Pharmacy Policy Bulletin: J-1441 Prevymis (letermovir) Oral Pellets – Commercial and Healthcare Reform	
Number: J-1441	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1441-002	**Original Date:** 10/02/2024
Effective Date: 04/25/2025	**Review Date:** 04/09/2025

Drugs Product(s):	• Prevymis (letermovir) oral pellets
FDA-Approved Indication(s):	• Prophylaxis of cytomegalovirus (CMV) infection and disease in adult and pediatric patients 6 months of age and older and weighing at least 6 kg who are CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT). • Prophylaxis of CMV disease in adult and pediatric patients 12 years of age and older and weighing at least 40 kg who are kidney transplant recipients at high risk (Donor CMV seropositive/Recipient CMV seronegative [D+/R-]).

Background:	• Prevymis (letermovir) oral pellet is a CMV deoxyribonucleic acid (DNA) terminase complex inhibitor. Prevymis impairs viral DNA processing and packaging by inhibiting the CMV DNA terminase complex. • Prevymis is also available as tablets and as an injection for intravenous (IV) infusion for prophylaxis of CMV in pediatrics and adults. • CMV is a prevalent β-herpesvirus that infects most humans of all ages, and the predicted overall CMV seroprevalence rate in the United States (US) is 50%. Individuals with normal immune systems seldom develop CMV symptoms after initial infection, with the virus remaining inactive or latent in the body for life. A weakened immune system provides the virus a chance to reactivate. 20-60% of solid organ transplant recipients and 30-70% of HSCT recipients develop symptomatic CMV infection. CMV-seronegative recipients who receive an organ from a CMV-seropositive donor [D+/R-] are at high risk of CMV disease after transplantation. CMV disease can lead to end-organ damage including gastrointestinal tract disease, pneumonia or retinitis. Transplant recipients who develop CMV infection post-transplant are at increased risk for transplant failure and death. CMV typically occurs between 30-90 days after transplantation. CMV infections remain one of the most common complications affecting transplant recipients, conveying higher risks of complications, graft loss, morbidity, and mortality. CMV infection is characterized by CMV replication regardless of

	symptoms and is defined as virus isolation or detection of viral proteins (antigens) or nucleic acid.
	• ICD-10 Code Information:
	  ○ Example: ICD-10: B25 “Cytomegaloviral disease” may apply to Prevymis oral pellets; however, the prescriber must confirm that the member is using Prevymis oral pellets for prophylaxis due to HSCT or kidney transplant.
	• Prescribing Considerations:
	  ○ Prevymis tablets is not recommended in pediatric HSCT recipients weighing less than 15 kg. Prevymis tablets is not recommended in pediatric HSCT recipients when co-administered with cyclosporine and weighing less than 30 kg.
	  ○ Treatment of Prevymis oral pellets may be continued through 200 days (~6.5 months) post-HSCT or kidney transplant.
	  ○ The safety and efficacy of Prevymis use for more than 200 days has not been studied in clinical trials.
	  ○ Prevymis has warnings or precautions for risk of adverse reactions or reduced therapeutic effect due to drug interactions (e.g., inducers of transporters [e.g., P-gp] and/or enzymes [e.g., UGTs]) and risk associated with hydroxypropyl betadex excipient in IV formulation.

Approval Criteria

I. Approval Criteria
When a benefit, coverage of Prevymis oral pellets may be approved when all of the following criteria are met **(A., B., and C.)**:

A. The member meets one (1) of the following criteria **(1. or 2)**:
  1. The member is 6 months of age and older and weighing at least 6 kg who is a cytomegalovirus (CMV) -seropositive recipient [R+] of an allogeneic hematopoietic stem cell transplant (HSCT).
  2. The member is 12 years of age and older and weighing at least 40 kg who is a kidney transplant recipient at high risk (Donor CMV seropositive/Recipient CMV seronegative [D+/R-]).

B. The member is using Prevymis oral pellets for the prophylaxis of CMV infection or disease.

C. The member meets one (1) of the following criteria **(1. or 2.)**:
  1. The member is unable to swallow tablets.
  2. The member is unable to use Prevymis tablets due to body weight dosing limitations.

II. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Prevymis oral pellets are not indicated for the treatment of CMV.
II. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
III. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 7-month authorization may be granted.

- Total cumulative authorizations do not exceed 7 months.

Automatic Approval Criteria

None.

References:

1. Prevymis [package insert]. Rahway, NJ: Merck Sharp & Dohme LLC; August 2024.
2. Razonable RR, Humar A. Cytomegalovirus in solid organ transplant recipients—guidelines of the American Society of Transplantation Infectious Diseases Community of Practice. *Clinical Transplantation*. 2019;33(9).
3. Azevedo L, Pierrotti L, Abdala E, et al. Cytomegalovirus infection in transplant recipients. *Clinics*. 2015;70(7):515-523.
4. Styczynski J. Who Is the Patient at Risk of CMV Recurrence: A Review of the Current Scientific Evidence with a Focus on Hematopoietic Cell Transplantation. *Infect Ther*. 2018;7:1-16
5. Kotton CN, Kumar D, Caliendo AM, et al. The Third International Consensus Guidelines on the management of cytomegalovirus in solid-organ transplantation. *Transplantation*. 2018;102(6):900-931.
6. National Comprehensive Cancer Network. NCCN Guidelines Version 2.2024 Prevention and Treatment of Cancer-Related Infections. Available at: https://www.nccn.org/professionals/physician_gls/pdf/infections.pdf. Accessed September 12, 2024.