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

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 pimozone 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

Revision Log
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

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>ganciclovir</td>
<td>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</td>
<td>6 mg/kg once daily for 5 days per week</td>
</tr>
<tr>
<td>(Cytovene®)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Drug Name | Dosing Regimen | Prevention of CMV disease in transplant recipients | Dose Limit/Maximum Dose
---|---|---|---
| | 5 mg/kg (given intravenously at a constant rate over 1 hour) every 12 hours for 7 to 14 days. | | 
| | 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 | Off-label regimen: 2 grams PO QID |

Valacyclovir (Valtrex®) Prevention of CMV disease in transplant recipients 2 grams PO QID

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 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)

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prophylaxis of CMV infection in adult CMV-seropositive recipients [R+] of an allogeneic stem cell transplant</td>
<td>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.</td>
<td>480 mg (or 240 mg when co-administered with cyclosporine) per day</td>
</tr>
</tbody>
</table>

VI. Product Availability

- Tablet: 240 mg, 480 mg
- Single-dose vials: 240 mg/12 mL, 480 mg/24 mL

VII. References


<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created</td>
<td>11.28.17</td>
<td>02.18</td>
</tr>
<tr>
<td>Per SDC: added redirection to valacyclovir or ganciclovir. Revised initial criteria to include scheduled transplant in addition to already received transplant.</td>
<td>06.14.18</td>
<td></td>
</tr>
<tr>
<td>1Q 2019 annual review: no significant changes; references reviewed and updated.</td>
<td>11.05.18</td>
<td>02.19</td>
</tr>
<tr>
<td>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.</td>
<td>10.09.19</td>
<td>02.20</td>
</tr>
</tbody>
</table>

**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.

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**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.

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