ValGANciclovir
Newborn use only

2021

Alert	**Cytotoxic agent.**
Indication	1. Treatment of severe or moderately severe, symptomatic congenital CMV, or 2. Treatment of acute severe CMV disease.
Action	Valganciclovir is an L-valyl ester salt (prodrug) of ganciclovir which, after oral administration, is rapidly converted to ganciclovir by intestinal and hepatic esterases. 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	Valcyte
Presentation	Valganciclovir hydrochloride powder for oral solution. The reconstituted solution contains 50 mg/mL valganciclovir and appears clear, colourless to brownish-yellow in colour.
Dose	16 mg/kg/dose 12 hourly* *In acute, severe CMV disease including hepatitis, use IV ganciclovir as initial therapy and change over to oral valganciclovir once clinically stable and able to tolerate oral feeds. Duration of treatment: 1. Treatment of severe or moderately severe, symptomatic congenital CMV – maximum 6 months. 2. Treatment of acute severe CMV disease – as per the disease progress and response.
Dose adjustment	Therapeutic hypothermia - Insufficient data to make recommendations. ECMO - Insufficient data to make recommendations. Renal impairment - Reduce dosage according to the severity of renal insufficiency[13] Hepatic impairment - Insufficient data to make recommendations.
Maximum dose	
Total cumulative dose	
Route	Oral
Preparation	**Cytotoxic agent.** Refer to local policy in regard to safety precautions/facilities required to reconstitute the powder for oral solution.
Administration	**Follow full cytotoxic precautions as per local policy.** Should be given with feeds and can be given with other medications.
Monitoring	Baseline 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. Blood CMV viral load as required
Contraindications	Hypersensitivity to valganciclovir, ganciclovir or to any of the excipients. 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	Active component of valganciclovir (i.e. ganciclovir) has both gonadal toxicity and carcinogenicity in animal models and its long-term safety after administration to young children is not established. Renal insufficiency. Due to the similarity of the chemical structure of ganciclovir and that of acyclovir, a cross-hypersensitivity reaction between these drugs is possible. Caution should be used when prescribing valganciclovir to patients with known hypersensitivity to aciclovir or to it's prodrug valaciclovir.
Drug interactions	Convulsions have been reported in patients receiving ganciclovir (metabolite of valganciclovir) and imipenem-cilastatin concurrently. Concurrent use of tacrolimus and ganciclovir increases nephrotoxicity. A pharmacodynamic interaction may occur during concomitant administration of zidovudine and valganciclovir (both have the potential to cause neutropenia and anaemia) and some patients may not tolerate concomitant therapy at full dosage.

	Note: interaction studies have only been performed in adults.
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	Not applicable
Incompatibility	Not applicable
Stability	The reconstituted solution should be discarded 49 days after reconstitution.
Storage	Store powder for reconstitution below 30°C. After reconstitution, the solution should be stored in the refrigerator (2-8°C). Do not freeze.
Excipients	Povidone, fumaric acid, sodium benzoate (E211), saccharin sodium, mannitol, tutti-frutti flavour.
Special comments	
Evidence	Efficacy and safety: Symptomatic congenital cytomegalovirus disease: A randomised controlled trial (RCT) 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 is sustained at 1 year of age, when 21% 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] [Ganciclovir: LOE II GORR B] An RCT of oral valganciclovir 16 mg/kg 12 hourly for 6 months versus 6 weeks in neonates ≥ 32 weeks and ≤ 30 days of age and weighing at least 1800 g at the initiation of therapy reported better total-ear hearing at 12 months in patients treated for 6 months compared to 6 weeks (73% vs. 57%, P = 0.01), which is modestly maintained at 24 months (77% vs. 64%, P = 0.04), without an increase in neutropenia. The 6-month group had better neurodevelopment scores at 24 months.[3] Valganciclovir treatment was associated with neutropenia,[3] although the incidence was markedly lower than previously observed with intravenous ganciclovir.[1, 2] [LOE II GOR B] There are case reports of the use of oral valganciclovir in extreme preterm infants.[9-12] **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.[4] [LOE II, GOR B] **Pharmacokinetics:** 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. Only a marginal decrease in AUC_{12} over time was noted after administration of the valganciclovir oral solution despite increased clearance, due to increased bioavailability, by 32% over the same period. The oral bioavailability of valganciclovir averaged 41.1% (95% CI, 30.8%–51.4%).[5] [LOE III, GOR B]
Practice points	
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Authors Contribution

Original author/s	Jing Xiao, Srinivas Bolisetty
Evidence Review	David Osborn
Expert review	Brendan McMullan, Alisson Kesson, Tony Lai
Nursing Review	Eszter Jozsa, Kirsty Minter
Pharmacy Review	Thao Tran
ANMF Group contributors	Nilkant Phad, Bhavesh Mehta, John Sinn, Jessica Mehegan, Michelle Jenkins, Helen Huynh, Simarjit Kaur
Final editing and review of the original	Ian Whyte

Electronic version	Cindy Chen, Ian Callander
Facilitator	Srinivas Bolisetty