Valcyte

Description

Valcyte (valganciclovir)

Background

Valcyte (valganciclovir) is an orally administered antiviral prodrug with no antiviral activity until converted in the body to ganciclovir (1). Ganciclovir is used in the treatment of Cytomegalovirus (CMV) by interfering with DNA synthesis. Adverse events known to be associated with ganciclovir usage can therefore be expected to occur with Valcyte. The bioavailability of ganciclovir for Valcyte is significantly higher than ganciclovir capsules (2,3). Therefore, Valcyte tablets cannot be substituted for ganciclovir capsules on a mg-per-mg basis (1,4).

In adult patients, Valcyte (valganciclovir) tablets are indicated for the treatment of cytomegalovirus (CMV) retinitis in patients with acquired immunodeficiency syndrome (AIDS). Valcyte tablets are also indicated 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-]). Adult patients should use the Valcyte tablets, not the Valcyte oral solution (1).

Regulatory Status

FDA approved indications:

Adult Patients
- **Treatment of Cytomegalovirus (CMV) Retinitis:** Valcyte tablets are indicated for the treatment of CMV retinitis in patients with acquired immunodeficiency syndrome (AIDS).

- **Prevention of CMV Disease:** Valcyte tablets are indicated 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:** Valcyte for oral solution and tablets are indicated for the prevention of CMV disease in kidney or heart transplant patients (4 months to 16 years of age) at high risk.

### Off-label indications:

Appropriate off-label indications include (6-12).

- Treatment of cytomegalovirus (CMV) disease in symptomatic patients
- Prevention of CMV infection in post-hematopoietic stem cell transplant (HSCT)
- Prevention of CMV infection in post solid organ transplant (including liver or lung)

In pediatric patients, both the tablets and oral solution of Valcyte (valganciclovir hydrochloride) are indicated for the prevention of CMV disease in kidney or heart transplant patients (4 months to 16 years of age) who are at high risk.

Cytomegalovirus (CMV) infections are among the most common infections that occur following solid organ transplantation. Organ transplant recipients at highest risk of CMV infection are those who are seronegative before transplantation and receive an organ from a seropositive donor (a combination commonly referred to as donor-positive/recipient-negative [D+/R-]); in these patients, latent CMV can be transmitted with the organ and subsequently reactivate, causing de novo or primary infection. The incidence of CMV disease in D+/R- transplantations is <5% (7).

Valcyte has a boxed warning of hematologic toxicity, carcinogenicity, teratogenicity, and impairment of fertility. Clinical toxicity of Valcyte, which is metabolized to ganciclovir, includes granulocytopenia, anemia, and thrombocytopenia. In animal studies, ganciclovir was carcinogenic, teratogenic, and caused temporary or permanent spermatogenesis.

Severe leukopenia, neutropenia, anemia, thrombocytopenia, pancytopenia, bone marrow depression, and aplastic anemia have been observed with the use of Valcyte or ganciclovir (1).

Valcyte should not be administered if the absolute neutrophil count is <500 cells/µL, the platelet count is <25,000/µL, or the hemoglobin is <8 g/dL (1).

Use with caution in patients with pre-existing cytopenias, or who have received or who are receiving myelosuppressive drugs or irradiation. Cytopenia may occur at any time during treatment and may worsen with continued dosing. Cell counts usually begin to recover within 3 to 7 days after discontinuing drug (1).
Advise women of childbearing potential to use effective contraception during treatment and for at least 30 days following treatment with Valcyte. Advise men to practice barrier contraception during and for at least 90 days following treatment (1).

Acute renal failure may occur in elderly patients with or without reduced renal function, patients receiving concomitant nephrotoxic drugs, or patients without adequate hydration (1). Monitor CBC with differential, platelets, ophthalmic, and renal function. Patients must maintain adequate hydration.

**Look alike / sound alike precaution:** Valtrex (valacyclovir).

**Policy**

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Valcyte may be considered **medically necessary** for the treatment of Cytomegalovirus (CMV) disease in symptomatic patients, or for the prevention of CMV disease in patients who are post solid organ transplant (including heart, liver, lung, kidney, or kidney-pancreas), post hematopoietic cell transplant (HCT), or under treatment for HIV.

Valcyte is considered **investigational** in patients who are CMV sero-negative recipients of a solid organ transplant from a CMV sero-negative donor and in patients with an absolute neutrophil count (ANC) less than 500 cells/μL, a platelet count less than 25,000/μL, or a hemoglobin less than 8 g/dL.

**Prior-Approval Requirements**

*Patients with an HIV diagnosis (one or more anti-retroviral claims in the last 12 months) are exempt from this PA requirement.*

**Diagnoses**

Patient must have **ONE** of the following:

1. **Treatment** of Cytomegalovirus (CMV) disease in symptomatic patients

2. **Prevention** (either prophylaxis or preemptive therapy) of CMV disease in patients who are:

   **ONE** of the following
1. Post solid organ transplant (including heart, liver, lung, kidney, or kidney-pancreas)
2. Post hematopoietic stem cell transplant (HSCT)

AND

1. Absolute neutrophil count (ANC) > 500 cells/μL
2. Platelet count > 25,000/μL
3. Hemoglobin > 8 g/dL

AND NOT

CMV sero-negative recipient of solid organ transplant from a CMV sero-negative donor (R-/D-)

Prior – Approval **Renewal Requirements**
Same as above

**Policy Guidelines**

**Pre - PA Allowance**
None

**Prior - Approval Limits**

Duration 12 months$^8$

**Prior – Approval **Renewal Limits**

Duration 12 months$^8$

**Rationale**

**Summary**

Valcyte (valganciclovir) is an orally administered antiviral prodrug with no antiviral activity until converted in vivo to ganciclovir, and subsequently to the active ganciclovir triphosphate. Ganciclovir triphosphate has in vitro and in vivo inhibitory activity against cytomegalovirus
(CMV). In adult patients, Valcyte (valganciclovir) tablets are indicated for the treatment of CMV retinitis in patients with acquired immunodeficiency syndrome (AIDS). Valcyte tablets are also indicated for the prevention of CMV disease in kidney, heart, or kidney-pancreas transplant patients at high risk. Appropriate off-label indications include the treatment of symptomatic CMV infection and the prevention of CMV disease in high-risk lung and liver transplant patients.

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Valcyte while maintaining optimal therapeutic outcomes.

References
6. Personal Communication, Gerald Medoff, MD, Infectious Diseases, Washington University Hospital, March 1, 2012, for treatment of symptomatic CMV infection, and off-label use post-transplant by recipients of lung and liver transplants.

11. Transplantation Proceedings 2011; 43, S1–S17


### Policy History

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<tr>
<td>June 2012</td>
<td>New Addition</td>
<td>Off-label: Added lung and liver to post solid organ transplant</td>
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<td>March 2013</td>
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### Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 12, 2014 and is effective July 1, 2014.

*Signature on File*

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