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

**Description**
Valganciclovir (Valcyte®) is a deoxynucleoside analogue cytomegalovirus (CMV) DNA polymerase inhibitor.

**FDA Approved Indication(s)**
Valcyte is indicated for:
- **Adult patients**
  - Treatment of CMV retinitis in patients with acquired immunodeficiency syndrome (AIDS)
  - Prevention of CMV disease in kidney, heart, and kidney-pancreas transplant patients at high risk (Donor CMV seropositive/Recipient CMV seronegative [D+/R-])
- **Pediatric patients**
  - Prevention of CMV disease in kidney transplant patients (4 months to 16 years of age) and heart transplant patients (1 month to 16 years of age) at high risk

**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 Valcyte is medically necessary when the following criteria are met:

**I. Initial Approval Criteria**

A. **CMV Prophylaxis in Heart, Kidney, or Kidney-Pancreas Transplant** (must meet all):
   1. Member has a history of heart, kidney, or kidney-pancreas transplant;
   2. Organ donor or recipient is CMV seropositive;
   3. Dose does not exceed 900 mg per day.
   **Approval duration:**
   - Heart or kidney-pancreas transplant: 6 months
   - Kidney transplant: 200 days

B. **CMV Retinitis** (must meet all):
   1. Diagnosis of CMV retinitis;
   2. Prescribed by or in consultation with an ophthalmologist;
   3. Age > 16 years;
   4. Member is human immunodeficiency virus (HIV)-positive;
   5. Dose does not exceed the following:
      a. Induction: 1800 mg per day for 21 days;
      b. Maintenance: 900 mg per day.
   **Approval duration:** 4 months

C. **CMV Prophylaxis in Liver or Lung Transplant** (off-label) (must meet all):
   1. Member has a history of liver or lung transplant;
   2. Organ donor or recipient is CMV seropositive;
   3. Dose does not exceed 900 mg per day.
Approval duration:
Liver transplant: 6 months
Lung transplant: 12 months

D. CMV-Associated Gastrointestinal Diseases (off-label) (must meet all):
1. Diagnosis of a CMV-associated gastrointestinal disease (e.g., CMV esophagitis, colitis);
2. Prescribed by or in consultation with an infectious disease specialist or gastroenterologist;
3. Age > 16 years;
4. Member is HIV-positive;
5. Dose does not exceed 1800 mg per day.
Approval duration: 42 days

E. 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. CMV Prophylaxis in Heart, Kidney, or Kidney-Pancreas Transplant (must meet all):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member meets one of the following (a or b):
   a. Heart or kidney-pancreas transplant: member has not received ≥ 6 months of therapy;
   b. Kidney transplant: member has not received ≥ 200 days of therapy;
3. If request is for a dose increase, new dose does not exceed 900 mg per day.
Approval duration:
Heart or kidney-pancreas transplant: Up to 6 months total
Kidney: Up to 200 days total

B. CMV Retinitis (must meet all):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Adherent to antiretroviral therapy (ART) as evidenced by pharmacy claims history;
3. If member has received ≥ 4 months of therapy, member meets one of the following (a or b):
   a. CD4 count is < 100 cells/mm³ (within the last 3 months);
   b. Continuation of therapy is recommended by an ophthalmologist;
4. If request is for a dose increase, new dose does not exceed 900 mg per day.
Approval duration: 3 months

C. CMV Prophylaxis in Liver or Lung Transplant (off-label) (must meet all):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member meets one of the following (a or b):
   a. Liver transplant: member has not received ≥ 6 months of therapy;
   b. Lung transplant: member has not received ≥ 12 months of therapy;
3. If request is for a dose increase, new dose does not exceed 900 mg per day.
Approval duration:
Liver transplant: Up to 6 months total
Lung transplant: Up to 12 months total

D. CMV-Associated Gastrointestinal Diseases (off-label) (must meet all):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Adherent to ART as evidenced by pharmacy claims history;
3. Member has experienced disease relapse since initial request;
4. If request is for a dose increase, new dose does not exceed 900 mg per day.
Approval duration: Duration of request or 3 months (whichever is less)

E. 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: Duration of request or 12 months (whichever is less); 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
   ART: antiretroviral therapy
   CMV: cytomegalovirus
   FDA: Food and Drug Administration
   HIV: human immunodeficiency virus

   Appendix B: Therapeutic Alternatives
   Not applicable

   Appendix C: Contraindications/Boxed Warnings
   • Contraindication(s): hypersensitivity
   • Boxed warning(s): hematologic toxicity, impairment of fertility, fetal toxicity, mutagenesis, and carcinogenesis

   Appendix D: General Information
   • Based on the 2009 Solid Organ Transplant Guidelines for CMV prophylaxis and the 2010 International guidelines, 3 to 6 months of prophylaxis therapy is recommended for donor+/recipient- heart transplant recipients and kidney/pancreas recipients. Three months of prophylactic therapy is recommended for recipient+ heart transplant recipients.
   • Based on the results of the IMPACT study, Valcyte prophylaxis for 200 days in kidney transplant patients resulted in a reduction in CMV disease. At 2 years post-transplant, CMV disease occurred in significantly less patients in the 200- vs. the 100-day group: 21.3% vs. 38.7%, respectively (p < 0.001).
   • Although Valcyte is not FDA approved for the prevention of CMV disease in liver transplant patients, consensus treatment guidelines support the use of Valcyte in this transplant type. The FDA has cautioned against valganciclovir prophylaxis in liver recipients due to high rate of tissue-invasive disease compared to oral ganciclovir.
   • Data supporting the use of Valcyte for lung transplant patients come from Finlen et al, who concluded that 12 months of Valcyte prophylaxis compared with 3 months provided a protective benefit with a CMV incidence of 12% vs 55% respectively (HR 0.13, CI: 0.03-0.61, p = 0.009). In another randomized clinical trial by Palmer et al, extending the duration of Valcyte prophylaxis from 3 months to 12 months decreased the incidence of CMV disease from 64% to 10% (p < 0.001).
   • Per CDC guidelines for the treatment of CMV retinitis, Valcyte may be used in combination with ganciclovir intraocular implant for patients with immediate sight-threatening lesions (adjacent to the optic nerve or fovea).
   • Chronic maintenance therapy is not routinely recommended for CMV gastrointestinal disease, unless there is concurrent retinitis or relapses have occurred.
   • The safety and efficacy of Valcyte for oral solution and tablets have not been established in children for prevention of CMV disease in pediatric liver transplant patients, in kidney transplant patients less than 4 months of age, in heart transplant patients less than 1 month of age, in pediatric AIDS patients with CMV retinitis, and in infants with congenital CMV infection. In 2010,
the FDA added an upper limit to pediatric dosing calculation to prevent Valcyte overdoing in children with low body weight, surface area and below normal serum creatinine.

### V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
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<tbody>
<tr>
<td><strong>Adult Dosage</strong></td>
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<tr>
<td>Prevention of CMV disease in heart or kidney-pancreas transplant patients</td>
<td>900 mg (two 450 mg tablets) PO QD within 10 days of transplantation until 100 days post-transplantation</td>
<td>900 mg/day</td>
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<tr>
<td>Prevention of CMV disease in kidney transplant patients</td>
<td>900 mg (two 450 mg tablets) PO QD within 10 days of transplantation until 200 days post-transplantation</td>
<td>900 mg/day</td>
</tr>
<tr>
<td>Treatment of CMV retinitis</td>
<td>Induction: 900 mg (two 450 mg tablets) PO BID for 21 days</td>
<td>Induction: 1800 mg/day; Maintenance: 900 mg/day</td>
</tr>
<tr>
<td>Prevention of CMV disease in liver transplantation†</td>
<td>900 mg (two 450 mg tablets) PO QD within 10 days of transplantation</td>
<td>900 mg/day</td>
</tr>
<tr>
<td>Prevention of CMV disease in lung transplantation†</td>
<td>900 mg (two 450 mg tablets) PO QD within 10 days of transplantation</td>
<td>900 mg/day</td>
</tr>
<tr>
<td>Treatment of CMV esophagitis† or colitis†</td>
<td>Doses are the same as for CMV retinitis</td>
<td>900 mg/day; 1800 mg/day during induction therapy</td>
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| **Pediatric Dosage**                             |                                                                               |                   |
| Prevention of CMV disease in kidney transplant patients 4 months to 16 years of age | Dose once a day within 10 days of transplantation until 200 days post-transplantation according to dosage algorithm (7 x body surface area [BSA] x creatinine clearance [CrCl]*) | Dosage is based on BSA and CrCl; not to exceed 900 mg/day |
| Prevention of CMV disease in heart transplant patients 1 month to 16 years of age | Dose once a day within 10 days of transplantation according to dosage algorithm (7 x BSA x CrCl*) | Dosage is based on BSA and CrCl; not to exceed 900 mg/day |

* Calculated using a modified Schwartz formula  
† Off-label indication

### VI. Product Availability
- Oral solution: 50 mg/mL
- Tablets: 450 mg

### VII. References

### Reviews, Revisions, and Approvals

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<th>Date</th>
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- **Policy created.**
- **Updated to new template (converted algorithm to bulleted criteria, added background and references).** Updated criteria to indicate donor (not recipient) should be seropositive for CMV prophylaxis in organ transplant per FDA labeling. Separated initial and continued approval durations for treatment of CMV and modified from “120 days total” for both to “4 months” for initial then “3 months” for continued per literature review. Added requirement for adherence to ART for continuation of CMV prophylaxis per literature review.
- **Converted to new template.**
  - All indications: modified general FDA approved maximum recommended dose statement to reflect actual max dose.
  - CMV prophylaxis in heart, kidney, or kidney-pancreas transplant: per consensus guidelines and/or Razonable et al, modified to include CMV seropositive recipients; increased approval duration for heart transplant from 100 days to 6 months/decreased approval duration for kidney-pancreas transplant from 200 days to 6 month-updated re-auth criteria to align with initial approval duration.
  - CMV retinitis: added prescriber specialty; modified age restriction from ≥ 16 years to > 16 per Clinical Pharmacology; CMV-associated GI diseases: separated from CMV retinitis criteria to indicate off-label indication; added prescriber specialty; modified age restriction from ≥ 16 years to > 16 per Clinical Pharmacology; modified initial approval duration from 4 months to 42 days per opportunistic infections in HIV guideline; for re-auth, added requirement for disease relapse.
  - Added off-label criteria set for CMV prophylaxis in liver or lung transplant per consensus treatment guidelines.
  - Updated references.
- **3Q 2018 annual review: no significant changes; references reviewed and updated.**
- **1Q 2019 annual review: no significant changes, references reviewed and updated.**

### 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.