Clinical Policy Title:	letermovir
Policy Number:	RxA.449
Drug(s) Applied:	Prevymis™
Original Policy Date:	03/06/2020
Last Review Date:	07/18/2022
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 CMV seropositive recipients [R+] of an allogeneic stem cell transplant	480 mg administered once daily orally or as an intravenous 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 (20 mg/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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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 intravenous 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

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has 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

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
CMV: cytomegalovirus
FDA: Food and Drug Administration
HSCT: hematopoietic stem cell transplant
HCT: hematopoietic cell transplant
DNA: deoxyribonucleic acid
CrCl: Creatinine Clearance

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ganciclovir	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.	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 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 post transplantation.	
valacyclovir (Valtrex®)	Prevention of CMV disease in transplant recipients 2 grams orally four times a day	Off-label regimen: 2 grams orally four times a day

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Patients receiving any of the following: pimozide, ergot alkaloids, pitavastatin and simvastatin when co-administered with cyclosporine.

*Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

- 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.
- Hepatic Impairment: Prevymis™ is not recommended for patients with severe (Child-Pugh C) hepatic impairment.
- Renal Impairment: No dosage adjustment necessary; Closely monitor serum creatinine levels in patients with CrCl less than 50 mL/min using Prevymis™ injection.

References

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Review/Revision History	Review/Revision 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
Policy was reviewed: 1. Clinical Policy statement was updated ‘‘The provision of provider samples does not guarantee coverage…”. 2. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 3. Initial Approval Criteria and Continued Therapy Approval Criteria was updated to remove HIM approval duration. 4. Appendix A was updated to include abbreviations HCT, CLCr and DNA. 5. Statement about drug listing format in Appendix B is updated to "Therapeutic alternatives are	07/06/2021	09/14/2021

listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 6. Appendix D was updated to include “Hepatic Impairment…” and “Renal Impairment…”. 7. References were reviewed and updated.		
Policy was reviewed: 1. Dosage Forms: Updated dosage form from Single-dose vials: 240 mg/12 mL, 480 mg/24 mL to Single-dose vials: 240 mg/12 mL, 480 mg/24 mL (20 mg/mL). 2. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 3. Appendix B, Drug Name: Updated to remove discontinued brand-name therapeutic alternative Cytovene®. 4. Disclaimer about contraindications "Contraindications listed reflect statements made in the manufacturer's package insert..." was added to Appendix C. 5. References were reviewed and updated.	03/28/2022	07/18/2022