MONOGRAPH

Foscarnet 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

Dosage/Dosage Adjustments | Administration | Compatibility | Monitoring

DRUG CLASS

Pyrophosphate analogue antiviral.[1, 2]

INDICATIONS AND RESTRICTIONS

- Foscarnet is used as an alternative in the treatment of herpes simplex virus (HSV) and cytomegalovirus (CMV) infection with proven or probable resistance to standard therapies or where first line therapies are unsuitable.[2, 3]

IV: Restricted (red) antiviral

ChAMP approval is required prior to prescription.

CONTRAINDICATIONS

- Hypersensitivity to foscarnet or any component of the formulation.[3-5]

PRECAUTIONS

Renal function:

- Renal function must be closely monitored throughout treatment and dose adjusted in cases of renal impairment. Adequate hydration should be maintained in all patients to minimise the potential of renal impairment. Renal impairment occurs to some degree in most patients treated with foscarnet. It may occur at any time and is usually reversible within one week of dose adjustment.[2-5]

Electrolyte disturbances:

- Clinically significant electrolyte disturbances may occur with foscarnet use including hypocalcaemia, hypophosphatemia, hyperphosphatemia, hypomagnesemia and hypokalemia.[2, 4, 6]
    - These electrolyte disturbances increase the risk of seizures and cardiac dysfunction.
    - Monitor and correct any deficiencies of electrolytes (especially calcium and magnesium) prior to and during foscarnet therapy.[3, 6]
    - Patients should be instructed to report any tingling, numbness or paraesthesia, which may be an indication of hypocalcaemia.[6]
- Foscarnet injection contains 240 micromol (5.5 mg) of sodium per mL, use with caution in patients with sodium restrictions.[1, 2, 5]
- If diuretics are indicated thiazide diuretics are preferred over loop diuretics as loop diuretics inhibit renal tubular secretion and may increase the degree of electrolyte disturbance and may impair foscarnet excretion.[5]

Skin irritation:

- Contact with skin or eyes may cause local irritation. If accidental exposure occurs, rinse immediately with cold water.[4]
- Staff administering foscarnet are recommended to wear an N95 mask and gloves as intermittent low dose exposure may pose an occupational hazard.[1]
- Foscarnet may cause genital irritation through urinary excretion – careful personal hygiene (e.g. cleaning of the genitals post urination) is recommended to reduce the potential for local irritation and ulceration. Regular nappy changes are also recommended in children wearing nappies.[2-5]
- Foscarnet is highly irritant. To avoid local irritation and thrombophlebitis, ensure that foscarnet is administered via a vein with adequate blood flow for rapid dilution and distribution.[3]

Other:

- Where possible, foscarnet should be avoided in patients receiving concurrent IV pentamidine due to additional risk of nephrotoxicity, serious hypocalcaemia, hypomagnesaemia and QT prolongation.[3, 5, 6]
- Use with caution in patients at increased risk of QT prolongation.[4, 6]
- Sexually active adolescent females should use effective contraception whilst being treated with foscarnet.[2, 5]
- Sexually active males are recommended to use barrier contraception and avoid fathering a child during, and for a minimum of 6 months after treatment with foscarnet.[5, 7]

FORMULATIONS

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

- 6 g/250 mL (24 mg/mL) solution for infusion.

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Neonates: Refer to Neonatal Medication Protocols

- Not routinely used in neonates, contact Infectious Disease or Clinical Microbiologist for advice.

Children ≥ 4 weeks of age: IV infusion:

Cytomegalovirus (CMV) - pre-emptive treatment in haematopoietic stem cell transplantation (HSCT) patients:

- **Induction:** 60 mg/kg/dose given 12 hourly for up to 2 weeks.[8, 9]
- **Maintenance:** 90 mg/kg/dose given once daily until PCR negative or an alternative agent can be considered.[8, 9]

Cytomegalovirus (CMV) disease:

- **Induction:** 60 mg/kg/dose given 8 hourly until symptom improvement (for 14 to 21 days) followed by maintenance therapy.[2, 7, 10]
- **Maintenance:** 90 to 120 mg/kg/dose given once daily.[2, 7]

Mucocutaneous herpes simplex virus (immunocompromised patient):

- 40 mg/kg/dose given 8 hourly for 14 to 21 days or until lesion(s) healed.[7]

Varicella zoster infection (HIV positive or exposed patient):

- 40 to 60 mg/kg/dose given 8 hourly for 7 to 10 days or until no new lesions have appeared for 48 hours.[3]

Renal impairment:

- eGFR calculator
- The eGFR calculator above calculates renal function in mL/minute/1.73m^2, **conversion to mL/minute/kg** (using the formula following) is required when interpreting the table below.

$$\text{eGFR} \times \left(\frac{\text{Body surface area in m}^2}{1.73} \right) = y$$

$$\left(\frac{y}{\text{patient weight in kg}} \right) = z \text{ mL/minute/kg}$$

CrCl (mL/minute/kg)	Recommended dose adjustment[3, 6]			
Recommended dose in normal renal function	40 mg/kg/dose 8 hourly	60 mg/kg/dose 8 hourly	90 mg/kg/dose 24 hourly	120 mg/kg/dose 24 hourly
> 1.4	40 mg/kg/dose 8 hourly	60 mg/kg/dose 8 hourly	90 mg/kg/dose 24 hourly	120 mg/kg/dose 24 hourly
> 1 - 1.4	30 mg/kg/dose 8 hourly	45 mg/kg/dose 8 hourly	70 mg/kg/dose 24 hourly	90 mg/kg/dose 24 hourly
> 0.8 - 1	35 mg/kg/dose 12 hourly	50 mg/kg/dose 12 hourly	50 mg/kg/dose 24 hourly	65 mg/kg/dose 24 hourly
> 0.6 - 0.8	25 mg/kg/dose 12 hourly	40 mg/kg/dose 12 hourly	80 mg/kg/dose 48 hourly	105 mg/kg/dose 48 hourly
> 0.5 - 0.6	40 mg/kg/dose 24 hourly	60 mg/kg/dose 24 hourly	60 mg/kg/dose 48 hourly	80 mg/kg/dose 48 hourly
≥ 0.4 - 0.5	35 mg/kg/dose 24 hourly	50 mg/kg dose 24 hourly	50 mg/kg/dose 48 hourly	65 mg/kg/dose 48 hourly
< 0.4	Not recommended	Not recommended	Not recommended	Not recommended

Note: for dosing recommendations for the 60 mg/kg/dose given 12 hourly for Cytomegalovirus (CMV) – induction of pre-emptive treatment in haematopoietic stem cell transplantation (HSCT) patients, discuss with ChAMP or Pharmacy.

Hepatic impairment:

No information regarding dose adjustments in hepatic impairment is available. Literature suggests no dosage adjustment required in mild to moderate hepatic impairment.[3]

Dosing in Overweight and Obese Children: There is very limited information regarding dosing of foscarnet 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.[11]

ADMINISTRATION

Hydration requirements:[1, 3, 4, 6]

- Adequate hydration should be given prior to and concurrently with foscarnet infusions to minimise renal toxicity.[3-6]
- Any dehydration should be corrected prior to commencement of foscarnet.[10, 12]

	Dose range	Hydration required
Pre-hydration for initial induction dose	All	10 to 20 mL/kg up to 750 mL to 1000 mL prior to the first dose.
Second and subsequent doses	90 to 120 mg/kg/dose	10 to 20 mL/kg up to 750 mL to 1000 mL given concurrently with each infusion
	40 to 60 mg/kg/dose	10 to 20 mL/kg up to 500 mL given concurrently with each infusion

- Oral hydration is also an option for those patients able to tolerate the required oral intake.[3, 6]

Administration:

IV infusion (central venous access device):

- The concentrated solution (24 mg/mL) may be used.[1, 3, 6]

IV infusion (peripheral vein):

- Dilute to a final concentration of 12 mg/mL or less with compatible fluid and infuse over 1 to 2 hours.[6, 7, 13]
- Foscarnet is highly irritant. To avoid local irritation and thrombophlebitis, ensure that foscarnet is administered via a vein with adequate blood flow for rapid dilution and distribution.[1, 6]

Duration of infusion:

- The required duration of infusion is dependent on the dose being administered with a maximum allowable rate of 1 mg/kg/minute.[1, 2, 6, 7]

Dose	Duration of infusion
≤ 60 mg/kg/dose	60 minutes
90 mg/kg/dose	1.5 to 2 hours
120 mg/kg/dose	2 hours

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

- Glucose 5%
- Sodium Chloride 0.9% [1]

Compatible at Y-site:

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

INCOMPATIBLE drugs:

- Any solution containing calcium (e.g. Hartmanns and Ringers)[1]

MONITORING

- Baseline renal function and electrolytes (including calcium, phosphate, potassium and magnesium) should be monitored every second day during induction then weekly thereafter.[2, 4, 6, 7]
- Monitor complete blood count regularly as needed.[2]
- Foscarnet may cause genital irritation through urinary excretion, careful personal hygiene is needed and children in nappies should be changed regularly and be closely monitored for genital irritation and ulceration.[2, 4]
- Patients should be instructed to report any tingling, numbness, abnormal muscle movements or muscle stiffness.[2, 10]

ADVERSE EFFECTS

Common: involuntary muscle contractions, seizures, headache, dizziness, anxiety, aggression, paraesthesia (may be managed with a slowing of infusion rate), cough, dyspnoea, fatigue, chills, malaise, fever, sweating, thrombophlebitis, genital ulceration, nausea, vomiting, diarrhoea, abdominal pain, anaemia, rash, itch, ECG changes, arrythmias, anaemia, thrombocytopenia, leucopenia, granulocytopenia, neutropenia.[2, 3, 7]

- *electrolyte disturbances:*
  - hypocalcaemia, hypokalaemia, hypomagnesaemia, hyperphosphataemia, hypophosphataemia, hyponatraemia
  - generally occurs within the first 2 weeks of treatment, correct any deficiencies as they occur
- *nephrotoxicity:*
  - generally occurs within the first 2 weeks of treatment, damage may be permanent, but is often reversible.
  - The risk is reduced by ensuring adequate hydration before and during treatment,

Infrequent: pulmonary haemorrhage, pneumonitis, cholestatic liver changes, hepatosplenomegaly, nephrogenic diabetes insipidus, oedema, neuropathy.[2]

Rare: muscle weakness, myopathy, oesophageal ulcers, acidosis, angioedema, glomerular nephritis, nephropathy, pancytopenia, severe cutaneous adverse reactions (SCARs), diabetes insipidus. [3, 7] .

STORAGE

- Store below 25°C and do not refrigerate.[1, 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 **foscarnet**. 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

1. Symons K. Ermer J. (editors). Australian injectable drugs handbook. Collingwood: The Society of Hospital Pharmacists of Australia; 2022.
2. Australian Medicines Handbook. Adelaide, S. Aust.: Australian Medicines Handbook; 2023 [cited 2023 30th October]. Available from: https://amhonline-amh-net-au.pklibresources.health.wa.gov.au/.
3. Up To Date - Paediatric Drug information [Internet]. Lexicomp. 2023 [cited 2023 November 6th]. Available from: https://www-uptodate-com.pklibresources.health.wa.gov.au/contents/table-of-contents/drug-information/pediatric-drug-information.
4. IBM Micromedex [Internet]. Truven Health Analytics. 2023 [cited 2023 November 6th]. Available from: http://www-micromedexsolutions-com.pklibresources.health.wa.gov.au/micromedex2/librarian.
5. MIMS Australia. MIMS online [full product information]. St Leonards, N.S.W: CMP Medica Australia.; 2023 [cited 2023 31th October].
6. Clinical Pharmacology powered by ClinicalKey [Internet]. Elsvier. 2023 [cited 2023 November 6th]. Available from: https://www-clinicalkey-com.pklibresources.health.wa.gov.au/pharmacology/.
7. Paediatric Formulary Committee. BNF for Children: 2023. London: BMJ Group Pharmaceutical Press; 2023.
8. Tomblyn M, Chiller T, Einsele H, Gress R, Sepkowitz K, Storek J, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. Biol Blood Marrow Transplant. 2009;15(10):1143-238.
9. Ljungman P, de la Camara R, Robin C, Crocchiolo R, Einsele H, Hill JA, et al. Guidelines for the management of cytomegalovirus infection in patients with haematological malignancies and after stem cell transplantation from the 2017 European Conference on Infections in Leukaemia (ECIL 7). Lancet Infect Dis. 2019;19(8):e260-e72.
10. Miller J, editor. AHFS Drug Information. Maryland: American Society of Health-System Pharmacists; 2022.

11. Ross EL, Heizer J, Mixon MA, Jorgensen J, Valdez CA, Czaja AS, Reiter PD. 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.
12. Electronic Medicines Compendium (emc). Surrey: DataPharm Ltd; 2023.
13. Pediatric Injectable Drugs. Maryland: American Society of Health -System Pharmacists; 2020.

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