



Effective Date: 02/2019
Last P&T Approval/Version: 01/26/2022
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Policy Number: C15922

Prevymis (letermovir)

PRODUCTS AFFECTED

Prevymis (letermovir)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:

Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:

Prophylaxis of cytomegalovirus (CMV) infection

REQUIRED MEDICAL INFORMATION:

This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

A. PROPHYLAXIS OF CYTOMEGALOVIRUS INFECTION:

1. Documentation that member as received, or is scheduled to receive, an allogeneic hematopoietic stem cell transplant (HSCT)
AND
2. Documentation that member is a confirmed CMV seropositive recipient (R+)
AND
3. Prescriber attests Prevymis (letermovir) will be initiated between Day 0 and Day 28 post-transplant

Drug and Biologic Coverage Criteria

AND

4. Prescriber attests the members medication profile has been reviewed and member it not concurrently receiving medications that are CONTRAINDICATED with Prevmis (letermovir) (i.e., pimozide, ergot alkaloids, pitavastatin and simvastatin when co-administered with cyclosporine)
AND
5. FOR IV THERAPY REQUESTS: Medical justification (with supporting documentation) must be provided explaining why the member is unable to use oral therapy AND Anticipated duration of IV therapy has been documented AND Member will be switched to oral Prevmis therapy as soon as he/ she is able to take oral medications (if applicable)
AND
6. ONE of the following:
 - (a) Documentation of inadequate treatment response, intolerance, contraindication, or non-susceptibility to treatment- ganciclovir (IV) AND valganciclovir
OR
 - (b) Request is for a continuation of therapy that was started at an in-patient setting (within the last 14days) and member is at time of request transitioning to an outpatient site of care [DISCHARGE DOCUMENTATION REQUIRED- WHICH INCLUDES SPECIALIST PRESCRIBER NOTES (SEE PRESCRIBER REQUIREMENTS), DURATION OF THERAPY; START AND END DATE]

CONTINUATION OF THERAPY:

NA

DURATION OF APPROVAL:

Per FDA label: to be continued through day 100 post transplantation.

PRESCRIBER REQUIREMENTS:

Prescribed by, or in consultation with, a physician who specializes in infectious disease, hematologist or a transplant specialist. [If prescribed in consultation, consultation notes must be submitted within initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

Tablets: 240 mg, 112 tablets per 100 days OR 480 mg, 112 tablets per 100 days- maximum 28 days per fill
Infusion: 240 mg (12 mL vial) 100 vials per 100 days OR 480 mg (24 mL vial) 100 vials per 100 days maximum 28 days per fill

*If Prevmis is co-administered with cyclosporine, the dose of Prevmis (letermovir) should be decreased to 240mg once daily

PLACE OF ADMINISTRATION:

The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-inpatient hospital facility-based location.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Oral and Intravenous

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Drug and Biologic Coverage Criteria

DRUG CLASS:

CMV Agents

FDA-APPROVED USES:

PREVYMIS is indicated for:

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

COMPENDIAL APPROVED OFF-LABELED USES:

None

APPENDIX

APPENDIX:

None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Prevymis (letermovir) inhibits the CMV DNA terminase complex (pUL51, pUL56, and pUL89) which is required for viral DNA processing and packaging. Biochemical characterization and electron microscopy demonstrated that letermovir affects the production of proper unit length genomes and interferes with virion maturation. Genotypic characterization of virus resistant to letermovir confirmed that letermovir targets the terminase complex.

Current therapy for CMV in allogeneic stem cells transplant patients is either prophylactic or preemptive therapy. Prophylactic therapy involves administering a drug to prevent infection in patients at increased risk, while preemptive therapy involves starting therapy based upon screening with a sensitive assay to detect early infection. The goal of preemptive therapy is to avoid disease progression. If the antimicrobial therapy is very toxic, preemptive therapy may be a more cautious approach. Medications used for CMV prophylaxis: Cytovene (ganciclovir), Foscarnet (foscarnet) (not an approved FDA indication), Acyclovir (Zovirax) (not an approved FDA indication, alternative therapy), Valtrex (valacyclovir) (not an approved FDA indication). Cytovene has been shown to be the most active product but the bone marrow toxicity side effect limits its use. High-dose Zovirax and Valtrex are less toxic than Cytovene but also have lower in vitro activity against CMV. Thus far, there are no comparative studies comparing Prevymis to any of the other antiviral medications.

Prophylaxis Therapy: Intravenous Cytovene, which has substantially greater anti-CMV activity than Zovirax or Valtrex, has been shown to be associated with a substantial reduction in both infection and disease (almost complete absence of disease) and is the most commonly used anti-CMV agent (1, 2, 3). IV Cytovene did not improve survival in these trials because it was associated with neutropenia and secondary bacterial and fungal infections. There was no difference in the risk of CMV disease at day 180 or survival between Cytovene prophylaxis and Cytovene given as preemptive therapy, although there was less CMV disease before day 100. Although survival improvement in individual Cytovene trials was not seen, the trials were underpowered to detect survival differences. However, in an observational study, patients who received prophylactic Cytovene had a survival benefit compared with patients who did not receive either antiviral prophylaxis or preemptive therapy (4). **Preemptive Therapy:** The efficacy of preemptive therapy has been demonstrated in several trials (3, 4, 5, 6, 7, 8). As an example, in a trial in which allogeneic HCT recipients who were CMV-seropositive or who had received a CMV-seropositive allograft were screened for CMV excretion by cultures from multiple sites, 72 patients who were virus excretors were randomly assigned to receive Cytovene (5 mg/kg IV twice daily for one week, then once daily for the first 100 days) or placebo (8). The primary adverse effect was neutropenia, which occurred in 30% of patients. Cytovene markedly reduced the incidence of CMV disease (3% versus 43%) and significantly increased overall survival. Another randomized trial showed that Foscarnet (90 mg/kg IV twice daily) was as effective as Cytovene (5 mg/kg IV twice daily) for preemptive

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therapy of CMV infection in allogeneic HCT recipients (9). As far as combination therapy is concerned, Cytovene with Foscarnivir, both at one-half of the usual dose, was not more effective than full-dose Cytovene (10). The combination regimen was also associated with more toxicity

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Prevyim (letermovir) that are not an FDA-approved indication or not included in this policy are considered not medically necessary. This is subject to change based on research and medical literature, or at the discretion of Molina Healthcare.

OTHER SPECIAL CONSIDERATIONS:

None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J3490	(NOC)

AVAILABLE DOSAGE FORMS:

Prevymis SOLN 480MG/24ML, Prevymis SOLN 240MG/12ML, Prevymis TABS 480MG, Prevymis TABS 240MG

REFERENCES

1. Kropelit D, McCormick D, Erb-Zohar K, et al. Pharmacokinetics and safety of the anti-human cytomegalovirus drug letermovir in subjects with hepatic impairment. *Br J Clin Pharmacol.* 2017a;83(12):2678-2686. doi: 10.1111/bcp.13376
2. Prevymis (letermovir) tablets and injection [prescribing information]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp; February 2021.
3. Centers for Disease Control and Prevention. Cytomegalovirus (CMV) and congenital CMV infection. 2017 December. URL: <https://www.cdc.gov/cmV/clinical/features.html>.
4. Ljungman P, Hakki M, and Boeckh M. Cytomegalovirus in hematopoietic stem cell transplant recipients. *Hematol Oncol Clin North Am.* 2011; 25(1):151–69.
5. Marty FM, Ljungman P, Chemaly RF, et al. Letermovir prophylaxis for cytomegalovirus in hematopoietic-cell transplantation. *N Engl J Med.* 2017; 377(25):2433-44.
6. 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.