BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

PREVYMIS™ (letermovir) 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 PREVYMIS (letermovir)

Criteria for Therapy:

Prescriber Qualifications
- Prescribed by an Infectious Disease Specialist, Hematologist, Oncologist, or Transplant Specialist, or in consultation with one of these specialists

Indication
- Prophylaxis of cytomegalovirus (CMV) infection and disease in CMV seropositive recipient (R+) of an allogeneic hematopoietic stem cell transplant

ORIGINAL EFFECTIVE DATE: 3/15/2018| ARCHIVE DATE: | LAST REVIEW DATE: 02/19/2026 | LAST CRITERIA REVISION DATE: 02/20/2025

- Prophylaxis of cytomegalovirus (CMV) disease in kidney transplant recipient at high risk (donor CMV seropositive/recipient CMV seronegative [D+/R−])

Age Requirement

- For hematopoietic stem cell transplant: 6 months of age and weight of at least 6 kilograms
- For kidney transplant: 12 years of age and weight of at least 40 kilograms

Baseline Clinical Evaluation

- Confirmed diagnosis of CMV infection or disease
- Not being treated for active CMV infection
- Does not have creatinine clearance of 10 mL/min or less or is not on dialysis
- Does not have severe hepatic impairment (Child Pugh Class C)

Alternative Therapies

- Failure (trial for at least three months duration), contraindication per FDA label, intolerance, or is not a candidate for:
  - Valcyte (valganciclovir) or generic valganciclovir unless at high risk for CMV
  - If available: generic equivalent **Note:** Failure, contraindication, or intolerance to the generic should be reported to the FDA (see Definitions section)

Safety

- No concomitant use with:
  - Pimozide
  - Ergot Alkaloids (e.g., ergotamine, dihydroergotamine)
  - Livalo (pitavastatin) or simvastatin when also used with cyclosporine
- No significant interacting drugs such as:
  - Nafcillin
  - Carbamazepine, phenobarbital, phenytoin, rifabutin, rifampin, or St. John's wort
  - Thioridazine
  - Bosentan
  - Efavirenz, etravirine, nevirapine
  - Atorvastatin, lovastatin when also used with cyclosporine
  - Modafinil

Documentation Requirements

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

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Criteria Approval Duration

- One time approval (includes number of days intravenous use and number of days oral use)
- Hematopoietic stem cell transplant: once daily oral or intravenous use through 100 days post transplant; may continue through 200 days if at risk for late CMV infection
- Kidney transplant: once daily oral or intravenous use through 200 days post transplant 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:

Prevymis (letermovir) is indicated for prophylaxis of cytomegalovirus (CMV) infection and disease in adult and pediatric individuals 6 months of age and older and weigh at least 6 kilogram who are CMV seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT). Prevymis (letermovir) is also indicated for prophylaxis of CMV disease in adult and pediatric individuals 12 years of age and older and weigh at least 40 kilograms who are kidney transplant recipients at high risk (i.e., donor CMV seropositive/recipient CMV seronegative [D+/R-]).

Hematopoietic cell transplant (HCT) recipients, especially those who have received allogeneic transplants, are at increased risk for a variety of infections depending upon their degree of immunosuppression and exposures. Infection in HCT recipients is associated with high morbidity and mortality. Viruses of major importance in HCT recipients include herpes simplex virus (HSV), varicella-zoster virus (VZV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), respiratory viruses (influenza, parainfluenza, respiratory syncytial virus, adenovirus), human herpes virus 6 (HHV-6), hepatitis B, and hepatitis C. Antiviral prophylaxis or preemptive therapy against some of these viruses is recommended.

The risk of CMV reactivation is significant in allogeneic HCT recipients. CMV prophylaxis has been studied using ganciclovir, valganciclovir, letermovir, foscarnet, acyclovir, and valacyclovir. CMV prophylaxis is used for patients at high risk for CMV disease.

Definitions:

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

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Allogeneic – transplantation of cells or tissues to a recipient that come from a genetically non-identical donor (i.e. genetically dissimilar)

Autologous – transplantation of cells or tissues to a recipient that come from a genetically identical donor

Primary prophylaxis – Primary prophylaxis involves the administration of an antimicrobial drug to prevent infection in patients at increased risk

Secondary prophylaxis – Secondary prophylaxis involves the administration of prophylactic doses of an antimicrobial drug to prevent recurrent infection

Pre-emptive therapy – Pre-emptive therapy involves starting antimicrobial therapy based upon screening with a sensitive assay (e.g., polymerase chain reaction) in an attempt to detect early infection. The goal of pre-emptive therapy is to avoid progression to invasive disease. Pre-emptive therapy may be favored over prophylaxis when the antimicrobial therapy is particularly toxic (e.g., for cytomegalovirus).

CMV infection:
- Isolation of virus or detection of viral proteins (antigens) or nucleic acid in any body fluid or tissue
  - Evidence of CMV replication regardless of symptoms

CMV disease:
- Evidence of end organ disease and CMV syndrome
  - Evidence of end organ disease is defined by the presence of appropriate clinical &/or signs together with documentation of CMV in tissue from the relevant organ
- Evidence of CMV infection with attributable symptoms
  - CMV disease can be further categorized as:
    - Viral syndrome (i.e., fever, malaise, leukopenia, and/or thrombocytopenia)
    - Tissue invasive ("end organ") disease

Risk of CMV
Risk of CMV reactivation is significant in allogeneic HCT recipients. Although some autologous HCT recipients reactivate CMV, the incidence of CMV disease is low in these patients. Both donor and recipient CMV serostatus significantly influence the risk of post-transplant CMV infection and CMV disease.

Factors associated with increased risk for CMV reactivation (high-risk stratum):
Patient meets **one** or more of the following criteria
- Human Leukocyte Antigen (HLA)-related (sibling) donor with at least one mismatch at one of the following three HLA-gene loci: HLA-A, -B or –DR
- Unrelated donor with at least one mismatch at one of the following four HLA-gene loci: HLA-A, -B, -C and -DRB1
- Haploidentical donor
- Use of umbilical cord blood as stem cell source
- Use of *ex vivo* T-cell-depleted grafts (including ex vivo use of alemtuzumab [Campath])
- Grade 2 or greater Graft-Versus-Host Disease (GVHD) requiring systemic corticosteroids (defined as the use of ≥ 1 mg/kg/day of prednisone or equivalent dose of another corticosteroid)

Clinically significant CMV infection (prophylaxis failure) defined as:

- The occurrence of either:
  - CMV end-organ disease
  - Initiation of anti-CMV pre-emptive therapy (PET) based on documented CMV viremia (using the Roche COBAS® AmpliPrep/COBAS TaqMan® assay, LLoQ is 137 IU/mL, which is approximately 150 copies/mL)
    - CMV viremia for high-risk stratum: a CMV DNA ≥ 150 copies/mL
    - CMV viremia for low-risk stratum: a CMV DNA > 300 copies/mL
- The clinical condition of the individual

Resources:

Prevymis (letermovir) tablet, pellets, injection product information, revised by Merck Sharp & Dohme Corp. 01-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 24, 2025.

Wingard JR. Prevention of viral infections in hematopoietic cell transplant recipients. In: UpToDate, Bow E, White N (Ed), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through October 2025. Topic last updated October 28, 2025. Accessed November 04, 2025.

Santos CAQ, Vella J, Brennan DC. Prevention of cytomegalovirus disease in kidney transplant recipients. In: UpToDate, Legendre C, Blumberg EA, Lam AQ, White N (Ed), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through October 2025. Topic last updated August 04, 2025. Accessed November 04, 2025.

Ljungman P, Boeckh M, Hirsch HH, et al.: Definitions of cytomegalovirus infection and disease in transplant patients for use in clinical trials. CID 2017; 64 (1): 87-91. Access May 21, 2019. Re-evaluated November 04, 2025.

Kotton CN, Kumar D, Manuel O, et al.: The Fourth International Consensus Guidelines on the Management of Cytomegalovirus in Solid-organ Transplantation. Transplantation 2025 July; 109 (7):1066-1110. Accessed November 04, 2025.

Khawaja F, Zamora D, Yong MK, et al.: American Society for Transplantation and Cellular Therapy Series #11: Updated Cytomegalovirus Guidelines in Hematopoietic Cell Transplant and Cellular Therapy Recipients. Transplant Cellular Therapy 2025; 31: 727-741 https://doi.org/10.1016/j.jtct.2025.06.025. Accessed November 04, 2025.