Clinical Policy: Letermovir (Prevymis)

Reference Number: CP.PHAR.367
Effective Date: 03.01.18
Last Review Date: 02.23
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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

It is the policy of health plans affiliated with Centene Corporation® 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 allogeneic HSCT;
2. Member is CMV-seropositive;
3. Prescribed by or in consultation with an oncology, hematology, infectious disease, or transplant specialist;
4. Age ≥ 18 years;
5. If request is for IV Prevymis, documentation supports inability to use oral therapy;
6. At the time of request, member is not receiving any of the following contraindicated agents:
   a. Pimozide or ergot alkaloids;
   b. Cyclosporine co-administered with pitavastatin or simvastatin;
7. Dose does not exceed 480 mg per day (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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 Centene benefit, or documentation supports that member is currently receiving for prophylaxis of CMV infection in adult CMV-seropositive recipients [R+] of an allogeneic HSCT and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Member has not received Prevymis therapy beyond 100 days post-transplantation;
4. If request is for a dose increase, new dose does not exceed 480 mg per day (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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies –

CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid 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
R+: seropositive recipients

Appendix B: Therapeutic Alternatives

Not applicable

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 HSCT) for allogeneic recipients involves administering prophylaxis to all allogeneic recipients at risk throughout the period from engraftment to 100 days after HSCT.
  - 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 HSCT.
- Positive response to therapy may be demonstrated if there is no evidence of CMV viremia.
- The 2021 American Society for Transplantation and Cellular Therapy Guideline for prevention of CMV infection after HCT states that primary prophylaxis in CMV-seropositive adult allogeneic recipients with alternative agents such as valganciclovir, ganciclovir, or foscarnet is generally not recommended.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Prophylaxis of CMV infection in adult CMV-seropositive recipients [R+] of an allogeneic HSCT	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
- Single-dose vials: 240 mg/12 mL, 480 mg/24 mL

VII. References

1. Prevymis Prescribing Information. Whitehouse Station, NJ: Merck and Co., Inc.: June 2022. Available at: https://www.merck.com/product/usa/pi_circulars/p/prevymis/prevymis_pi.pdf. Accessed October 24, 2022.
2. Clinical Pharmacology [database online]. Elsevier, Inc.; 2022. Available at: https://www.clinicalkey.com/pharmacology/. Accessed October 24, 2022.
3. 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.
4. 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.
5. 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.
6. Boeckh M, Ljungman P. How we treat cytomegalovirus in hematopoietic cell transplant recipients. Blood 2009; 113:5711-9.
7. Schmidt-Hieber, M., Schwarck, S., Stroux, A. et al. Immune reconstitution and cytomegalovirus infection after allogeneic stem cell transplantation: the important impact of in vivo T cell depletion. Int J Hematol (2010) 91: 877-885.
8. Hakki M, Aitken SL, Danziger-Isakov L, et al. American Society for Transplantation and Cellular Therapy Series: #3-Prevention of Cytomegalovirus Infection and Disease After Hematopoietic Cell Transplantation. Transplant Cell Ther. 2021 Sep; 27(9):707-719.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3490	Unclassified drugs
J8499	Prescription drug, oral, non chemotherapeutic, nos

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2019 annual review: no significant changes; references reviewed and updated.	11.05.18	02.19
1Q 2020 annual review: added pathway to approval to bypass valacyclovir or ganciclovir trial for members who are high risk for CMV infection; added information for defining high risk in Appendix D; references reviewed and updated.	10.09.19	02.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: no significant changes; added additional definitions of high risk to Appendix D; added coding implications; references reviewed and updated.	10.20.20	02.21
1Q 2022 annual review: no significant changes; converted HIM-Medical Benefit to HIM; references reviewed and updated.	09.14.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.22.22	
1Q 2023 annual review: removed redirection to valacyclovir or ganciclovir per 2021 American Society for Transplantation and Cellular Therapy Guidelines and bypass that was allowed for CMV-seropositive recipients as this is the only indicated use for Prevymis, added requirement for initial approval that member is CMV-seropositive; for continued therapy added the following requirement to support existing approval duration: Member has not received Prevymis therapy beyond 100 days post-transplantation; added HCPCS code J8499; references reviewed and updated.	10.24.22	02.23

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.