09-J4000-88

Original Effective Date: 06/15/24

Reviewed: 05/14/25

Revised: 06/15/25

Subject: Danicopan (Voydeya™) Tablets

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Paroxysmal Nocturnal Hemoglobinuria (PNH) is an uncommon, life-threatening hemolytic anemia; the incidence of PNH ranges from 0.1 to 0.2 per 100,000 persons per year. PNH results from an acquired genetic deficiency in the cytolytic complement cascade that renders red blood cells (RBCs) susceptible to lysis. Chronic destruction of PNH RBCs by complement leads to serious morbidities. Increased hemolysis at night, hypothesized to result from decreased blood pH and activation of the complement system, leads to characteristic bloody morning urination. Excessive or persistent intravascular hemolysis in persons with PNH results in anemia, hemoglobinuria, and complications related to the presence of plasma-free hemoglobin (e.g., thrombosis, abdominal pain, dysphagia, erectile dysfunction, and pulmonary hypertension). Extravascular hemolysis in PNH can also occur and result in reticuloendothelial destruction in the liver and spleen. Complement inhibitors are used in the treatment of PNH to reduce hemolysis and transfusion requirements.

Danicopan (Voydeya) is an inhibitor of factor D of the alternative complement pathway and prevents the cleavage of factor B, the downstream effectors, and amplification of the terminal pathway. This prevents C3 fragment-mediated extravascular hemolysis (EVH). Danicopan is Food and Drug Administration (FDA) approved for the treatment of extravascular hemolysis in adults with paroxysmal nocturnal hemoglobinuria (PNH) in combination with ravulizumab or eculizumab. Ravulizumab and eculizumab are complement 5 (C5) inhibitors that target membrane attack complex (MAC) mediated intravascular hemolysis (IVH).

The efficacy of danicopan was evaluated in a randomized, double-blind, placebo-controlled study in adults with PNH and clinically significant EVH. EVH was defined as anemia (hemoglobin $\leq$ 9.5 g/dL) with absolute reticulocyte count $\geq$ 120 x 10^9/L with or without transfusion support. Patients had been receiving a stable dose of ravulizumab or eculizumab for the previous 6 months or longer. Patients

received danicopan or placebo for 12 weeks in combination with ravulizumab or eculizumab. The mean change from baseline in hemoglobin level at week 12 was significantly improved with danicopan as compared to placebo (2.9 vs 0.5 g/dL, p = 0.0007). The proportion of patients with hemoglobin increase of > 2 g/dL in the absence of transfusion were higher in the danicopan as compared to placebo (59.5% vs 0%). The proportion of patients with transfusion avoidance, change in fatigue score, and change in absolute reticulocyte count was also significantly improved with danicopan as compared to placebo. The most common adverse reactions occurring included vomiting and pyrexia. Danicopan has a Risk Evaluation and Mitigation Strategy (REMS) program due to the risk for serious and life-threatening infection caused by encapsulated bacteria, including *Streptococcus pneumoniae, Neisseria meningitidis, and Haemophilus influenzae* type B.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of danicopan (Voydeya) **meets the definition of medical necessity** when:

1. **Paroxysmal Nocturnal Hemoglobinuria (PNH)**
    a. Flow cytometry to confirm PNH in both red and white blood cells (with at least 5% granulocyte or monocyte clone size) – documentation must be provided
    b. **ALL** of the following – documentation must be provided:
        i. Member has been receiving a stable dose of eculizumab (Soliris, Bkemv, Epysqli) or ravulizumab (Ultomiris) for at least 6 months
        ii. Member has anemia with a hemoglobin less than or equal to 9.5 g/dL– lab documentation must be provided
        iii. Member has an absolute reticulocyte count of greater than or equal to 120 x 10^9/L – lab documentation must be provided
    c. The member will receive treatment in combination with eculizumab (Soliris, Bkemv, Epysqli) or ravulizumab (Ultomiris)
    d. The member will not receive treatment in combination with pegcetacoplan (Empaveli), iptacopan (Fabhalta), or crovalimab (Piasky)
    e. **ONE** of the following:
        i. Member has been vaccinated against encapsulated bacteria (e.g., Streptococcus pneumoniae, Neisseria meningitidis) at least 2 weeks prior to therapy initiation
        ii. Member has been vaccinated against encapsulated bacteria less than 2 weeks prior to therapy initiation and will receive prophylactic antibiotics for at least 2 weeks following vaccination

f. There is no evidence of an active infection caused by encapsulated bacteria (e.g., Streptococcus pneumoniae, Neisseria meningitidis, or Haemophilus influenzae type B)

g. The dose does not exceed 200 mg three times a day

Approval duration: 6 months

Continuation of danicopan **meets the definition of medical necessity** when **ALL** of the following are met

1. Member has a history of beneficial response to danicopan therapy for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) - examples of beneficial response include decreased requirement for transfusions, stabilization of hemoglobin, decrease in absolute reticulocyte count)– documentation must be provided
2. The member has been previously approved for danicopan in the treatment of PNH by Florida Blue or another health plan in the past 2 years, **OR** the member has previously met all indication-specific criteria for coverage
3. Member has been revaccinated against encapsulated bacteria (e.g., Streptococcus pneumoniae, Neisseria meningitidis) at least 2 weeks prior to therapy initiation according to current medical guidelines for vaccination while on danicopan therapy
4. There is no evidence of an active infection caused by encapsulated bacteria (e.g., Streptococcus pneumoniae, Neisseria meningitidis, or Haemophilus influenzae)
5. The member will receive treatment in combination with eculizumab (Soliris, Bkemv, Epysqli) or ravulizumab (Ultomiris)
6. The member will not receive treatment in combination with pegcetacoplan (Empaveli), iptacopan (Fabhalta), or crovalimab (Piasky)
7. The dose does not exceed 200 mg three times a day

Approval duration: 1 year

NOTE: Quest Diagnostics® can perform the Flow cytometry assay (PNH with FLAER) used in the diagnosis of PNH

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

Danicopan is Food and Drug Administration (FDA) approved for the treatment of extravascular hemolysis in adults with paroxysmal nocturnal hemoglobinuria in combination with ravulizumab or eculizumab.

PRECAUTIONS:

Boxed Warning

Life-threatening and fatal infections caused by encapsulated bacteria have occurred in persons treated with complement inhibitors and may become rapidly life-threatening or fatal if not recognized and treated early.

- Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in persons with complement deficiencies.
- Immunize members at least 2 weeks prior to administering the first dose of danicopan unless the risks of delaying therapy outweigh the risks of developing an infection.
- Monitor members for early signs of infections and evaluate immediately if infection is suspected.
- Danicopan is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS).

Contraindications

- Danicopan is contraindicated in persons with unresolved serious infection caused by encapsulated bacteria.

Precautions/Warnings

- Assess liver enzymes before treatment initiation and periodically during treatment. Consider interruption or discontinuation if elevations are clinically significant or if the patient becomes symptomatic.
- Monitor serum lipids periodically during treatment and initiate cholesterol-lowering medication if indicated.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, Not Otherwise Specified

ICD-10 Diagnosis Codes That Support Medical Necessity

D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request

DEFINITIONS:

None

RELATED GUIDELINES:

Eculizumab (Soliris), 09-J1000-17

Pegcetacoplan (Empaveli), 09-J4000-04

Ravulizumab (Ultomiris), 09-J3000-26

Iptacopan (Fabhalta) capsules, 09-J4000-80

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2025 [cited 2025 May 1]. Available from: http://www.clinicalpharmacology.com/.
2. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2025 May 1].
3. Voydeya (danicopan)[package insert]. Alexion Pharmaceuticals Inc. Boston, MA. Mar 2024.
4. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2025 [2025 May 1]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 05/14/25.

GUIDELINE UPDATE INFORMATION:

06/15/24	New Medical Coverage Guideline.

06/15/25	Review and revision to guideline; consisting of including use with eculizumab biosimilars and updating agents not to be used in combination.