BlueCross BlueShield Arizona

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PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**3/15/2018**
LAST REVIEW DATE:	**2/17/2022**
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PREVYMIS™ (letermovir) oral

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.**

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Criteria:

- **Criteria for therapy:** Prevymis (letermovir) 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 an Infectious Disease Specialist, Hematologist, Oncologist, or Transplant Specialist depending upon indication or use
  2. Individual is 18 years of age or older
  3. A confirmed diagnosis of **prophylaxis** of cytomegalovirus (CMV) infection and disease in adult CMV-seropositive recipient [R+] of an allogeneic hematopoietic stem cell transplant (HSCT)
  4. Individual has failure, contraindication per FDA label, intolerance to Valcyte (valganciclovir) **or** generic valganciclovir **unless** individual is at high-risk for CMV (See Definitions section)
  5. Initiation of therapy is between day 0 and day 28 post-transplantation
  6. Individual is not being treated for an active CMV infection
  7. Individual does not have a CrCl of 10 mL/min or less or is on dialysis
  8. Individual does not have severe hepatic impairment (Child-Pugh Class C)
  9. There are **NO** FDA-label contraindications, such as:
     a. Concurrent use with Pimozide
     b. Concurrent use with Ergot Alkaloids
     c. Concurrent use with Livalo (pitavastatin) or simvastatin when also used with cyclosporine
  10. There are no significant interacting drugs

  Approval duration:
  One-time approval through day 100 post-transplantation (includes intravenous use)
  - 240 mg: One-time approval through day 100 post-transplantation (includes intravenous use)
  - 480 mg: One-time approval through day 100 post-transplantation (includes intravenous use)

- 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**

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Description:

Prevymis (letermovir) is indicated for prophylaxis of cytomegalovirus (CMV) infection and disease in adult CMV seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT). Prevymis (letermovir) is an anti-viral agent active against CMV.

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:

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).

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

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- 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) product information, revised by Merck Sharp & Dohme Corp. 02-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 21, 2021.

Wingard JR. Prevention of viral infections in hematopoietic cell transplant recipients. In: UpToDate, Bow E, Bond S (Ed), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Topic last updated November 29, 2021. Accessed December 23, 2021.