BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 3/15/18
LAST REVIEW DATE: 3/15/18
LAST CRITERIA REVISION DATE:
ARCHIVE DATE:

PREVYMIS™ (letermovir) oral tablet

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.**

PREVYMIS™ (letermovir) oral tablet (cont.)

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 agents 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

Factors associated with increased risk for CMV reactivation (high risk stratum):

- Human Leukocyte Antigen (HLA)-related donor with at least one mismatch at one of the following three HLA-gene loci: HLA-A, -B or –DR;
- Haploidentical donor;
- Unrelated donor with at least one mismatch at one of the following four HLA-gene loci: HLA-A, -B, -C and -DRB1;
- Use of umbilical cord blood as stem cell source;
- Use of *ex vivo* T-cell-depleted grafts;
- Grade 2 or greater Graft-Versus-Host Disease (GVHD) requiring systemic corticosteroids

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 $\geq$ 150 copies/mL
        - CMV viremia for low risk stratum: a CMV DNA > 300 copies/mL
- The clinical condition of the individual

PREVYMIS™ (letermovir) oral tablet (cont.)

Prevymis (letermovir)

Medication class:
- Antivirals, CMV Agents

FDA-approved indication(s):
- Prevymis is a CMV DNA terminase complex inhibitor indicated for prophylaxis of cytomegalovirus (CMV) infection and disease in adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT).

Recommended Dose:
- 480 mg once daily orally or as an intravenous (IV) infusion over 1 hour through 100 days post-transplant
  - Initiated between day 0 and day 28 post-transplantation (before or after engraftment)

Maximum dosage
- There is no well-established maximum dose for the approved indication

Available Dosage Forms:
- Tablet: 240 mg; 480 mg.
- Injection: 240 mg/12 mL (20 mg/mL) or 480 mg/24 mL (20 mg/mL) in a single-dose vial.

Warnings, Precautions, and other Clinical Information:
- Tablet and injection may be used interchangeably, no dosage adjustment is necessary when switching formulations
- Injection formulation contains hydroxypropyl betadex, a cyclodextrin; each mL contains 150 mg of hydroxypropyl betadex
- Hydroxypropyl betadex is eliminated by glomerular filtration; elimination is decreased with severe renal impairment
- With CrCl < 50 mL/min who are receiving Prevymis injection, accumulation of hydroxypropyl betadex may occur
- When used with cyclosporine, reduce Prevymis dose to 240 mg once daily
- Prevymis is not recommended for patients with severe hepatic impairment (Child-Pugh Class C)
- There is insufficient information on dosing & safety of Prevymis in patients with CrCl < 10 mL/min or those on dialysis
- Use with rifampin is not recommended, there is no information provided on the effect of other CYP3A4 inducers
- Prevymis is a moderate inhibitor of CYP3A4, but when it is used with cyclosporine, the combination becomes a strong inhibitor of CYP3A4 metabolism
- When Prevymis is used with cyclosporine, use of repaglinide, atorvastatin, or lovastatin is not recommended
- Prevymis reduces the exposure of voriconazole due to induction of voriconazole elimination
- Prevymis is active against viral populations showing resistance to cidofovir, foscarnet, and ganciclovir
- Cidofovir, foscarnet, and ganciclovir are active against viral populations showing resistance to Prevymis

PREVYMIS™ (letermovir) oral tablet (cont.)

Criteria:

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

1. Prescriber is an Infectious Disease Specialist, Hematologist, Oncologist, or Transplant Specialist
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. Initiation of therapy is between day 0 and day 28 post-transplantation
5. Individual has failure, contraindication or intolerance to Valcyte (valganciclovir) **or** generic valganciclovir
6. There are **NO** contraindications.
    - Contraindications include:
        - Use with Pimozide
        - Use with Ergot Alkaloids
        - Use with Livalo (pitavastatin) or simvastatin when also used with cyclosporine

Initial approval duration: One time approval through day 100 post-transplantation
240 mg: One time approval through day 100 post-transplantation
480 mg: One time approval through day 100 post-transplantation

Resources:

Prevymis. Package Insert. Revised by manufacturer 11/2017. Accessed 02-15-18.

UpToDate: Prevention of viral infections in hematopoietic cell transplant recipients. Current through Feb 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/prevention-of-viral-infections-in-hematopoietic-cell-transplant-recipients?source=see_link#H357744304

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

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Office notes, labs, and medical testing relevant to the request that show medical justification are required.