MONOGRAPH

Ganciclovir Monograph - Paediatric

Scope (Staff):	Medical, Pharmacy, Nursing
Scope (Area):	All Clinical Areas

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

QUICKLINKS

DRUG CLASS

Guanine analogue antiviral.[1, 2]

Ganciclovir is a High Risk Medicine.

INDICATIONS AND RESTRICTIONS

Ganciclovir is used in the treatment and prophylaxis of cytomegalovirus (CMV) disease in immunocompromised patients and the management of congenital CMV disease if oral therapy with valganciclovir is not tolerated.[1, 3]

IV: 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 ganciclovir, valganciclovir, aciclovir or any component of the formulation.[1, 4]

PRECAUTIONS

- Ganciclovir should be treated as a cytotoxic agent with the appropriate handling precautions. Refer to the policy on Cytotoxic/Biotherapy Agents Administration within the Clinical Practice Manual for further information. [1, 5, 6]
- Concomitant use of imipenem/cilastatin may further increase the risk of seizures - avoid combination.[1, 2]
- Ganciclovir administration may cause irritation or phlebitis at the injection site due to the high pH (approximately 11) of the solution. Administration via a vein with adequate blood flow is recommended.[5]
- Ganciclovir is potentially teratogenic and carcinogenic.[2, 5]
- Sexually active adolescent females should use effective contraception whilst being treated with ganciclovir and for at least 30 days after ceasing therapy.[4, 6, 7]
- Sexually active males are recommended to use barrier contraception during and for a minimum of 90 days after treatment with ganciclovir. Based on animal studies, ganciclovir may cause temporary or permanent inhibition of spermatogenesis.[4, 6, 7]

Patients with bone marrow suppression may be more susceptible to myelosuppression; an alternative agent (e.g. foscarnet) should be considered if:

- Neutrophil count is less than $0.5x10^9$ cells/L or
- Platelet count is less than $25\ x10^9$ cells/L or
- Haemoglobin is less than 80g/L.[1, 2, 6]

FORMULATIONS

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

- 500 mg powder for injection vial

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Neonates: Refer to Neonatal Medication Protocols

Child ≥ 4 weeks:

Intravenous - Induction therapy:

- 5 mg/kg/dose 12 hourly (usually given for 14 to 21 days followed by maintenance therapy).[3]
- The dose may be increased to a maximum of 7.5 mg/kg/dose 12 hourly on the recommendation of Infectious Diseases dependent on clinical response.[7]

Intravenous - Maintenance/Prevention of CMV in immunocompromised patients:

- 5 mg/kg/dose once daily.[3]

Oral switch:

Oral switch to valganciclovir may be a suitable alternative. Contact ChAMP, Infectious Diseases or Clinical Microbiology for further advice.[3]

Renal impairment:

- eGFR calculator

Dosage adjustment is required in cases of impaired renal function (with eGFR of less than 70 mL/minute/1.73m^2).

eGFR (mL/minute/1.73m^2)	Induction dose[4, 7]	Maintenance dose[4, 7]
≥70 mL/minute/1.73m^2	5 mg/kg/dose 12 hourly	5 mg/kg/dose 24 hourly
≥ 50 to <70 mL/minute/1.73m^2	2.5 mg/kg/dose 12 hourly	2.5 mg/kg/dose 24 hourly
≥ 30 to < 50 mL/minute/1.73m^2	2.5 mg/kg/dose 24 hourly	1.25 mg/kg/dose 24 hourly
≥ 10 to < 30mL/minute/1.73m^2	1.25 mg/kg/dose 24 hourly	0.625 mg/kg/dose 24 hourly
< 10mL/minute/1.73m^2	1.25 mg/kg/dose 3 times per week	0.625 mg/kg/dose 3 times per week

Intermittent Haemodialysis or Peritoneal Dialysis:

Give all doses after dialysis sessions[4]

Below dosing assumes three times a week dialysis session.

Induction Dose[4, 7]	Maintenance Dose[4, 7]
1.25 mg/kg/dose 3 times per week	0.625 mg/kg/dose 3 times per week

Continuous Renal Replacement Therapy (CVVHD or CVVHDF):

Induction Dose[4, 7]	Maintenance Dose[4, 7]
2.5 mg/kg/dose 12 hourly	2.5 mg/kg/dose 24 hourly

Hepatic impairment:

No dosage adjustment is required in hepatic impairment; however caution should be taken in patients with severe impairment.[2, 7]

Dosage reduction required with myelosuppression:

Treatment with ganciclovir should be interrupted if:

- Neutrophil count is less than $0.5x10^9$ cells/L
- Platelet count is less than 25 $x10^9$ cells/L or
- Haemoglobin is less than 80g/L. [2, 4]

Treatment may be reconsidered if there is evidence of bone marrow recovery:

- Neutrophil count > 0.75 x 10^9 cells/L
- Platelets > 50 $x10^9$/L [2, 4]

Dosing in Overweight and Obese Children: There is limited information regarding dosing of ganciclovir in overweight and obese patients. Given the volume of distribution, consideration should be given to dosing based on adjusted body weight on a case-by-case basis.[8]

RECONSTITUTION & ADMINISTRATION

- Ganciclovir infusion should **not** be prepared by staff on the ward – the order must be sent to Pharmacy Compounding Service (PCS) for preparation in a cytotoxic drug safety cabinet.[5]

Ganciclovir must be handled as a cytotoxic agent.[1, 2, 4-7]

- Ganciclovir is a potential teratogen and carcinogen in humans and may inhibit spermatogenesis. Proper procedures for the handling and disposal of cytotoxic agents should be followed.[6]
- Refer to PCH Medication Management Manual Cytotoxic and/or Biotherapy Agents Safety for further information.

Administration:

- Administer via IV infusion over at least 60 minutes at a concentration of 10 mg/mL or less.[1, 4-6]
- Ensure the infusion is administered into a vein with adequate blood flow due to the risk of irritation or phlebitis from the high pH of the solution.[5-7]
- Too rapid infusion can result in increased toxicity and excessive plasma levels.[7]

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

- Sodium chloride 0.9%
- Glucose 5%
- Hartmann's
- Ringer's[5]

Compatible at Y-site:

Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.

INCOMPATIBLE drugs:

- Bacteriostatic water for injection[5]

MONITORING

- Prior to each dose, the patient's hydration status should be assessed.[5]
- Haematological function (full blood count), electrolytes and renal function should be monitored at least 2 or 3 times per week during the induction phase, then weekly throughout maintenance.[1, 4, 6, 7]
- Hepatic function should be measured at baseline and then monitored at least monthly throughout treatment.[4, 7]
- Patients should also be monitored for virological response.[4, 7]

ADVERSE EFFECTS

Common: myelosuppression (including granulocytopenia, neutropenia, leucopenia, thrombocytopenia, anaemia), fever, gastrointestinal tract disturbance (including nausea, vomiting, anorexia, dyspepsia, abdominal pain, flatulence, diarrhoea, constipation), central nervous system (CNS) reactions (headache, confusion, anxiety, hallucinations, insomnia, abnormal thoughts, seizures, peripheral neuropathy, fatigue), pain and phlebitis at the injection site, sweating, rash, itch, increased serum creatinine and blood urea, myalgia, raised liver enzymes, eye inflammation and/or pain.[1, 6, 7]

Infrequent: chest pain, chills, mouth ulceration, cough, dry mouth, drowsiness, arthralgia, arrhythmia, deafness, haematuria, alopecia, hypotension, male infertility, visual impairment, tremor.[1, 6, 7]

Rare: agranulocytosis, cholestasis, dysphasia, encephalopathy, cranial nerve palsy, rhabdomyolysis, Stevens-Johnson syndrome. [1, 6, 7]

Extravasation:

Ganciclovir has a high pH and may result in irritation or phlebitis at the infusion site. If any signs of extravasation, refer to PCH Medication Management Manual – Cytotoxic Biotherapy Agents Extravasation.[5]

STORAGE

- Store unopened vials below 30˚C[2, 5]
- Store products prepared by PCS between 2 and 8˚C.[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 **ganciclovir**. 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

References

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2. MIMS Australia. MIMS online [full product information]. St Leonards, N.S.W: CMP Medica Australia.; 2022 [cited 2023 21st Mar].
3. Royal Australian College of General Practitioners, Pharmaceutical Society of Australia, Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists. AMH: Children's Dosing Companion. Adelaide: Australian Medicines Handbook Pty Ltd; 2022.
4. Clinical Pharmacology powered by ClinicalKey [Internet]. Elsvier. 2023 [cited 2023 June 20th]. Available from: https://www-clinicalkey-com.pklibresources.health.wa.gov.au/pharmacology/.
5. Symons K. Ermer J. (editors). Australian injectable drugs handbook. Collingwood: The Society of Hospital Pharmacists of Australia; 2022.
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7. Up To Date - Paediatric Drug information [Internet]. Lexicomp. 2022 [cited 2023 May 29th]. Available from: https://www-uptodate-com.pklibresources.health.wa.gov.au/contents/table-of-contents/drug-information/pediatric-drug-information.
8. Ross EL, Heizer J, Mixon MA, Jorgensen J, Valdez CA, Czaja AS, et al. Development of recommendations for dosing of commonly prescribed medications in critically ill obese children. American Journal of Health-System Pharmacy. 2015;72(7):542-56.

Useful resources (including related forms)
PCH Medication Management Manual – Cytotoxic Biotherapy Agents Extravasation.
PCH Medication Management Manual - Cytotoxic and/or Biotherapy Agents Safety
PCH Medication Management Manual - Cytotoxic/Biotherapy Agents Administration

This document can be made available in alternative formats on request.

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