Clinical Policy: Letermovir (Prevymis)

Reference Number: PA.CP.PHAR.367
Effective Date: 11.28.17
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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. Received an allogeneic HSCT;
2. Prescribed by or in consultation with an oncology, hematology, infectious disease, or transplant specialist;
3. Age ≥ 18 years;
4. If request is for IV Prevymis, must provide medical justification why the patient cannot use oral therapy;
5. 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;
6. Dose does not exceed:
   a. 240 mg orally or intravenously once daily when co-administered with cyclosporine;
   b. 480 mg administered orally or intravenously once daily.

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 (e.g., no evidence of CMV viremia);
3. If request is for a dose increase, new dose does not exceed:
   a. 240 mg orally or intravenously once daily when co-administered with cyclosporine;
   b. 480 mg administered orally or intravenously once daily.

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®)*	Treatment of CMV retinitis 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. Prevention of CMV disease in transplant recipients Induction: 5 mg/kg (given intravenously at a constant rate over 1 hour) every 12 hours for 7 to 14 days. 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.	6 mg/kg once daily for 5 days per week
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.
*May require prior authorization

Appendix C: 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.
- Prevymis is contraindicated in patients receiving pimozide or ergot alkaloids:
  - Concomitant administration of Prevymis in patients receiving pimozide may result in increased concentrations of pimozide due to inhibition of cytochrome P450 3A (CYP3A) by letermovir, which may lead to QT prolongation and torsades de pointes.
  - Ergot alkaloids: Concomitant administration of Prevymis in patients receiving ergot alkaloids may result in increased concentrations of ergot alkaloids (ergotamine and

dihydroergotamine) due to inhibition of CYP3A by letermovir, which may lead to ergotism.

- Prevymis is contraindicated with pitavastatin and simvastatin when co-administered with cyclosporine.
  - Concomitant administration of Prevymis in combination with cyclosporine may result in significantly increased pitavastatin or simvastatin concentrations, which may lead to myopathy or rhabdomyolysis.

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

Tablets: 240 mg, 480 mg
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 17, 2017.
2. Cytovene Prescribing Information. South San Francisco, CA: Genentech, Inc.: July 2017. Available at https://www.gene.com/download/pdf/cytovene_prescribing.pdf. Accessed November 17, 2017.
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 17, 2017.
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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date