Ganciclovir (Cytovene®)

Class:
Ganciclovir is a nucleoside analogue of guanosine and a homologue of acyclovir. Valganciclovir is the valyl ester prodrug of ganciclovir

Antiviral Activity:
Ganciclovir has activity against nearly all herpesviruses. It has little activity against vaccina virus, human papilloma virus, or RNA viruses such as influenza A. Its main use is in the treatment and/or prophylaxis of CMV infection in immunocompromised patients.

Mechanism of Action:
Ganciclovir is phosphorylated to its triphosphate form (ganciclovir triphosphate), which competitively inhibits incorporation of deoxyguanosine triphosphate into elongating DNA. Short subgenomic CMV DNA fragments continue to be synthesized in the presence of ganciclovir. These DNA fragments are not packaged into virions and are therefore not considered infectious.

Mechanism of Resistance:
Mutations producing an inability to phosphorylate ganciclovir are the most common mechanism of resistance.

Pharmacokinetics:
Intravenous ganciclovir achieves higher C_{max} values then oral ganciclovir. However, oral ganciclovir produces serum concentrations that are more sustained over the course of the day. The absolute bioavailability of oral ganciclovir is approximately 8.5%. The absolute bioavailability of ganciclovir from administration of valganciclovir tablets with food is approximately 60%. The plasma protein binding of ganciclovir is negligible (<2%). The kidneys are the primary route of elimination for ganciclovir.

Adverse Effects:
The main dose-limiting adverse effect is bone marrow suppression, resulting in granulocytopenia, anemia and thrombocytopenia. Elevations in serum creatinine, diarrhea, nausea, fever, rash and neurotoxicity have also been seen with ganciclovir use.

Dosage:
Capsule 250mg, 500mg
Powder for injection 500mg

Induction therapy:

> Ganciclovir 5 mg/kg (constant intravenous infusion over 1 h every 12 h for 2 to 3 weeks)

Maintenance therapy (AIDS patients with CMV retinitis)

Ganciclovir 5 mg/kg intravenously daily OR 1000 mg orally three times a daily OR valganciclovir 900 mg (two 450-mg tablets daily)

Primary prophylaxis (CMV retinitis in patients with AIDS)

Ganciclovir 1000 mg orally three times daily OR valganciclovir 900 mg orally daily

Intravitreal therapy (for CMV retinitis)

induction – ganciclovir 400mg two to three times a week
maintenance therapy – ganciclovir 400 mg weekly

Disease state based dosing:
Renal Impairment:
Ganciclovir (Table 3) and Valganciclovir (Table 4) must be dose adjusted in renal insufficiency.

Hepatic Impairment:
No dose adjustment necessary

Contraindications/Warnings/ Precautions:
Ganciclovir should not be administered if the absolute neutrophil count is less than 500 cells/µL or the platelet count is less than 25,000 cells/µL.

Drug Interactions:
Ganciclovir has additive toxicities with other medications that cause bone marrow suppression and drugs that inhibit replication of rapidly dividing cells.

Pregnancy:
Category C: Risk unknown. Human studies inadequate.

Monitoring requirements:
CBC, LFTs, ophthalmologic exam, serum creatinine/BUN

Brand names/Manufacturer:
Cytovene®/Hoffmann La Roche Inc
Ganciclovir/Ranbaxy Pharmaceuticals Inc