Clinical Policy: Letermovir (Prevymis)

Reference Number: PA.CP.PHAR.367
Effective Date: 11.28.17
Last Review Date: 01.19

Revision Log

Description
Letermovir (Prevymis™) is a cytomegalovirus (CMV) DNA terminase complex inhibitor.

FDA Approved Indication(s)
Prevymis is indicated for prophylaxis of CMV infection and disease in adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT).

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with PA Health & Wellness that Prevymis is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Prophylaxis of CMV Infection in Adult CMV-Seropositive Recipients of an Allogeneic HSCT (must meet all)**:**

1. Member has received or is scheduled to receive an allogeneic HSCT;
2. Prescribed by or in consultation with an oncology, hematology, infectious disease, or transplant specialist;
3. Age ≥ 18 years;
4. Failure of valacyclovir or ganciclovir, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for ganciclovir*
5. If request is for IV Prevymis, documentation supports inability to use oral therapy;
6. At the time of request, member has none of the following contraindications:
   a. Member is receiving pimozide or ergot alkaloids;
   b. Member is receiving cyclosporine co-administered with pitavastatin or simvastatin;
7. Dose does not exceed 480 mg per day or 240 mg per day if co-administered with cyclosporine).

Approval duration: Through Day 100 post-transplantation

B. Other diagnoses/indications

1. Refer to PA.CP.PMN.53.

II. Continued Therapy

A. Prophylaxis of CMV Infection in Adult CMV-Seropositive Recipients of an Allogeneic HSCT (must meet all)**:**
1. Currently receiving medication via PA Health &Wellness benefit or member has met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 480 mg per day or 240 mg per day if co-administered with cyclosporine).

Approval duration: Through Day 100 post-transplantation

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health &Wellness benefit or member has met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
   Approval duration: Through Day 100 post-transplantation; or
2. Refer to PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CMV: cytomegalovirus
FDA: Food and Drug Administration
HSCT: hematopoietic stem cell transplant

Appendix B: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ganciclovir (Cytovene®)	<u>Treatment of CMV retinitis</u> Induction: 5 mg/kg (given intravenously at a constant rate over 1 hour) every 12 hours for 14 to 21 days. Maintenance: 5 mg/kg (given intravenously at a constant-rate over 1 hour) once daily for 7 days per week, or 6 mg/kg once daily for 5 days per week. <u>Prevention of CMV disease in transplant recipients</u> Induction: 5 mg/kg (given intravenously at a constant rate over 1 hour) every 12 hours for 7 to 14 days.	6 mg/kg once daily for 5 days per week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Maintenance: 5 mg/kg (given intravenously at a constant-rate over 1 hour) once daily, 7 days per week, or 6 mg/kg once daily, 5 days per week until 100 to 120 days posttransplantation.	
valacyclovir (Valtrex®)	Prevention of CMV disease in transplant recipients 2 grams PO QID	Off-label regimen: 2 grams PO QID

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): patients receiving any of the following - pimozide, ergot alkaloids, pitavastatin and simvastatin when co-administered with cyclosporine
- Boxed warning(s): none reported

Appendix D: General Information

- Prophylaxis strategy against early CMV replication (i.e., < 100 days after hematopoietic cell transplant [HCT]) for allogeneic recipients involves administering prophylaxis to all allogeneic recipients at risk throughout the period from engraftment to 100 days after HCT.
  - CMV prophylaxis has been studied using a variety of agents, including ganciclovir, valganciclovir, foscarnet, acyclovir, and valacyclovir.
- Preemptive strategy targets antiviral treatment to those patients who have evidence of CMV replication after HCT.
- Positive response to therapy may be demonstrated if there is no evidence of CMV viremia.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Prophylaxis of CMV infection in adult CMV-seropositive recipients [R+] of an allogeneic stem cell transplant	480 mg administered once daily PO or as an IV infusion over 1 hour through 100 days post-transplant. If co-administered with cyclosporine, the dosage of should be decreased to 240 mg once daily.	480 mg (or 240 mg when co-administered with cyclosporine) per day

VI. Product Availability

Tablet: 240 mg, 480 mg
Single dose vials: 240 mg/12 mL, 480 mg/24 mL

VII. References

1. Prevymis Prescribing Information. Whitehouse Station, NJ: Merck and Co., INC.: November 2017. Available at: https://www.merck.com/product/usa/pi_circulars/p/prevymis/prevymis_pi.pdf, accessed November 5, 2018.
2. Cytovene Prescribing Information. South San Francisco, CA: Genentech, Inc.: August 2018. Available at https://www.gene.com/download/pdf/cytovene_prescribing.pdf. Accessed November 5, 2018.
3. Valtrex Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline: December 2013. Available at https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Valtrex/pdf/VALTREX-PI-PIL.PDF. Accessed November 5, 2018.
4. Ljungman P, de La Camara R, Milpied N, Volin L, Russell CA, Crisp A, Webster A; Valacyclovir International Bone Marrow Transplant Study Group. Randomized study of valacyclovir as prophylaxis against cytomegalovirus reactivation in recipients of allogeneic bone marrow transplants. Blood. 2002;99:3050-6.
5. Winston DJ, Yeager AM, Chandrasekar PH, Snydman DR, Petersen FB, Territo MC; Valacyclovir Cytomegalovirus Study Group. Randomized comparison of oral valacyclovir and intravenous ganciclovir for prevention of cytomegalovirus disease after allogeneic bone marrow transplantation. Clin Infect Dis. 2003;36:749-58. Epub 2003 Mar 3.
6. Tomblyn M, Chiller T, Einsele H, et al. Guidelines for Preventing Infectious Complications among Hematopoietic Cell Transplantation Recipients: A Global Perspective. Biol Blood Marrow Transplant. 2009; 15: 1143-1238.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2019 annual review: per SDC: added redirection to valacyclovir or ganciclovir. Revised initial criteria to include scheduled transplant in addition to already received transplant.references reviewed and updated.	01/19	