Clinical Policy Title:	letermovir
Policy Number:	RxA.449
Drug(s) Applied:	Prevymis™
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

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

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Letermovir (Prevymis™)	Prophylaxis of CMV infection in adult CMVseropositive 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 Prevymis should be decreased to 240 mg once daily.	480 mg (or 240 mg when co-administered with cyclosporine) per day

Dosage Forms

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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 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
Commercial: 100 days
Medicaid: 100 days
HIM: 100 days

II. Continued Therapy Approval

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

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
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
Commercial: 100 days
Medicaid: 100 days
HIM: 100 days

III. Appendices

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.	6 mg/kg once daily for 5 days per week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	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.	
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.

References

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3. Valtrex Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline: December 2019. Available at https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Valtrex/pdf/VALTREX-PI-PIL.PDF. Accessed July 22, 2020.

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.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Line of Business Policy Applies to was updated to all lines of business. 3. Initial and Continued approval duration was updated to include Medicaid, Commercial & HIM approval duration. 4. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance…”. 5. References were reviewed and updated.	7/22/2020	9/14/2020