Ganciclovir
Newborn Use Only

2017

Alert	**IV ganciclovir is a cytotoxic agent.**
Indication	1) Treatment of severe or moderately severe, symptomatic congenital CMV, or 2) Treatment of acute severe CMV disease.
Action	Synthetic nucleoside analogue of 2-deoxyguanosine that inhibits replication of herpes viruses. Sensitive human viruses include cytomegalovirus, herpes simplex virus 1 and 2, herpes virus type 6, 7 and 8, Epstein-Barr virus, varicella zoster virus and hepatitis B virus.
Drug Type	Antiviral
Trade Name	Cymevene
Presentation	Injection containing ganciclovir sodium 500 mg (for reconstitution)
Dosage/Interval	6 mg/kg/dose 12 hourly. Infants may be switched to oral valganciclovir if clinically stable and able to take oral medications. IV ganciclovir should generally not be used for more than 6 weeks. Please note, oral valganciclovir is the oral prodrug of ganciclovir and prescribed at a different dose.
Route	IV
Preparation/Dilution	**IV ganciclovir is a cytotoxic agent.** Contact Pharmacy to order reconstituted/pre-diluted product. Final concentration should not be higher than 10 mg/mL.
Administration	**IV ganciclovir is a cytotoxic agent. Follow full cytotoxic precautions as per local policy.** IV infusion over 30 minutes with a syringe pump. Central line is preferred as medication has high pH and can cause tissue irritation. Peripheral cannula may be used for short-term treatment but the IV site should be monitored carefully.
Monitoring	Full blood count, particularly neutrophil count, should be followed weekly for 6 weeks, then at week 8, then monthly for the duration of therapy. Liver function tests monthly throughout therapy. Renal function tests.
Contraindications	Hypersensitivity to ganciclovir, valganciclovir, aciclovir or valacyclovir. Patients with: • absolute neutrophil count below 0.5 x 10^9/L or • platelet count below 25 x 10^9/L unless thrombocytopenia is related to CMV disease, or • haemoglobin less than 80 g/L (8 g/dL).
Precautions	Ganciclovir has both gonadal toxicity and carcinogenicity in animal models and its long-term safety after administration to young children is not established.[1]
Drug Interactions	Convulsions have been reported in patients receiving ganciclovir and imipenem-cilastatin concurrently. Concurrent use of tacrolimus and ganciclovir increases nephrotoxicity.
Adverse Reactions	Commonly causes neutropenia. If absolute neutrophil count (ANC) falls below 0.5 x 10^9/L and if it is thought not to be due to CMV disease, withhold medication until ANC is above 0.75 x 10^9/L then restart medication at half dose. If ANC falls below 0.5 x 10^9/L again, consider discontinuing the medication. Can also cause anaemia and thrombocytopenia. Discontinue medication if platelet count below 25 x 10^9/L or haemoglobin less than 80 g/L occurs and is thought not to be due to CMV disease.
Compatibility	<u>Fluids:</u> Glucose 5%, sodium chloride 0.9%. <u>Drugs via Y-site:</u> Anidulafungin, caspofungin, filgrastim, fluconazole, linezolid, remifentanil.
Incompatibility	Fluids: Amino acid/glucose. Lipid emulsion. Drugs: Adrenaline (epinephrine) hydrochloride, amikacin, aminophylline, ampicillin, aztreonam, benzatropine, benzylpenicillin, cefazolin, cefepime, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, clindamycin, dobutamine, dopamine, erythromycin, esmolol, gentamicin,

	hydralazine, hydrocortisone sodium succinate, imipenem-cilastatin, lidocaine (lignocaine), magnesium sulfate, methylprednisolone sodium succinate, metronidazole, midazolam, morphine sulfate, mycophenolate mofetil, noradrenaline (norepinephrine), pentamidine, pethidine, phenylephrine, piperacillin-tazobactam (EDTA-free), potassium acetate, pyridoxine, sodium ascorbate, sodium bicarbonate, suxamethonium, tacrolimus, thiamine, ticarcillin-clavulanate, tobramycin, vancomycin, vecuronium, verapamil.
Stability	Compounding centres that are licensed by the Australian Therapeutic Goods Administration to reconstitute and/or further dilute cytotoxic medicines and have validated aseptic procedures and regular monitoring of aseptic technique may apply a shelf life of 15 days at 2 to 8°C (refrigerate, do not freeze) to ganciclovir IV infusions reconstituted with water and further diluted with sodium chloride 0.9% or glucose 5%. Please contact your Pharmacy Department for more information or refer to expiry date on the product.
Storage	Unused vials: Store below 30°C. Pre-diluted solution: Store at 2 to 8°C (or as instructed on product label by compounding facility)
Special Comments	
Evidence summary	**Efficacy and safety:** **Symptomatic congenital cytomegalovirus disease:** A randomised, controlled trial in infants ≥ 32 weeks GA of 6 weeks IV ganciclovir 6 mg/kg every 12 hours demonstrated more infants had improved hearing or maintained normal hearing between baseline and 6 months in the IV ganciclovir group versus placebo (84% vs 59%, p = 0.06) and fewer infants had worsening hearing (0% vs 41%, p < 0.01).[1] This effect was sustained at 1 year of age, when 21% of infants in the treatment group had worsening hearing versus 68% in the placebo group (p < 0.01)[1]. Two-thirds of the treatment group developed significant neutropenia[1]. At 12 months, infants treated with 6 weeks IV ganciclovir had fewer developmental delays.[2] [LOE II, GOR B – see below for recommendation]. There are case reports of the use of 10–12 mg/kg/day in 2 divided doses in extreme preterm infants.[10-14] **International Congenital Cytomegalovirus Recommendations Group:** Ganciclovir is now available as an oral prodrug, valganciclovir. A recent RCT now recommends valganciclovir treatment for congenitally-infected neonates ≥ 32 weeks of life, with moderate to severe symptomatic disease, to be commenced within the first month of life and for 6 months. Antiviral therapy should not be administered to neonates with asymptomatic congenital cytomegalovirus infections. Antiviral therapy is not routinely recommended for asymptomatic congenital cytomegalovirus infection with isolated sensorineural hearing loss or for neonates with mildly symptomatic congenital cytomegalovirus infection.[3] **Pharmacokinetics:** In symptomatic newborns with CMV, the mean elimination half-life of ganciclovir was 2.4 hours.[4] A target AUC_{12} (area under the concentration-time curve over a 12-h period) of 27 mg x h/L has been defined.[5] The clearance of intravenous ganciclovir nearly doubled and the AUC_{12} was reduced by almost one-half during the first 6 weeks of life.[5] Based on these data, it appears ganciclovir 6 mg/kg every 12 hours may be insufficient to achieve the pharmacokinetic target despite evidence for clinical and virological efficacy.[5] A pharmacokinetic study showed that oral valganciclovir 16 mg/kg every 12 hours achieved similar concentrations to IV ganciclovir 6 mg/kg every 12 hours. [5] [LOE III, GOR B]
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