DESCRIPTION	Valganciclovir, a guanine analogue is a prodrug of ganciclovir. It inhibits viral DNA polymerase and DNA synthesis following phosphorylation by viral and cellular enzymes.[1,2] Valganciclovir is used in the treatment and prophylaxis of cytomegalovirus (CMV) in immunosuppressed patients.[1]
ChAMP INDICATIONS AND RESTRICTIONS	**Oral: Category B: Monitored** ChAMP team to be informed of use and will review if ongoing therapy is required and does not meet specified indications. **Standard Indications:** • CMV prophylaxis post solid organ transplant • CMV retinitis Section 100 criteria may apply prescribers to complete the declaration form and return to the Pharmacy department: Attention S100 technician: http://cahs.hdwa.health.wa.gov.au/__data/assets/pdf_file/0010/70111/Valganciclovir_Hydrochloride.pdf
FORMULATIONS	450mg tablets 50mg/mL powder for oral solution
DOSAGE	The doses listed below fall within the standard range. Higher doses may be prescribed for certain situations. This should be in consultation with Infectious Diseases or Microbiology consultants. $BSA\ (m^2) = \sqrt{\frac{Height\ (cm) \times Weight\ (kg)}{3600}}$ $CrCl\ (mL/minute/1.73m^2) = \frac{36.5 \times Height\ (cm)}{Serum\ Creatinine(micromoles/L)}$.[7,8] Note: Use a value of 150mL/minute to calculate the dose if the calculated creatinine clearance exceeds this value.[4,5] **Oral:** **Cytomegalovirus prophylaxis post transplant:** Infants 4 months and older to adolescents 16 years and under: 7 x BSA x CrCl given once daily. The dose should be rounded to the nearest 25mg, should not exceed 900mg daily and should be commenced within 10 days of the transplant.[1,4,5] Adolescents 16 years and over: 900mg once daily commencing within 10 days of the transplant.[1,3] **Cytomegalovirus retinitis (adolescents 16 years and older):** Induction: 900mg twice daily for 21 days Maintenance: 900mg once daily.[5] **Neonates:** Not routinely used in neonates, contact Infectious Disease or Microbiology consultants for advice. Suggested dose 16mg/kg/dose 12 hourly.[4,5,6]
DOSAGE ADJUSTMENT	**Dosage adjustment required in renal impairment:** Dosage adjustment may be required in cases of impaired renal function (with creatinine clearance of less than 60mL/min).[1] http://cahs.hdwa.health.wa.gov.au/__data/assets/pdf_file/0003/106986/01_Guidlines_for_calculating_CLcr.pdf The following dose adjustments are to be applied to adolescents with a recommended dose in normal renal function of 900mg. For younger children, the dose calculation stated above already takes into account the individuals renal function and no further adjustment is required.[5]

	Valganciclovir induction: CrCl > 60mL/minute = normal dosing CrCl 40-59 mL/minute = 50% 12 hourly CrCl 25-39mL/minute = 50% 24 hourly CrCl 10-24mL/minute = 50% 48 hourly CrCl <10mL/minute = avoid use, consider IV ganciclovir.[2,3,5] Valganciclovir maintenance: CrCl > 60mL/minute = normal dosing CrCl 40-59 mL/minute = 50% 24 hourly CrCl 25-39mL/minute = 50% 48 hourly CrCl 10-24mL/minute = 50% twice weekly CrCl <10mL/minute = avoid use, consider IV ganciclovir.[2,3,5]
RECONSTITUTION	Valganciclovir is potentially carcinogenic and mutagenic. Proper procedures for the handling and disposal of cytotoxic agents should be followed.[3,9] Reconstitute with 91mL of water as follows: tap bottle until all powder flows freely; add the total volume of water for reconstitution, replace the cap and shake vigorously to dissolve the powder. Once reconstituted, remove the cap and push the bottle adaptor into the neck of the bottle. Replace the child resistant cap to assure the correct seating of the bottle adaptor. Store reconstituted solution in the refrigerator and discard any remaining suspension after 49 days.[3]
ADMINISTRATION	**Valganciclovir should be handled as a cytotoxic agent** Valganciclovir is a potential teratogen and carcinogen in humans and inhibits spermatogenesis. Proper procedures for the handling and disposal of cytotoxic agents should be followed. Patients, parents and carers should be instructed not to crush the tablets.[3,9] Refer to the Paediatric Nursing Practice Manual Section 2.8.2 for further information. **Oral:** Best taken with food to aid in absorption.[1,5]
MONITORING	Haematological function (full blood picture, FBP), electrolytes, renal function and liver function should be measured at baseline. FBP should then be measured 2 to 3 times per week during induction and weekly thereafter. Electrolytes and renal function should be monitored 2 to 3 times weekly, whilst liver function should be measured at least monthly throughout treatment.[1] Neutropenia is usually dose dependent and occurs within the first 1 to 2 weeks of therapy. Aim to maintain a neutrophil count of more than 0.5 $x10^9$ cells/L throughout treatment. In the event of severe neutropenia or thrombocytopenia, treatment can be temporarily interrupted as neutrophil counts tend to return to normal range within 2 to 5 days. Dose reduction should be considered if significant anaemia or leucopenia occurs.[1,4]
ADVERSE EFFECTS	As ganciclovir is the active metabolite of valganciclovir, any side effect seen with ganciclovir may also occur with valganciclovir.[1] **Common:** anaemia, neutropenia (severe neutropenia more common with CMV retinitis), thrombocytopenia, fever, diarrhoea, vomiting, abdominal pain, constipation, oral candidiasis, headache, fatigue, insomnia, dizziness, seizures, confusion, itch, dermatitis, sweating, cough, decreased creatinine clearance (more common in transplant recipients),graft rejection, retinal detachment, upper respiratory tract infection, electrolyte abnormalities.[1,5,9] **Rare:** allergic reaction, local and systemic infection, oedema, hyper or hypotension, peripheral oedema.[4,5]
COMPATIBLE FLUIDS	Not applicable
PRECAUTIONS	Patients with bone marrow suppression, receiving myelosuppressive drugs or irradiation may be more susceptible to the myelosupporessive effects of valganciclovir. Dose adjustment may be required. Consider the need for valganciclovir if: neutrophil count is <0.5 x 10^9 cells/L, platelet count is <25 x 10^9 /L

	or Haemoglobin is < 80g/L.[1] Valganciclovir may lower the seizure threshold in people with epilepsy or a history of CNS disorders. Concomitant use of imipenem may further increase the risk of seizures.[1] Sexually active adolescent females should use effective contraception whilst taking valganciclovir and for at least 30 days after ceasing therapy. Sexually active males are recommended to use barrier contraception during and for a minimum of 90 days after treatment with valganciclovir.[1,4,5,6] Valganciclovir should be treated as a cytotoxic agent with the appropriate handling precautions. Refer to the Paediatric Nursing Practice Manual Section 2.8.2 for further information.[3,5] Parents and carers should be instructed to wash thoroughly with soap and water any skin or mucous membrane that is accidently exposed to broken or crushed tablets, oral powder for reconstitution or oral solution. If ocular exposure occurs, the eye should be washed with plain water.[4,5]
COMMENTS	Patients should be instructed to maintain adequate fluid intake.[4,5]

Please note: The information contained in this guideline is to assist with the preparation and administration of **valganciclovir**. Any variations to the doses recommended should be clarified with the prescriber prior to administration

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