RATIONALE FOR INCLUSION IN PA PROGRAM

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: Valcyte is a cytomegalovirus (CMV) nucleoside analogue DNA polymerase inhibitor indicated for: (1)

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
1. Prevention of CMV Disease: Valcyte for oral solution and tablets are indicated for the 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.
Off-label indications: (6-10).

- 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 transplant patients (4 months to 16 years of age) and heart transplant patients (1 month to 16 years of age) who are at high risk (1).

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 (1).

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. Monitor CBC with differential, platelets, ophthalmic, and renal function. Patients must maintain adequate hydration (1).

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

**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 (1).

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Valcyte while maintaining optimal therapeutic outcomes (1-10).

**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.

