

Clinical Policy: Letermovir (Prevymis)

Reference Number: ERX.NPA.60

Effective Date: 03.01.18

Last Review Date: 02.22

Line of Business: Commercial, Medicaid

[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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Prevymis is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Prophylaxis of CMV Infection in 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, clinically significant adverse effects are experienced, or member is at high risk for CMV (see *Appendix D*);
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

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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. 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. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

Approval duration: Through Day 100 post-transplantation; or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ganciclovir (Cytovene®)	<u>Prevention of CMV disease in transplant recipients</u> Induction: 5 mg/kg (given IV at a constant rate over 1 hour) every 12 hours for 7 to 14 days Maintenance: 5 mg/kg (given IV 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/day for 5 days per week
valacyclovir (Valtrex®)	<u>Prevention of CMV disease in transplant recipients*</u> 1-2 grams PO QID	8 grams/day

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.

**Off-label*

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.
- High risk for CMV:
 - Human leukocyte antigen (HLA)-related (sibling) donor with at least one mismatch at one of the following three HLA-gene loci: HLA-A, -B or -DR

- Unrelated donor with at least one mismatch at one of the following four HLA-gene loci: HLA-A, -B, -C and -DRB1
- Haploidentical donor
- Use of umbilical cord blood as stem cell source
- Use of ex vivo T-cell-depleted grafts (including ex vivo use of alemtuzumab)
- Grade 2 or greater graft-versus-host disease (GVHD) requiring systemic corticosteroids (defined as the use of ≥ 1 mg/kg/day of prednisone or equivalent dose of another corticosteroid)
- CMV-seropositive recipient
- CMV-seronegative recipients who receive a graft from CMV-seropositive donor

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 QD.	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.: February 2021. Available at https://www.merck.com/product/usa/pi_circulars/p/prevymis/prevymis_pi.pdf. Accessed September 14, 2021.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: <http://www.clinicalpharmacology-ip.com>. Accessed September 14, 2021.
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, Snyderman 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. *Int J Hematol* (2010) 91: 877. <https://doi.org/10.1007/s12185-010-0597-6>.
8. Tomblyn M, Chiller T, Einsele H, Gress R, Sepkowitz K, Storek J, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant* 15:1143-1238.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	11.28.17	02.18
1Q 2019 annual review: added redirection to valacyclovir or ganciclovir; revised initial criteria to include scheduled transplant in addition to already received transplant; 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
1Q 2021 annual review: no significant changes; added additional definitions of high risk to Appendix D; references reviewed and updated.	10.20.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	09.14.21	02.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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