Clinical Policy: Letermovir (Prevymis)

Reference Number: LA.PHAR.367
Effective Date: 03.16.23
Last Review Date: ~~06.25.23~~02.2311.27.23
Line of Business: Medicaid

Revision Log

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

****Please note: This policy is for medical benefit****

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

FDA Approved Indication(s)
Prevymis is indicated for:

~~Pprophylaxis of CMV infection and disease in adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT).~~

- ~~Prophylaxis of CMV disease in adult kidney transplant recipients at high risk (Donor CMV seropositive/Recipient CMV seronegative [D+/R-])~~Prophylaxis of CMV infection and disease in adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT).
- Prophylaxis of CMV disease in adult kidney transplant recipients at high risk (Donor CMV seropositive/Recipient CMV seronegative [D+/R-])

Policy/Criteria
~~Prior Authorization is required.~~ *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 Louisiana Healthcare Connections 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 any of the following (a or b):
   a. 480 mg per day; if ~~(240 mg per day if co-administered with cyclosporine).~~
   b. ~~240 mg per day~~If co-administered with cyclosporine: 240 mg per day.

Approval duration: Through Day 100 post-transplantation

B. ~~B.~~ Prophylaxis of CMV in Adult Kidney Recipients at High Risk (must meet all):
1. Member has received or scheduled to receive an allograft kidney transplant from a CMV-seropositive donor;
2. Member is CMV-seronegative;
3. Prescribed by or in consultation with a nephrologist 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:
   Pimozide or ergot alkaloids;
   a. Cyclosporine co-administered with pitavastatin or simvastatin;
7. Dose does not exceed any of the following (a or b):
   a. 480 mg per day;
   b. If co-administered with cyclosporine: 240 mg per day.

Approval duration: Through Day 200 post-transplantation

~~B.~~C. ~~C.~~ 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 LA.PMN.255
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 LA.PMN.53

~~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 PDL (Medicaid), the no coverage criteria policy for Medicaid: LA.PMN.255; or~~
   ~~b. For drugs NOT on the PDL (Medicaid), the non-formulary policy for Medicaid: LA.PMN.16; or~~
~~2. If the requested us (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: LA.PMN.53 for Medicaid.~~

II. Continued Therapy

~~a. A. All Indications Prophylaxis of CMV Infection~~ **in Section I** (must meet all)**:**
~~**Adult CMV-Seropositive Recipients of an Allogeneic HSCT** (must meet all)**:**~~

Formatted: Font: Bold

A. Currently receiving medication via Louisiana Healthcare Connections benefit, or documentation supports that member is currently receiving Prevymis for a covered indication~~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;

1. Member is responding positively to therapy;
2. One of the following (a or b);
   a. HSCT: Member has not received Prevymis therapy beyond 100 days post-~~post-transplantation~~ transplantation; ~~;~~
   b. Kidney transplant: Member has not received Prevymis therapy beyond 200 days post-transplantation;
3. If request is for a dose increase, new dose does not exceed any of the following (a or b):
   a. 480 mg per day
   b. If co-administered with cyclosporine: 240mg per day.

~~2. 480 mg per day (240 mg per day if co-administered with cyclosporine).~~

Approval duration: Through Day 100 post-transplantation (for HSCT) or Day 200 (for kidney transplant) post-transplantation

B. ~~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 LA.PMN.255
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 LA.PMN.53

~~3. 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 PDL (Medicaid), the no coverage criteria policy for Medicaid: LA.PMN.255; or~~
~~b. For drugs NOT on the PDL (Medicaid), the non-formulary policy for Medicaid: LA.PMN.16; or~~

~~4. If the requested us (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: LA.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 policy~~ies~~ – LA.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
D+: donor CMV seropositive
HSCT: hematopoietic stem cell transplant
R+: seropositive recipients
R-: recipient CMV seronegative

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~~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

Indication	Dosing Regimen	Maximum Dose
Prophylaxis of CMV disease in adult kidney transplant recipients at high risk (Donor CMV seropositive/Recipient CMV seronegative [D+/R-]	480 mg administered once daily PO or as an IV infusion over 1 hour through 200 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~~

1. Prevymis Prescribing Information. Whitehouse Station, NJ: Merck and Co., Inc.: June 2023. Available at: https://www.merck.com/product/usa/pi_circulars/p/prevymis/prevymis_pi.pdf . Accessed June 21, 2023.
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. Kidney Transplant
9. Kotton CN, Kumar D, Caliendo AM, et al. The Third International Consensus Guidelines on the Management of Cytomegalovirus in Solid-organ Transplantation. Transplantation 2018; 102:900.

10. Razonable RR, Humar A. Cytomegalovirus in solid organ transplant recipients-Guidelines of the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant 2019; 33:e13512.
–Limaye AP, Budde K, Humar A, et al. Letermovir vs Valganciclovir for prophylaxis of cytomegalovirus in high-risk kidney transplant recipients: A randomized clinical trial. JAMA 2023. ~~2023. Available at: 2022. Available at: https://www.merck.com/product/usa/pi_circulars/p/prevymis/prevymis_pi.pdf. Accessed June 21, 2023.pdf. Accessed October 24, 2022.~~
~~2. Clinical Pharmacology [database online]. Elsevier, Inc.; 2022. Available at: https://www.clinicalkey.com/pharmacology/https://www.clinicalkey.com/pharmacology/. Accessed October 24, 2022.~~
~~*HSCT*~~
~~3. Ljungman P, de La Camara R, Milpied N, Volin L, Russell CA, Crisp A, Webster A;~~

~~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 International Bone Marrow Transplant Study Group. Randomized study of valacyclovir as prophylaxis against cytomegalovirus reactivation in recipients of allogeneic valacyclovir as prophylaxis against cytomegalovirus reactivation in recipients of allogeneic bone marrow transplants. Blood. 2002;99:3050-6.~~
~~4. bone marrow transplants. Blood. 2002;99:3050-6.~~
~~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. 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.~~
~~Tomblyn M, Chiller T, Einsele H, et al. Guidelines for Preventing Infectious ComplicationsInfectious Complications among Hematopoietic Cell Transplantation Recipients: A Global Perspective. Biol Blood Marrow Transplant. 2009; 15: 1143-1238 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. Boeckh M, Ljungman P. How we treat cytomegalovirus in hematopoietic cell transplant recipients. Blood 2009; 113:5711-9.~~

Formatted: Font color: Black, Not Expanded by / Condensed by

Formatted: Font color: Auto, Condensed by 0.05 pt

Schmidt-Hieber, M., Schwarck, S., Stroux, A. et al. Immune reconstitution and cytomegalovirusand
cytomegalovirus infection after allogeneic stem cell transplantation: the important impact
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.
Kidney Transplant

9. Kotton CN, Kumar D, Caliendo AM, et al. The Third International Consensus Guidelines
on the Management of Cytomegalovirus in Solid-organ Transplantation. Transplantation
2018; 102:900.
10. Razonable RR, Humar A. Cytomegalovirus in solid organ transplant recipients-
Guidelines of the American Society of Transplantation Infectious Diseases
Community of Practice. Clin Transplant 2019; 33:e13512.
11. Limaye AP, Budde K, Humar A, et al. Letermovir vs Valganciclovir for prophylaxis of
cytomegalovirus in high-risk kidney transplant recipients: A randomized clinical trial.
JAMA 2023.

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
C9399	Unclassified drugs or biologicals
J3490	Unclassified drugs
J8499	Prescription drug, oral, non chemotherapeutic, nos

Reviews, Revisions, and Approvals	Date	LDH~~P&T~~ Approval Date
Converted corporate to local policy	02.23	03.16.23
Updated other diagnoses/indications ~~criteria~~criteria. Added blurb that this policy is for medical benefit only. Updated new indication for prophylaxis of CMV disease in adult kidney transplant recipients at high risk to policy; added HCPCS code C9399.	~~06.25.230~~ ~~6.25.23~~11.27.23	

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. LHCC 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.

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 LHCC-level administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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 LHCC has no control or right of control. Providers are not agents or employees of LHCC.

This clinical policy is the property of LHCC. 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.