

Clinical Policy: Valganciclovir (Valcyte)

Reference Number: CP.PCH.06

Effective Date: 12.01.17

Last Review Date: 02.20

Line of Business: Commercial, HIM*

[Revision Log](#)

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.

**For Health Insurance Marketplace (HIM), valganciclovir oral solution 50 mg/mL is non-formulary and cannot be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

FDA Approved Indication(s)

Valcyte is indicated for:

- Adult patients
 - Treatment of CMV retinitis in patients with acquired immunodeficiency syndrome (AIDS).
 - For the prevention of CMV disease in kidney, heart, or kidney-pancreas transplant patients at high risk (donor CMV seropositive/recipient CMV seronegative [D+/R-]).
- Pediatric patients
 - Prevention of CMV disease in kidney (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.

It is the policy of health plans affiliated with Centene Corporation® 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

(For HIM, approve valganciclovir tablets 450 mg only. Refer to HIM.PA.103 for valganciclovir oral solution 50 mg/mL)

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: 1,800 mg per day for 21 days;
 - b. Maintenance: 900 mg per day.

Approval duration: 4 months

(For HIM, approve valganciclovir tablets 450 mg only. Refer to HIM.PA.103 for valganciclovir oral solution 50 mg/mL)

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 – 6 months; Lung – 12 months

(For HIM, approve valganciclovir tablets 450 mg only. Refer to HIM.PA.103 for valganciclovir oral solution 50 mg/mL)

D. CMV-Associated Gastrointestinal Diseases (off-label) (must meet all):

1. Diagnosis of 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 1,800 mg per day.

Approval duration: 42 days

(For HIM, approve valganciclovir tablets 450 mg only. Refer to HIM.PA.103 for valganciclovir oral solution 50 mg/mL)

E. 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 HIM.PHAR.21 for health insurance marketplace.

II. Continued Therapy

A. CMV Prophylaxis in Heart, Kidney, or Kidney-Pancreas Transplant (must meet all):

1. Currently receiving medication via Centene benefit 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

(For HIM, approve valganciclovir tablets 450 mg only. Refer to HIM.PA.103 for valganciclovir oral solution 50 mg/mL)

B. CMV Retinitis (must meet all):

1. Currently receiving medication via Centene benefit 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

(For HIM, approve valganciclovir tablets 450 mg only. Refer to HIM.PA.103 for valganciclovir oral solution 50 mg/mL)

C. CMV Prophylaxis in Liver or Lung Transplant (off-label) (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member meets one of the following:
 - 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

(For HIM, approve valganciclovir tablets 450 mg only. Refer to HIM.PA.103 for valganciclovir oral solution 50 mg/mL)

D. CMV-Associated Gastrointestinal Diseases (off-label) (must meet all):

1. Currently receiving medication via Centene benefit 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)

(For HIM, approve valganciclovir tablets 450 mg only. Refer to HIM.PA.103 for valganciclovir oral solution 50 mg/mL)

E. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
Approval duration: Duration of request or 12 months (whichever is less); 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 HIM.PHAR.21 for health insurance marketplace.

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 and HIM.PHAR.21 for health insurance marketplace.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AIDS: acquired immunodeficiency syndrome

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 overdosing in children with low body weight, surface area and below normal serum creatinine.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Adult Dosage		
Prevention of CMV disease in heart or kidney-pancreas transplant patients	900 mg (two 450 mg tablets) PO QD within 10 days of transplantation until 100 days post-transplantation	900 mg/day
Prevention of CMV disease in kidney transplant patients	900 mg (two 450 mg tablets) PO QD within 10 days of transplantation until 200 days post-transplantation	900 mg/day
Treatment of CMV retinitis	Induction: 900 mg (two 450 mg tablets) PO BID for 21 days Maintenance: 900 mg (two 450 mg tablets) PO QD	Induction: 1,800 mg/day; Maintenance: 900 mg/day
Prevention of CMV disease in liver transplantation [†]	900 mg (two 450 mg tablets) PO QD within 10 days of transplantation	900 mg/day
Prevention of CMV disease in lung transplantation [†]	900 mg (two 450 mg tablets) PO QD within 10 days of transplantation	900 mg/day
Treatment of CMV esophagitis [†] or colitis [†]	Doses are the same as for CMV retinitis	900 mg/day; 1,800 mg/day during induction therapy
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-	Dosage is based on BSA and CrCl; not to exceed 900 mg/day

Indication	Dosing Regimen	Maximum Dose
	transplantation according to dosage algorithm (7 x body surface area [BSA] x creatinine clearance [CrCl]*)	
Prevention of CMV disease in heart transplant patients 1 month to 16 years of age	Dose once a day within 10 days of transplantation until 100 days post-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
- Tablet: 450 mg

VII. References

1. Valcyte Prescribing Information. South San Francisco, CA: Genentech USA, Inc.; August 2018. Available at <http://www.valcyte.com/>. Accessed September 26, 2019.
2. Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: herpes: cytomegalovirus disease: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at <https://aidsinfo.nih.gov/guidelines/brief-html/4/adult-and-adolescent-opportunistic-infection/337/cytomegalovirus>. Accessed September 26, 2019.
3. Kotton CN, Kumar D, Caliendo AM, et al. The third international consensus guidelines on the management of cytomegalovirus in solid-organ transplantation. *Transplantation*. June 2018; 102 (6): 900-931.
4. Zamora MR, Davis RD, Leonard C. Management of cytomegalovirus infection in lung transplant recipients: evidence-based recommendations. *Transplantation* 2005;80: 157–163.
5. Razonable RR, Humar A, and the AST Infectious Disease Community of Practice. Cytomegalovirus in solid organ transplantation. *Am J Transplant*. 2013 Mar;13 Suppl 4:93-106.
6. Marcelin JR, Beam E, Razonable RR. Cytomegalovirus infection in liver transplant recipients: Updates on clinical management. *World Journal of Gastroenterology : WJG*. 2014;20(31):10658-10667. doi:10.3748/wjg.v20.i31.10658.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Added off-label use for GI diseases in HIV-positive patients. Modified approval duration for heart, kidney-	08.01.17	11.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
pancreas, and liver transplants to 6 months. Added prescriber requirement for retinitis and GI diseases. Added reauthorization criteria for CMV retinitis based on CD4 count per CDC recommendations. Added prescriber restriction for CMV retinitis and associated GI diseases.		
3Q 2018 annual review: no significant changes from previously approved corporate policy; new policy for HIM line of business.	04.25.18	08.18
1Q 2019 annual review: no significant changes, references reviewed and updated.	11.05.18	02.19
1Q 2020 annual review: no significant changes; references reviewed and updated.	9.26.19	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.

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Note:

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

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