Written By: Michael Verbosky, PharmD, BCOP, BCPS; Matt Snyder, PharmD, BCOP; Timothy Kubal, MD, MBA
Institution: Moffitt Cancer Center

Pegcetacoplan (Empaveli) Use in Paroxysmal Nocturnal Hemoglobinuria

Description: This PQI will focus on the role of pegcetacoplan in the management of paroxysmal nocturnal hemoglobinuria (PNH).

Background: Pegcetacoplan is a pegylated peptide that targets the proximal complement protein C3 and can inhibit both intravascular and extravascular hemolysis, providing an option for patients with refractory or breakthrough disease. It is the first C3 inhibitor approved for:[1]

- Paroxysmal nocturnal hemoglobinuria
- Additional indications – see prescribing information[1]

Most common adverse reactions (≥ 20%):[1]

- Injection site reactions, infections, diarrhea, abdominal pain

PQI Process:

- Confirm PNH diagnosis; assess patient's need for treatment and prior therapies received
- Review the patient's medical history for contraindications to pegcetacoplan
  - Hypersensitivity to pegcetacoplan or any component of formulation
  - Patients with unresolved serious infection due to encapsulated bacteria (S. *pneumoniae*, N. *meningitidis*, or H. *influenzae)*
- Black box warning
  - Vaccinate against encapsulated bacteria (per current ACIP recommendations for patients receiving complement inhibitors[2]) ≥ 2 weeks before starting pegcetacoplan, unless treatment delay poses greater risk
  - If urgent pegcetacoplan therapy needed < 2 weeks after vaccination, give antibacterial prophylaxis for 2 weeks
- Evaluate pregnancy status prior to use in patients who may become pregnant
- Dosing and Administration
  - Confirm correct dose, frequency, and timing (if switching from another product)
    - Pegcetacoplan 1080 mg subcutaneously (subQ) twice weekly
      - ➢ If LDH > 2x ULN: Adjust to 1080 mg every 3 days
  - Administer subQ using either:
    - Commercially available infusion pump with a reservoir of at least 20 mL, or
    - Single-use, disposable on body injector
  - Switching from eculizumab: overlap with eculizumab for 4 weeks
  - Switching from ravulizumab: start pegcetacoplan ≤ 4 weeks after last dose of ravulizumab
  - While no dose adjustments for renal or hepatic impairment are provided in the manufacturer's labeling, no clinically significant differences in pharmacokinetics have been found in patients with reduced kidney or liver function
- Availability – dispensed only though restricted program under a Risk Evaluation and Mitigation Strategy (REMS)
  - All prescribing providers and dispensing pharmacies must be enrolled in REMS program (telephone: 1-888-343-7073 or at www.empavelirems.com)

- Monitoring - hemoglobin, LDH at baseline, periodically, and twice weekly for ≥ 4 weeks after dose change
  - Avoid silica reagents in coagulation panels as drug may artificially prolong aPTT levels
  - Monitor for signs/symptoms of hemolysis for ≥ 8 weeks after last dose

Patient-Centered Activities:

- Counsel patients to watch for/report:
  - Signs/symptoms of severe infections (fever, chills, rash, shortness of breath, stiff neck/back, headache, high heart rate, light sensitivity) while on the drug and for 2 months after stopping
  - Serious hypersensitivity reactions (anaphylaxis, facial swelling, rash, urticaria)
  - Signs/symptoms of hemolysis (fever, weakness, dizziness, confusion, dark urine, yellowing of skin/eyes/mouth)
  - Other common adverse events (injection-site reactions, rash, diarrhea, abdominal pain, fatigue, cough, headache, joint pain)
- Administration & Storage
  - Store vials in refrigerator (36-46°F / 2-8°C) in original carton, protected from light
  - Prior to use, allow vial to reach room temperature (68-77°F / 20-25°C) for ~30 minutes
  - Prepare/administer pegcetacoplan using aseptic use technique via infusion pump or injector
    - Infusion pump: subQ over 30-60 minutes (abdomen, thighs, hips, upper arms; ensure infusion sites are ≥3 inches apart if multi-infusion sets needed)
      - Refer to full infusion pump instructions for use here[3]
    - Injector: subQ in abdomen only; rotate sites
      - Refer to full injector instructions for use here[4]
  - Avoid tender/bruised/red/hard skin, tattoos, scars, stretch marks.
  - If a dose is missed, administer ASAP, then resume regular schedule
- Safety
  - Carry a *Patient Safety Card* regarding serious infection risk during treatment and for 2 months after last dose
  - Advise females of reproductive age to use contraception during therapy and for 40 days after last dose
  - Notify provider of any new medications/supplements
  - Emphasize the importance of adhering to recommended vaccination schedule
- Patient Assistance: NCODA Financial Assistance Tool
  - ApellisAssist program offers disease/drug education, financial assistance, insurance support, and drug self-administration training (1-866-MY-APL-ASSIST (1-866-692-7527) or at www.empaveli.com)

References:

1. EMPAVELI [prescribing information]. Waltham, MA: Apellis Pharmaceuticals, Inc.; 2023.
2. Centers for Disease Control and Prevention. Clinical guidance for managing meningococcal disease risk in patients receiving complement inhibitor therapy. CDC. Updated June 21, 2024. Accessed August 21, 2025. https://www.cdc.gov/meningococcal/hcp/clinical-guidance/complement-inhibitor.html
3. Apellis Pharmaceuticals, Inc. *EMPAVELI: Instructions for Use (Infusion Pump)*. Revised July 2025. Accessed August 21, 2025. https://pi.apellis.com/files/IFU_Empaveli.pdf
4. Apellis Pharmaceuticals, Inc. *EMPAVELI Injector: Instructions for Use*. Revised July 2025. Accessed August 21, 2025. https://pi.apellis.com/files/IFU_EMPAVELIinjector.pdf