MONOGRAPH

Valganciclovir Monograph - Paediatric

Scope (Staff):	Medical, Pharmacy, Nursing
Scope (Area):	All Clinical Areas – Perth Children's Hospital (PCH)

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

⚠ HIGH RISK MEDICINE ⚠

QUICKLINKS

DRUG CLASS

Guanine analogue.[1]

Valganciclovir is a High Risk Medicine.

INDICATIONS AND RESTRICTIONS

- Valganciclovir is used in the treatment and prophylaxis of cytomegalovirus (CMV) in immunosuppressed patients.[1]
- Valganciclovir may also be recommended for neonates and infants diagnosed with moderate to severe symptomatic congenital cytomegalovirus (CMV) infection given potential benefits to long-term audiological and neurodevelopmental outcomes. Refer to the CMV Neonatal Pathway for further information. [2]
- Valganciclovir has antiviral activity against human herpes virus-6 (HHV-6) and human herpes virus-8 (HHV-8) and may be used for maintenance therapy in immunosuppressed patients with severe and/or CNS infection with these viruses [2].

Oral: Monitored (orange) antiviral

- If the use is consistent with a standard approved indication, this must be communicated to ChAMP by documenting that indication on all prescriptions (inpatient and outpatient).

- The ChAMP team will review if ongoing therapy is required and/or if the order does not meet ChAMP Standard Indications.
- If use is not for a standard approved indication, phone approval must be obtained from ChAMP before prescribing.

CONTRAINDICATIONS

- Hypersensitivity to valganciclovir, ganciclovir or any component of the formulation. [1-4]
- Caution should be used in patients with a history of allergy to other guanine analogues (aciclovir, famciclovir, penciclovir and valaciclovir).[2, 4]

PRECAUTIONS

- Patients with bone marrow suppression, receiving myelosuppressive drugs or irradiation may be more susceptible to the myelosuppressive effects of valganciclovir. Dose adjustment may be required.

  Consider the need for valganciclovir and use with caution if:

  - neutrophil count is <0.5 x 10^9 cells/L **or**
  - platelet count is <25 x 10^9 cells/L **or**
  - haemoglobin is < 80g/L.[1-3]
- Valganciclovir is category D in pregnancy and has the potential to cause birth defects.[5] 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.[1-3]
- Valganciclovir **must** be treated as a cytotoxic agent with the appropriate handling precautions. Refer to Cytotoxic/Biotherapy Agents Administration for further information.[2, 6]
  - The dosing syringe provided in the packaging of the Valcyte® brand of valganciclovir suspension only shows the increments in milligrams and not millilitres. The syringe provided should be removed and a suitable device displaying millilitres should be provided with each prescription.
  - Parents and carers should be instructed to wash thoroughly with soap and water any skin or mucous membrane that is accidently exposed to valganciclovir. If ocular exposure occurs, the eye should be washed with plain water.[2, 5, 6]
- Parents and carers of patients in nappies taking valganciclovir should be instructed to avoid contact with faecal matter and urine and to use disposable nappies.
  - Gloves should be worn whilst changing nappies and nappies double-bagged before disposal. Inpatients nappies should be disposed of into purple cytotoxic waste bins.
- Valganciclovir should not be disposed of via waste water or household waste. Unused/expired medicines should be returned to pharmacy for disposal.[5]

FORMULATIONS

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required:

- 450mg tablets
- 50mg/mL powder for oral solution 100mL

  Note: After reconstitution, the minimal usable volume is 88mL, this volume should be taken into account when determining the quantity to prescribe.[5]

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Neonates: Refer to Neonatal Medication Protocols

***Oral - Treatment*:**

Valganciclovir tablets can be considered if the calculated dose is within 10% of the available tablet strength of 450mg.[2, 5]

Symptomatic congenital CMV disease in neonates (≥32 weeks gestation and ≥1.8kg) and infants:

- 16mg/kg/dose (to a maximum of 900mg) given 12 hourly for 6 months.[2, 6, 7]

Commence within the first month of life. The efficacy of valganciclovir commenced after 1 month of age is uncertain. Dose should be adjusted monthly to account for weight gain.[7, 8]

Active CMV disease children 1 month to <12 months:

- 16mg/kg/dose given 12 hourly. Discuss duration of therapy with Infectious Diseases.[9]

Active CMV disease children ≥ 12 months:

- 7 x Body surface area (BSA) x eGFR (to a maximum of 900mg per dose) given twice daily calculated using the equations and links below. Discuss duration of therapy with Infectious Diseases.[9]

Oral - Prophylaxis

Secondary CMV prophylaxis (maintenance) after induction therapy for CMV retinitis or CMV disease in an immunocompromised host:

- Initial treatment is generally commenced with IV ganciclovir, oral step down to valganciclovir may be appropriate in consultation with Infectious Diseases or Clinical Microbiology for those at ongoing risk of CMV reactivation.

Children 1 month to <12 months:16mg/kg/dose (to a maximum of 900mg) given once daily.[9]

Children ≥12 months: 7 x BSA x eGFR (to a maximum of 900mg per dose) given once daily calculated using the equations and links below.[9]

CMV prophylaxis post solid organ transplant:

Infants ≥1 month:

- 7 x BSA x eGFR given once daily calculated using the equations and links below.[7]

  The dose should not exceed 900mg daily and should be commenced within 10 days of the transplant.[1, 7]

$$\text{BSA } (m^2) = \sqrt{\frac{\text{Height (cm) x Weight (kg)}}{3600}}$$

eGFR calculator (Google Chrome)

Note: Use a value of 150mL/minute/1.73m^2 to calculate the dose if the calculated eGFR exceeds this value.[1, 7]

Renal impairment:

- eGFR calculator (Google chrome)

Dosage adjustment may be required in cases of impaired renal function (with creatinine clearance of less than 60mL/min).[1]

Cytomegalovirus prophylaxis post solid organ transplant:
Infants ≥1 month:
The dose calculation stated above takes into account renal function and no other dose reductions are required.[2]

Cytomegalovirus prophylaxis post solid organ transplant:
Adolescents 16 to 18 years:
The following dose adjustments are to be applied to adolescents with a recommended dose in normal renal function of 900mg and those patients using a 16mg/kg/dose.

Valganciclovir induction:

- eGFR ≥60mL/minute = normal dosing
- eGFR 40-59 mL/minute = 50% of the standard dose given12 hourly
- eGFR 25-39mL/minute = 50% of the standard dose given 24 hourly
- eGFR 10-24mL/minute = 50% of the standard dose given 48 hourly
- eGFR <10mL/minute = avoid use, consider dose adjusted IV ganciclovir.[2, 3]
- Intermittent haemodialysis or peritoneal dialysis: valganciclovir is not recommended.[2]

Valganciclovir maintenance:

- eGFR ≥60mL/minute = normal dosing
- eGFR 40-59 mL/minute = 50% of the standard dose given 24 hourly
- eGFR 25-39mL/minute = 50% of the standard dose given 48 hourly
- eGFR 10-24mL/minute = 50% of the standard dose given twice weekly
- eGFR <10mL/minute = avoid use, consider dose adjusted IV ganciclovir.[2, 3]
- Intermittent haemodialysis or peritoneal dialysis: valganciclovir is not recommended.[2]

Dosage adjustment required in hepatic impairment:

- There is no specific information available, no adjustments appear to be required.[2]

Dosage adjustment required in haematologic toxicity:

- Patients with bone marrow suppression, receiving myelosuppressive drugs or irradiation may be more susceptible to the myelosupporessive effects of valganciclovir.[1, 2]
- Neutropenia is often dose dependent and usually occurs within the first one to two weeks of therapy.[1]
- Dose adjustment may be required. Consider the need for valganciclovir and use with caution if:
    - neutrophil count is $<0.5 \times 10^9$ cells/L **or**
    - platelet count is $<25 \times 10^9$ cells /L **or**
    - haemoglobin is < 80g/L.[1, 2]

Contact Infectious Diseases, Clinical Microbiology or Pharmacy for advice.

- If bone marrow suppression occurs while on treatment (particularly neutropaenia with a neutrophil count of $< 0.5 \times 10^9$ cells/L), valganciclovir may need to be ceased temporarily to enable bone marrow recovery.

RECONSTITUTION & ADMINISTRATION

Valganciclovir must be handled as a cytotoxic agent

- Valganciclovir is a potential teratogen and carcinogen. Proper procedures for the handling and disposal of cytotoxic agents should be followed.[1, 2, 5]
- Refer to Cytotoxic/Biotherapy Agents Administration within the CAHS Medication Management Manual for further information.
- Valganciclovir powder for oral solution should be reconstituted in Pharmacy within a Powder Enclosure Cabinet to avoid exposure through powder inhalation.[2]

Reconstitution:

Reconstitute as per the product information with 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 ensure the correct sealing of the bottle adaptor.[5]

Store reconstituted solution in the refrigerator between 2 and 8 degrees and discard any remaining suspension after 49 days.[2, 3, 5]

- **Note:** After reconstitution, the minimal usable volume is 88mL, this volume should be taken into account when determining the quantity to prescribe.[5]

Administration:

Valganciclovir **must** be treated as a cytotoxic agent with the appropriate handling precautions. Refer to Cytotoxic/Biotherapy Agents Administration for further information.[2, 6]

- Patients, parents and carers should be instructed not to crush or break the oral tablets and to use gloves when handling both the tablets and/or oral solution.[2, 3]
- Parents and carers should be instructed to wash thoroughly with soap and water any skin or

mucous membrane that is accidently exposed to valganciclovir. If ocular exposure occurs, the eye should be washed with plain water.[2, 5, 6]

- Shake the oral solution well before administration and do not use the measuring device for any other medications.[2, 5]
- Best taken with food to aid absorption.[1, 2, 7]

COMPATIBILITY

Not applicable

MONITORING

- Haematological function, electrolytes, renal function and liver function should be measured at baseline and then regularly (two to three times a week during induction and weekly during maintenance) throughout treatment.[1]
- Neutropenia is usually dose dependent and usually occurs within the first one to two weeks of therapy.
    - Aim to maintain a neutrophil count of > 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 leucopaenia recurs following treatment interruption. Contact Infectious Diseases for advice.[1]
- Monitoring for neonates and infants with congenital CMV should follow the Cytomegalovirus CMV Neonatal Pathway.

Therapeutic drug monitoring

- Valganciclovir is a pro-drug of ganciclovir.[1, 10]
- Ganciclovir levels may be monitored on the advice of Infectious Diseases or Clinical Microbiology Consultants.
- Contact the duty Biochemist **prior** to collection of the sample.[10]

Collection tube:

- **Paediatric and neonatal –** Lithium Heparin (Dark Green top) 1 mL (No Gel) or Serum (Red top) 1 mL (No Gel).
- **Minimum volume required:** 0.1mL[10]

ADVERSE EFFECTS

As valganciclovir is rapidly converted to ganciclovir any side effect seen with ganciclovir may also occur with valganciclovir.[1, 2]

Common: anaemia, anxiety, asthenia, neutropenia (severe neutropenia more common with CMV retinitis), thrombocytopenia, fever, local and systemic infection, hypotension, peripheral oedema, diarrhoea, vomiting, abdominal pain, chest pain, constipation, oral candidiasis, headache, fatigue, insomnia, depression, dizziness, seizures, confusion, itch, dermatitis, sweating, cough, decreased creatinine clearance (more common in transplant recipients), eye pain, electrolyte abnormalities, abnormal hepatic function, peripheral neuropathy.[1, 2, 4]

Infrequent: alopecia, arrhythmia, deafness, haematuria, hallucination, oral ulceration, pancreatitis, psychotic disorder, tremor, visual impairment.[1, 4]

Rare: allergic reaction.[1, 2, 4]

STORAGE

- **Tablets:** Store below 25°C.[5]
- **Powder for oral solution:** Store below 30°C prior to reconstitution, after reconstitution store in the refrigerator between 2°C and 8°C and discard 49 days after reconstitution[4, 5]

INTERACTIONS

This medication may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

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

Related CAHS internal policies, procedures and guidelines
Antimicrobial Stewardship Policy
ChAMP Empiric Guidelines and Monographs
KEMH Neonatal Medication Protocols
Cytomegalovirus CMV Neonatal Pathway
Cytotoxic/Biotherapy Agents Administration

References

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