BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

EMPAVELI™ (pegcetacoplan) subcutaneous injection
FABHALTA® (iptacopan) oral
VOYDEYA™ (danicopan) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for EMPAVELI (pegcetacoplan)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a Hematologist, Nephrologist, or Transplant Specialist or is in consultation with a Hematologist, Nephrologist, or Transplant Specialist

Indication
- Paroxysmal nocturnal hemoglobinuria (PNH)

ORIGINAL EFFECTIVE DATE: 02/17/2022 | ARCHIVE DATE: | LAST REVIEW DATE: 02/19/2026 | LAST CRITERIA REVISION DATE: 02/19/2026

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Age Requirement

- **ONE** of the following:
  - **Paroxysmal nocturnal hemoglobinuria**: 18 years of age or older
  - **Complement 3 glomerulopathy (C3G) or primary immune complex membranoproliferative glomerulonephritis (IC MPGN):** 12 years of age or older

Baseline Clinical Evaluation

- Negative pregnancy test before starting treatment
- **For Paroxysmal nocturnal hemoglobinuria (PNH) ALL** of the following**:**
  - Clinical signs or symptoms of PNH (e.g., red blood cell transfusion dependence, dyspnea, severe fatigue, thrombosis, organ dysfunction, uncontrolled pain)
  - High sensitivity flow cytometry showing absence or deficiency of glycosylphosphatidylinositol (GPI) anchored proteins (e.g., CD55, CD59) on at least two cell lineages (e.g., granulocytes and red blood cells)
  - Hemoglobin is less than or equal to 10 g/dL despite stable doses (for at least six months) of previous treatment with or without use of a complement 5 inhibitor
- **For Complement 3 glomerulopathy (C3G) or primary immune complex membranoproliferative glomerulonephritis (IC MPGN) to reduce proteinuria ALL** of the following:
  - Biopsy proven results is **ONE** of the following:
    1. Native kidney with recurrent complement 3 glomerulopathy
    2. Post transplant kidney with recurrent complement 3 glomerulopathy
    3. Native kidney with primary immune complex membranoproliferative glomerulonephritis
  - Estimated glomerular filtration rate (eGFR) greater than or equal to 30 mL/min/1.73 meter squared
  - Proteinuria greater than or equal to 1 g/day
  - Urine protein to creatinine ratio (UPCR) greater than or equal to 1 g/g

Alternative Therapies

- **For Paroxysmal nocturnal hemoglobinuria:** Failure (trial for at least three months duration), contraindication, intolerance to transfusions, corticosteroids, supplements (such as iron, folate, and vitamin B) with or without a complement 5 inhibitor
- **For Complement 3 glomerulopathy (C3G) or primary immune complex membranoproliferative glomerulonephritis (IC MPGN):** Failure (trial for at least three months duration), contraindication, intolerance to **BOTH** of the following:
  - Optimized doses of angiotensin converting enzyme inhibitors or angiotensin receptor blockers, with or without sodium glucose co transporter 2 inhibitors
  - Stable dose of immune suppressants (corticosteroid, mycophenolate or tacrolimus)

Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

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Safety

- Immunized against *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B at least two weeks prior to first dose unless risks of delaying therapy outweigh infection risk
- No use in individuals not vaccinated against encapsulated bacteria unless risks of delaying therapy outweigh infection risk
- No unresolved serious infection caused by encapsulated bacteria
- Safety and effectiveness in recurrent immune complex membranoproliferative glomerulonephritis (IC MPGN) following kidney transplant have not been established

Additional Requirements

- Empaveli, Fabhalta, and Voydeya will not be used in combination
- Empaveli and Fabhalta will not be used chronically with Soliris or Ultomiris except for four week overlap when switching from Soliris
- **For Paroxysmal nocturnal hemoglobinuria:** Switching from C5 inhibitors is **ONE** of the following:
  - Soliris (eculizumab) to Empaveli allow a four week overlap then stop Soliris
  - Ultomiris (ravulizumab) to Empaveli start Empaveli no more than four weeks after last dose of Ultomiris

Documentation Requirements

- A completed request form must be submitted including:
  - Chart notes
  - Lab results
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualification

- Continues to be seen by a Hematologist, Nephrologist, or Transplant Specialist or is in consultation with a Hematologist, Nephrologist, or Transplant Specialist

Clinical Response

- **For paroxysmal nocturnal hemoglobinuria (PNH):** Achieves and maintained **TWO** of the following:
  - Increase or stabilization of hemoglobin
  - Normalization of absolute reticulocyte count
  - Decrease in frequency of red blood cell transfusions
  - Decrease in lactase dehydrogenase
  - Decrease in pain or fatigue

- **For Complement 3 glomerulopathy (C3G) or primary immune complex membranoproliferative glomerulonephritis (IC MPGN):** Achieves and maintains **BOTH** of the following:
  - At least a 50 percent reduction in urine protein to creatinine ratio (UPCR)
  - Stabilization or improvement in estimated glomerular filtration rate (eGFR)

Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- Immunized against *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B at least two weeks prior to first dose unless risks of delaying therapy outweigh infection risk
- No use in individuals not vaccinated against encapsulated bacteria unless risks of delaying therapy outweigh infection risk
- No unresolved serious infection caused by encapsulated bacteria
- Safety and effectiveness in recurrent immune complex membranoproliferative glomerulonephritis (IC MPGN) following kidney transplant have not been established

Additional Requirements

- Empaveli, Fabhalta, and Voydeya will not be used in combination
- Empaveli and Fabhalta will not be used chronically with Soliris or Ultomiris except for four week overlap when switching from Soliris
- **For Paroxysmal nocturnal hemoglobinuria:** Switching from C5 inhibitors is **ONE** of the following:
  - Soliris (eculizumab) to Empaveli allow a four week overlap then stop Soliris
  - Ultomiris (ravulizumab) to Empaveli start Empaveli no more than four weeks after last dose of Ultomiris

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement
- Lab values that confirm safe use

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

Medical Necessity Requirements for **FABHALTA** (iptacopan)

PHARMACY COVERAGE GUIDELINE

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FABHALTA® (iptacopan) oral
VOYDEYA™ (danicopan) oral
Generic Equivalent (if available)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a Hematologist or Nephrologist or is in consultation with a Hematologist or Nephrologist

Indication
- **ONE** of the following:
  - Paroxysmal nocturnal hemoglobinuria (PNH)
  - Primary Immunoglobulin A nephropathy (IgAN), used to reduce proteinuria
  - Complement 3 glomerulopathy (C3G), used to reduce proteinuria

Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- **For Paroxysmal nocturnal hemoglobinuria (PNH) ALL** of the following**:**
  - Clinical signs or symptoms of PNH (e.g., red blood cell transfusion dependence, dyspnea, severe fatigue, thrombosis, organ dysfunction, uncontrolled pain)
  - High sensitivity flow cytometry showing absence or deficiency of glycosylphosphatidylinositol (GPI) anchored proteins (e.g., CD55, CD59) on at least two cell lineages (e.g., granulocytes and red blood cells)
  - Hemoglobin is less than or equal to 10 g/dL despite stable doses (for at least six months) of previous treatment with or without use of a complement 5 inhibitor
- **For Primary Immunoglobulin A nephropathy (IgAN), to reduce proteinuria ALL** of the following:
  - Biopsy proven IgAN
  - Urine protein to creatinine ratio (UPCR) is at least 1.0 grams per gram or greater
  - Estimated glomerular filtration rate (eGFR) is at least 20 milliliters per minute per 1.73 square meters
- **For C3 glomerulopathy (C3G), to reduce proteinuria ALL** of the following:
  - Biopsy proven, native kidney with C3 glomerulopathy
  - Estimated glomerular filtration rate (eGFR) greater than or equal to 30 mL/min/1.73 meter squared
  - Urine protein to creatinine ratio (UPCR) greater than or equal to 1 g/g

Alternative Therapies
- **For Paroxysmal nocturnal hemoglobinuria:** Failure (trial for at least three months duration), contraindication, intolerance to transfusions, corticosteroids, supplements (such as iron, folate, and vitamin B) with or without a complement 5 inhibitor
- **For Primary Immunoglobulin A nephropathy (IgAN)**
  - On a stable dose of maximally tolerated renin angiotensin system (RAS) inhibitor with or without a stable dose of a sodium glucose cotransporter 2 (SGLT 2) inhibitor
- **For Complement 3 glomerulopathy (C3G):** Failure (trial for at least three months duration), contraindication, intolerance to **ALL** of the following:
  - Optimized doses of angiotensin converting enzyme inhibitors or angiotensin receptor blockers, with or without sodium glucose cotransporter 2 inhibitors
  - Corticosteroid and/or mycophenolate

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Generic Equivalent (if available)

Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- Immunized against *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B at least two weeks prior to first dose unless risks of delaying therapy outweigh infection risk
- No use in individuals not vaccinated against encapsulated bacteria unless risks of delaying therapy outweigh infection risk
- No unresolved serious infection caused by encapsulated bacteria
- Safety and effectiveness with recurrent C3G following kidney transplant have not been established
- No use with strong CYP2C8 inhibitors (e.g., gemfibrozil)
- No use in severe renal impairment (estimated glomerular filtration rate less than 25 milliliters per minute per 1.73 square meters) with or without hemodialysis
- No use in severe hepatic impairment (Child Pugh Class C)
- Empaveli, Fabhalta, and Voydeya will not be used in combination
- Empaveli and Fabhalta will not be used chronically with Soliris or Ultomiris

Additional Requirements

- **For Paroxysmal nocturnal hemoglobinuria:** Switching from C5 inhibitors is **ONE** of the following:
  - Soliris (eculizumab) to Fabhalta start Fabhalta no later than one week after last dose of Soliris
  - Ultomiris (ravulizumab) to Fabhalta start Fabhalta no later than six weeks after last dose of Ultomiris

Documentation Requirements

- A completed request form must be submitted including:
  - Chart notes
  - Lab results: UPCR, estimated glomerular filtration rate, flow cytometry results
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualification

- Continues to be seen by a Hematologist or Nephrologist or is in consultation with a Hematologist or Nephrologist

Clinical Response

- **For Paroxysmal nocturnal hemoglobinuria (PNH)**: Achieved and maintained **TWO** of the following:

  - Increase or stabilization of hemoglobin
  - Normalization of absolute reticulocyte count
  - Decrease in frequency of red blood cell transfusions
  - Decrease in lactase dehydrogenase
  - Decrease in pain or fatigue
- **For Primary Immunoglobulin A nephropathy (IgAN):**
  - Reduction in urine protein to creatinine ratio (UPCR)
- **For Complement 3 glomerulopathy (C3G):**
  - At least a 50 percent reduction in urine protein to creatinine ratio (UPCR)
  - Stabilization or improvement in estimated glomerular filtration rate (eGFR)

Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- Immunized against *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B at least two weeks prior to first dose unless risks of delaying therapy outweigh infection risk
- No use in individuals not vaccinated against encapsulated bacteria unless risks of delaying therapy outweigh infection risk
- No unresolved serious infection caused by encapsulated bacteria
- Safety and effectiveness with recurrent C3G following kidney transplant have not been established
- No use with strong CYP2C8 inhibitors (e.g., gemfibrozil)
- No use in severe renal (estimated glomerular filtration rate less than 25 milliliters per minute per 1.73 square meters) with or without hemodialysis
- No use in severe hepatic impairment (Child Pugh Class C)
- Empaveli, Fabhalta, and Voydeya will not be used in combination
- Empaveli and Fabhalta will not be used chronically with Soliris or Ultomiris

Additional Requirements

- **For Paroxysmal nocturnal hemoglobinuria:** Switching from C5 inhibitors is **ONE** of the following:
  - Soliris (eculizumab) to Fabhalta start Fabhalta no later than one week after last dose of Soliris
  - Ultomiris (ravulizumab) to Fabhalta start Fabhalta no later than six weeks after last dose of Ultomiris

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use: UPCR, estimated glomerular filtration rate, flow cytometry

PHARMACY COVERAGE GUIDELINE

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Generic Equivalent (if available)

Continuation Therapy Criteria Approval Duration
- 12 months OR end of plan year

Medical Necessity Requirements for VOYDEYA (danicopan)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a Hematologist or is in consultation with a Hematologist

Indication
- **Paroxysmal nocturnal hemoglobinuria (PNH)** used as add on therapy to a C5 inhibitor

Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Clinical signs or symptoms of PNH (e.g., red blood cell transfusion dependence, dyspnea, severe fatigue, thrombosis, organ dysfunction, uncontrolled pain)
- High sensitivity flow cytometry showing absence or deficiency of glycosylphosphatidylinositol (GPI) anchored proteins (e.g., CD55, CD59) on at least two cell lineages (e.g., granulocytes and red blood cells)
- Hemoglobin is less than or equal to 10 g/dL despite stable doses (for at least six months) of a complement 5 inhibitor
- Absolute reticulocyte count is greater than 120 × 10^9 per liter
- Liver enzymes assessed before treatment initiation and monitored periodically

Alternative Therapies
- Failure (trial for at least six months duration), contraindication, intolerance to stable dose of Soliris (eculizumab) or Ultomiris (ravulizumab) for treatment of extravascular hemolysis with use to be as add on therapy to a C5 inhibitor

Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- Immunized against *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B at least two weeks prior to first dose unless risks of delaying therapy outweigh infection risk
- No use in individuals not vaccinated against encapsulated bacteria unless risks of delaying therapy outweigh infection risk

- No unresolved serious infection caused by encapsulated bacteria
- No use in severe hepatic impairment (Child Pugh Class C)
- Empaveli, Fabhalta, and Voydeya will not be used in combination
- Voydeya has not been shown to be effective as monotherapy and should only be prescribed as add on therapy to a C5 inhibitor

Documentation Requirements

- A completed request form must be submitted including:
  - Chart notes
  - Lab results: flow cytometry, absolute reticulocyte count, liver enzymes
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualification

- Continues to be seen by a Hematologist or is in consultation with a Hematologist

Clinical Response

- Achieved and maintained **TWO** of the following:
  - Increase or stabilization of hemoglobin
  - Normalization of absolute reticulocyte count
  - Decrease in frequency of red blood cell transfusions
  - Decrease in lactase dehydrogenase
  - Decrease in pain or fatigue

Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- Immunized against *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B at least two weeks prior to first dose unless risks of delaying therapy outweigh infection risk
- No use in individuals not vaccinated against encapsulated bacteria unless risks of delaying therapy outweigh infection risk

- No unresolved serious infection caused by encapsulated bacteria
- No use in severe hepatic impairment (Child Pugh Class C)
- Empaveli, Fabhalta, and Voydeya will not be used in combination
- Voydeya has not been shown to be effective as monotherapy and should only be prescribed as add on therapy to a C5 inhibitor

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use: flow cytometry, absolute reticulocyte count, liver enzymes

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

Description:

Empaveli (pegcetacoplan) and Fabhalta (iptacopan) are indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH). Empaveli is also indicated for treatment of adult and pediatric patients aged 12 years and older with C3 glomerulopathy (C3G) or primary immune-complex membranoproliferative glomerulonephritis (IC-MPGN), to reduce proteinuria. Fabhalta is also indicated for reduction of proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) =1.5 g/g. This indication is approved under accelerated approval based on reduction of proteinuria. It has not been established whether Fabhalta slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.

Voydeya (danicopan) is a complement factor D inhibitor indicated as add-on therapy to Ultomiris (ravulizumab) or Soliris (eculizumab) for the treatment of extravascular hemolysis (EVH) in adults with paroxysmal nocturnal hemoglobinuria (PNH). Voydeya (danicopan) has not been shown to be effective as monotherapy and should only be prescribed as an add-on to Ultomiris (ravulizumab) or Soliris (eculizumab).

PNH is a rare, acquired disorder in which hematopoietic stem cells that cause reduced or absent glycosylphosphatidylinositol (GPI)-anchored proteins on the cell surface. GPI-linked complement inhibitors

prevent over activation of the alternative pathway of complement (APC) which is a component of innate immunity. The functional components of APC are C3 and C5 convertases and cytolytic membrane attack complex (MAC). Loss of the GPI-linked complement inhibitors on red blood cells (RBCs) leads to paroxysmal intravascular hemolysis (IVH) and an increased risk for thrombosis, organ dysfunction, and hypocellular or dysplastic bone marrow. Some individuals with PNH may have clinically significant aplastic anemia or myelodysplastic syndrome. Common clinical symptoms include fatigue, dyspnea, hemoglobinuria, abdominal pain, bone marrow suppression, erectile dysfunction, thrombosis, and renal insufficiency.

PNH is categorized into one of three categories: hemolytic (classical) PNH, subclinical PNH and PNH with bone marrow failure. Complement inhibitors including Soliris (eculizumab), Ultomiris (ravulizumab-cwvz), and Empaveli (pegcetacoplan) are primarily used to treat symptomatic hemolytic PNH to manage anemia-related symptoms, thrombosis, pain, and organ dysfunction. Clinical benefit includes stabilization of hemoglobin, decreases in transfusion and reduction in hemolysis. Soliris (eculizumab) and Ultomiris (ravulizumab-cwvz) are both complement 5 inhibitors that target IVH. Soliris administered as an intravenous infusion. Ultomiris is administered as an intravenous infusion in adult or pediatric patients one month of age and older or as a subcutaneous injection for maintenance in adult patients. Subcutaneous dosing of Ultomiris is not approved for use in pediatric patients.

Empaveli (pegcetacoplan) is a pegylated pentadecapeptide that targets complement C3. In binding to complement protein C3 and its activation fragment C3b, pegcetacoplan regulates the cleavage of C3 and the generation of downstream effectors of complement activation. It acts in the complement cascade that controls both C3b-mediated extravascular hemolysis (EVH) and terminal complement-mediated intravascular hemolysis.

Fabhalta (iptacopan) binds to Factor B of the alternative complement pathway and regulates the cleavage of C3, generation of downstream effectors, and the amplification of the terminal pathway. In PNH, IVH is mediated by the downstream MAC, while EVH is facilitated by C3b opsonization. Iptacopan acts proximally in the alternative pathway of the complement cascade to control both C3b-mediated EVH and terminal complement-mediated IVH. Fabhalta is available as a capsule and is given twice daily.

Empaveli (pegcetacoplan) is administered subcutaneously via an infusion pump at doses 1,080 milligrams twice weekly. For lactase dehydrogenase (LDH) levels greater than 2 times the upper limit of normal (ULN), adjust the dose to every 3 days. The LDH is monitored twice weekly for at least 4 weeks after a dose increase. An Empaveli REMS program requires prescribers to enroll in and educate patients regarding the risks of bacterial infections and the need for preventative vaccinations against encapsulated bacteria.

Voydeya (danicopan) binds reversibly to complement Factor D and selectively inhibits the alternative complement pathway. Voydeya (danicopan) prevents the cleavage of complement Factor B into the Ba and Bb fragments which are required for the formation of the alternative pathway (AP) complement component C3 convertase (C3bBb), the generation of downstream effectors including C3 fragment opsonization, and the amplification of the terminal pathway. In PNH, intravascular hemolysis (IVH) is mediated by the terminal membrane attack complex (MAC), while extravascular hemolysis (EVH) is facilitated by C3 fragment opsonization. Voydeya (danicopan) acts proximally in the alternative pathway of the complement cascade to control preferentially C3 fragment-mediated EVH, while co-administered Ultomiris (ravulizumab) or Soliris (eculizumab) is anticipated to maintain control over MAC-mediated IVH.

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Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Paroxysmal Nocturnal Hemoglobinuria therapies:

Compliment Factor B inhibitor (CFBi)	FABHALTA (iptacopan)
Compliment Factor D inhibitor (CFDi)	VOYDEYA (danicopan)
Compliment 3 inhibitor (C3i)	EMPAVELI (pegcetacoplan)
Compliment 5 inhibitor (C5i)	SOLIRIS (eculizumab)
Compliment 5 inhibitor (C5i)	ULTOMIRIS (ravulizumab)
Compliment 5 inhibitor (C5i)	PIASKY (crovalimab-akkz)

Resources:

Empaveli (pegcetacoplan) subcutaneous injection product information, revised by Apellis Pharmaceutical, Inc. 07-2025. Available at DailyMed https://dailymed.nlm.nih.gov/dailymed/. Accessed November 03, 2025.

Fabhalta (iptacopan) cap product information, revised by Novartis Pharmaceutical Corporation. 03-2025. Available at DailyMed https://dailymed.nlm.nih.gov/dailymed/. Accessed November 03, 2025.

Voydeya (danicopan) tab product information, revised by Alexion Pharmaceuticals Inc. 03-2024. Available at DailyMed https://dailymed.nlm.nih.gov/dailymed/. Accessed November 03, 2025.

Brodsky RA DeZern AE. Clinical manifestations and diagnosis of paroxysmal nocturnal hemoglobinuria. In: UpToDate, Larson RA, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through December 2025. Topic last updated November 27, 2024. Accessed January 15, 2026.

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Fervenza FC, Sethi S. Membranoproliferative glomerulonephritis: Classification, clinical features, and diagnosis In: UpToDate, Glassock RJ, Lam AQ (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through December 2025. Topic last updated August 12, 2024. Accessed January 15, 2026.

Java A, Brennan DC. Membranoproliferative glomerulonephritis: Recurrence of idiopathic disease after transplantation In: UpToDate, Vella J, Lam AQ (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through December 2025. Topic last updated September 06, 2024. Accessed January 15, 2026.

Fervenza FC, Sethi S. Membranoproliferative glomerulonephritis: Treatment and prognosis In: UpToDate, Glassock RJ, Lam AQ (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through December 2025. Topic last updated March 29, 2024. Accessed January 15, 2026.

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