NOT be used in combination with pegcetacoplan (Empaveli™)‡, iptacopan (Fabhalta®)‡, or crovalimab (PiaSky®)‡.
    *(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 requests (1 year)
  - Patient has received an initial authorization for Voydeya; AND
  - According to the prescriber, patient is continuing to derive benefit from Voydeya. Examples of benefit include increase in or stabilization of hemoglobin levels, decreased transfusion requirements or transfusion independence, reductions in hemolysis, improvement in Functional Assessment of Chronic illness Therapy (FACIT)-Fatigue score; 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.)*
  - Voydeya will be used in combination with Soliris or Ultomiris; AND
  - Voydeya will NOT be used in combination with Empaveli, Fabhalta, or PiaSky.
    *(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.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of danicopan (Voydeya) when the patient has not been on a stable dose of Soliris or Ultomiris or will be using Voydeya in combination with Empaveli, Fabhalta, or PiaSky to be **not medically necessary.****

Based on review of available data, the Company considers the continued use of danicopan (Voydeya) when the patient is not deriving benefit from Voydeya 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 danicopan (Voydeya) when the patient selection criteria are not met (except those noted above as **not medically necessary****) to be **investigational.***

Background/Overview

Voydeya is a factor D inhibitor approved as add-on therapy to ravulizumab (Ultomiris) or eculizumab (Soliris) for the treatment of extravascular hemolysis (EVH) in adults with paroxysmal nocturnal hemoglobinuria. It works by inhibiting factor D, a complement system protein that plays a key role in the amplification of the complement system response. It is dosed orally three times a day and carries a black box warning similar to other complement inhibitors for the risk of serious infections caused by encapsulated bacteria.

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Paroxysmal Nocturnal Hemoglobinuria (PNH)
PNH is an acquired hematopoietic stem cell disorder associated with an acquired somatic mutation of the phosphatidylinositol glycan class A (PIGA) gene. Mutations disrupt the first step in glycophosphatidylinositol (GPI) synthesis, which causes an absence of the GPI anchor and a deficiency of GPI proteins. The absence of GPI proteins on erythrocytes makes them susceptible to attack by complement and intravascular hemolysis. Intravascular hemolysis associated with PNH leads to release of free hemoglobin, leading to anemia, hemoglobinuria, thrombosis, dysphagia, abdominal pain, pulmonary hypertension, renal impairment, and erectile dysfunction. The prevalence of PNH is estimated to be between 0.5-1.5 per million people in the general population, with an approximately equal male to female distribution. Although PNH can affect any age group, the median age at diagnosis is during the fourth decade of life. The primary clinical finding is hemolysis of red blood cells by complement, which leads to hemoglobinuria that is most prominent in the morning. Those with PNH are also susceptible to repeated, potentially life-threatning thromboses. Underlying bone marrow dysfunction may also be present and those who are severely affected may have pancytopenia. Many patients also have acquired aplastic anemia. Although less common, some patients have concomitant myelodysplasia, For unknown reasons, PNH may rarely develop into acute leukemia.

Signs and symptoms of PNH may vary with some patients exhibiting mild and stable disease for many years while other patients have severe symptoms that rapidly progress to life-threatening. However, chronic hemolysis is central to all of the symptoms and physical findings associated with PNH. Fatigue, rapid heartbeat, headaches, and chest pain and difficulty breathing while exercising can result from mild hemolysis. With severe hemolysis, disabling fatigue, dysphagia, and painful contractions of the abdomen and esophagus may occur. It is estimated that 15-30% of patients with PNH develop blood clots, particularly venous thrombosis. Diagnosis of PNH is suspected in those with unexplained hemoglobinuria or abnormally high serum lactate dehydrogenase (LDH) levels. However, flow cytometry is the main diagnostic test for the identification of PNH cells.

The only curative treatment for PNH is allogeneic hematopoietic stem cell transplant, but this is associated with significant morbidity and mortality and is typically only recommended for patients with severe bone marrow failure. The current standard of care treatments include the complement C5 inhibitor products ravulizumab (Ultomiris) and eculizumab (Soliris). Approximately 10-20% of patients treated with a C5 inhibitor experience clinically significant extravascular hemolysis which can result in continued symptoms of anemia and require blood transfusions. Additional newer treatment options for this condition include pegcetacoplan (Empaveli), a self-administered subcutaneous complement C3 inhibitor; iptacopan (Fabhalta), an oral selective inhibitor of complement factor B; and crovalimab (PiaSky), a monoclonal antibody that binds to complement C5.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Voydeya was approved in March 2024 as add-on therapy to ravulizumab or eculizumab for the treatment of extravascular hemolysis (EVH) in adults with paroxysmal nocturnal hemoglobinuria (PNH).

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 federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Voydeya in adults with PNH and clinically significant EVH was assessed in a multiple-region, randomized, double-blind, placebo-controlled study. Clinically significant EVH was defined by anemia (hemoglobin $\leq$ 9.5 g/dL) with absolute reticulocyte count $\geq$ 120 x 10^9/L with or without transfusion support. The study enrolled patients with PNH who had been treated with a stable dose of ravulizumab or eculizumab for at least the previous 6 months. Voydeya was administered orally at 150 mg three times a day, escalated to 200 mg three times a day depending on the clinical response.

Patients were randomized to Voydeya or placebo in a 2:1 ratio for 12 weeks in addition to background ravulizumab or eculizumab treatment. After Week 12, all patients received Voydeya in combination with their background ravulizumab or eculizumab treatment up to Week 24. After Week 24, patients could enter a long-term extension period and continue to receive Voydeya with background ravulizumab or eculizumab.

Efficacy was based on the change in hemoglobin (Hgb) level from Baseline to Week 12 and was established based on demonstration of superiority of Voydeya in combination with ravulizumab or eculizumab compared to placebo in combination with ravulizumab or eculizumab in all efficacy measures with statistically significant results. In the Voydeya group (n=24), the mean change from Baseline to Week 12 was 2.9 g/dL. In the Placebo group (n=21), the mean change from Baseline to Week 12 was 0.5. The treatment difference was 2.4 g/dL (95% CI: 1.7, 3.2) with a p value of 0.0007.

References

1. Voydeya [package insert]. Alexion Pharmaceuticals, Inc. Boston, MA. Updated April 2024.
2. Voydeya New Drug Review. IPD Analytics. Updated May 2024.

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Policy History

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11/07/2024 Medical Policy Committee review
11/13/2024 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 11/2025

*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.

**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.

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‡ 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.