BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

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EMPAVELI™ (pegcetacoplan)

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

EMPAVELI™ (pegcetacoplan)

Criteria:

- **Criteria for initial therapy:** Empaveli (pegcetacoplan) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Hematologist.

  2. Individual is 18 years of age or older

  3. A confirmed diagnosis of paroxysmal nocturnal hemoglobinuria (PNH) by the following:
     a. Laboratory confirmation with high-sensitivity flow cytometry showing the absence or deficiency of glycosylphosphatidylinositol (GPI)-anchored proteins (e.g., CD55, CD59) on at least 2 cell lineages (e.g., granulocytes and red blood cells)

  4. Individual is currently on Soliris (eculizumab) with a stable dose for at least 3 months with **ALL** of the following:
     a. Hemoglobin is less than 10.5 g/dL in last 60 days
     b. Absolute reticulocyte count (ARC) is greater than 1.5 times the upper limit of normal (ULN)
     c. Has received at least 1 red blood cell (RBC) transfusion in the previous 12 months
     d. Plan is to continue Soliris (eculizumab) for ONLY 4 weeks after starting Empaveli

  5. Individual has been immunized against *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B at least 2 weeks prior to first dose of Empaveli

  6. There are **NO** contraindications.
     a. Contraindications include:
        i. Individuals who are not currently vaccinated against certain encapsulated bacteria (e.g., *Streptococcus pneumoniae*, *Neisseria meningitidis* types A, C, W, Y and B and *Haemophilus influenzae* type B. unless the risks of delaying treatment outweigh the risks of developing a serious bacterial infection with an encapsulated organism
        ii. Individuals with unresolved serious infection caused by encapsulated bacteria

  7. Will not be used in combination with Soliris (eculizumab) or Ultomiris (ravulizumab-cwvz)
     (Note: When switching from Soliris (eculizumab) to Empaveli, a 4-week drug overlap is required)

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Empaveli (pegcetacoplan) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by physician specializing in the patient's diagnosis or is in consultation with a Hematologist.

  2. Individual's condition has responded while on therapy
     a. Response is defined as individual has achieved and maintained **TWO** of the following:

i. Increase or stabilization of hemoglobin
ii. Normalization of absolute reticulocyte count (ARC)
iii. Decrease in frequency of red blood cell (RBC) transfusions
iv. Decrease in lactase dehydrogenase (LDH)
v. Decrease in pain or fatigue

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications

5. Will not be used in combination with Soliris (eculizumab) or Ultomiris (ravulizumab-cwvz)

Renewal duration: 12 months

- 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:

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired disorder in which hematopoietic stem cells that causes 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 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. Eculizumab and ravulizumab-cwvz are both complement 5 inhibitors that target intravascular hemolysis.

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

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generation of downstream effectors of complement activation. It acts in the complement cascade that controls both C3b-mediated extravascular hemolysis and terminal complement-mediated intravascular hemolysis.

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.

Resources:

Empaveli (pegcetacoplan). Product information, revised by manufacturer 05/2021, at DailyMed https://dailymed.nlm.nih.gov/dailymed/. Accessed July 08, 2021.

UpToDate.com. Treatment and prognosis of paroxysmal nocturnal hemoglobinuria. Accessed September 30, 2021.

UpToDate.com. Clinical manifestations and diagnosis of paroxysmal nocturnal hemoglobinuria. Accessed September 22, 2021.

Hillmen P, Szer J, Weitz I, et al. Pegcetacoplan versus Eculizumab in Paroxysmal Nocturnal Hemoglobinuria. *N Engl J Med.* 2021;384(11):1028-1037.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.