letermovir (Prevymis™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO130

Description

Letermovir (Prevymis) is an orally administered antiviral agent that inhibits cytomegalovirus (CMV) deoxyribonucleic acid (DNA) terminase complex which helps prevent CMV infection in adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT).

Length of Authorization

- Initial: up to 100 days post-transplant
- Renewal: no renewal

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
letermovir (Prevymis)	240 mg tablet	Prophylaxis for CMV Infection	30 tablets/30 days
	480 mg tablet		

Initial Evaluation

I. Letermovir (Prevymis) may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, an oncologist, hematologist, infectious disease, or transplant specialist; **AND**
   C. Member will be using letermovir (Prevymis) for the prevention of CMV infection or disease; **AND**
   D. Member is cytomegalovirus (CMV)-seropositive**; AND**
   E. Member is an allogeneic hematopoietic stem cell transplant (HSCT) recipient with a high risk of CMV reactivation; **AND**
   F. Documentation of transplant date has been recorded in chart notes; **AND**
   G. If the request is for letermovir (Prevymis) 240 mg, it will be used in combination with cyclosporine.

II. Letermovir (Prevymis) is considered investigational when used for all other conditions, including but not limited to:
   A. Prevention of CMV infection or disease in all other settings EXCEPT HSCT
   B. Treatment for CMV infection or disease

Supporting Evidence

I. Per label, letermovir (Prevymis) has only been FDA-approved in the setting of CMV prophylaxis in adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT). Safety and efficacy in the pediatric population has not been established.

II. Considering the complexity of care for patients receiving HSCT, the agent requested must be prescribed by, or in consultation with, an oncologist, hematologist, infectious disease, or transplant specialist.

III. The safety and efficacy of letermovir (Prevymis) was studied in a multicenter, double-blind, placebo-controlled, Phase 3 trial in adult CMV-seropositive recipients [R+] of those who have received an allogeneic hematopoietic stem cell transplant (HSCT). Of the 325 participants who received letermovir (Prevymis), 38% failed prophylaxis compared to 61% in the placebo arm [95% CI (32.5, 14.6)].

IV. A review by Chen et al. 2018 demonstrated that among the six antiviral therapies studied, ganciclovir and letermovir were the most effective in reducing incidence of CMV reactivation when used as universal prophylaxis agents. Results further suggest that patients undergoing allogeneic HSCT would significantly benefit from universal prophylaxis with an agent that is tolerable after HSCT. The data suggest that although effective at reducing CMV reactivation and disease, ganciclovir use cannot be recommended as a universal prophylaxis agent because of an increased risk of myelosuppression and subsequent drug discontinuation. In contrast, the data suggests that letermovir has an excellent safety profile with no myelosuppression, and its use should be considered for this indication in patients at risk. Letermovir was associated with a decrease in CMV-related outcomes and all-cause mortality through 24 weeks after HSCT. Data around acyclovir found that although a delay in the onset of CMV reactivation was demonstrated, acyclovir showed nonsignificant efficacy in preventing CMV disease. Valacyclovir, which has a greater bioavailability than acyclovir was compared with acyclovir and found to be associated with a lower rate of viremia with similar rate of survival to acyclovir in CMV R+ or D+ allogeneic HCT recipients. High-dose acyclovir and valacyclovir are less myelosuppressive than ganciclovir and appear to have some efficacy for CMV prophylaxis, but these agents have inferior in vitro activity against CMV than ganciclovir. Though ganciclovir has promising efficacy, treatment is limited in this HSCT patient due to its increased risk of myelosuppression.

Investigational or Not Medically Necessary Uses

I. There is a lack of strong scientific evidence from randomized controlled trials supporting safety and efficacy for the following indications below:
   A. Prevention of CMV infection or disease in all other settings EXCEPT HSCT
   B. Treatment for CMV infection or disease

References

1. Prevymis [Prescribing Information]. Whitehouse Station, NJ: MERCK & CO, Inc. November 2017.
2. Chen K, Cheng MP, Hammond SP, et al. Antiviral Prophylaxis for Cytomegalovirus Infection in Allogeneic Hematopoietic Cell Transplantation. Blood Adv. 2018 Aug 28; 2(16): 2159–2175. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6113617/
3. UpToDate, Inc. Prevention of viral infections in hematopoietic cell transplant recipients. UpToDate [database online]. Waltham, MA. Last updated April 27, 2020. Available at: http://www.uptodate.com/home/index.html.

Policy Implementation/Update:

Action and Summary of Changes	Date
Removed requirement of valacyclovir or ganciclovir trial given reduced efficacy and/or safety in comparison to letermovir	10/2020
Policy created	11/2019