Clinical Policy: Letermovir (Prevymis)

Reference Number: CP.PHAR.367
Effective Date: 03.01.18
Last Review Date: 02.20
Line of Business: Commercial, Medicaid, HIM-Medical Benefit 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. 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*);
   **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: Through Day 100 post-transplantation

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is

NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

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 or prophylaxis of CMV infection in adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant 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 or 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 Centene benefit and documentation supports positive response to therapy.
   Approval duration: Through Day 100 post-transplantation; or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

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, CP.PMN.53 for Medicaid and HIM-Medical Benefit 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

Appendix B: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ganciclovir (Cytovene®)	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. Maintenance: 5 mg/kg (given intravenously at a constant-rate over 1	6 mg/kg once daily for 5 days per week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	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 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.
- 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 alemtuzamab)

- 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)

V. Dosage and Administration

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

VI. Product Availability

- Tablet: 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.: November 2017. Available at: https://www.merck.com/product/usa/pi_circulars/p/prevymis/prevymis_pi.pdf, Accessed October 8, 2019.
2. Cytovene Prescribing Information. South San Francisco, CA: Genentech, Inc.: August 2018. Available at https://www.gene.com/download/pdf/cytovene_prescribing.pdf. Accessed November 5, 2018.
3. Valtrex Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline: December 2013. Available at https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Valtrex/pdf/VALTREX-PI-PIL.PDF. Accessed November 5, 2018.
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8. Schmidt-Hieber, M., Schwarck, S., Stroux, A. et al. Int J Hematol (2010) 91: 877. https://doi.org/10.1007/s12185-010-0597-6.

9. 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
Per SDC: added redirection to valacyclovir or ganciclovir. Revised initial criteria to include scheduled transplant in addition to already received transplant.	06.14.18	
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

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.