MONOGRAPH

Fosfomycin 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

Phosphonic acid antibacterial agent.[1, 2]

INDICATIONS AND RESTRICTIONS

Fosfomycin is active against a range of Gram-positive and Gram-negative bacteria including multidrug-resistant Gram-negative bacteria (e.g. extended spectrum beta-lactamase's [ESBLs]). It is not active against *Pseudomonas aeruginosa.*[2, 3]

Oral fosfomycin is reserved for the treatment of multidrug-resistant urinary tract infections (UTIs). Oral formulations are generally not suitable for the initial treatment of pyelonephritis as they do not achieve adequate concentrations in the kidney tissue.

Oral and IV: Restricted (red) antibiotic

ChAMP approval is required prior to prescription. Document the indication, the ChAMP approver, and the date and time on the prescription or in the medication chart indication box.

IV fosfomycin is a **Special access scheme product**. SAS application(s) must be completed in accordance with the TGA regulations.

CONTRAINDICATIONS

- Hypersensitivity to fosfomycin or any component of the formulation.[4-6]
- Fosfomycin is contraindicated in patients with severe renal insufficiency (creatinine clearance < 10 mL/min/1.73m^2), patients undergoing haemofiltration, haemodialysis or peritoneal dialysis.[5]

PRECAUTIONS

- Doses should be prescribed as fosfomycin base as there are different salt formulations available which are **not** equivalent.[7]
- 1 gram of fosfomycin base is equivalent to 1.4 grams of fosfomycin calcium; 1.3 grams fosfomycin sodium; and 1.9 grams of fosfomycin trometamol.[8]

Oral:

- Fosfomycin sachets should be used with caution in patients with fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency as each sachet contains 2.2 grams of sucrose.[1, 5]
- 1.9 grams of fosfomycin trometamol is equivalent to 1 gram of fosfomycin base.[8]
- Sodium bicarbonate and urinary alkalinisers (e.g. Ural® and Citravescent®) make fosfomycin less effective and should be avoided whilst taking fosfomycin and for 2 days after the last dose.[1]
- Oral fosfomycin is not routinely used for initial treatment of pyelonephritis as adequate tissue levels may not be reliably achieved.[1, 4] Use as an oral switch following initial IV therapy may be considered in consultation with Infectious Diseases or Clinical Microbiology.[9]

IV:

- IV fosfomycin has a high sodium content (each 1 gram of fosfomycin contains 320 mg (14 mmol) of sodium) and patients should follow a low sodium diet whilst on IV fosfomycin, especially in patients on doses over 16 grams per day.[6, 10]
- There is a risk of hypokalaemia due to the high sodium load with the use of IV fosfomycin and care should be taken in patients with cardiac insufficiency, hypertension, hyperaldosteronism, hypernatraemia or pulmonary oedema.[2, 6]
- Hepatic injury (steatosis and hepatitis), agranulocytosis and neutropenia have been reported with fosfomycin use.[6]

FORMULATIONS

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

- 3 gram (fosfomycin base) sachet of granules for oral solution as fosfomycin trometamol
- 2 g, 4 g or 8 g (fosfomycin base) IV Powder for reconstitution as fosfomycin sodium

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Neonates: Refer to Neonatal Medication Protocols for IV therapy. Oral fosfomycin is not routinely used in neonates.

Doses should be prescribed as fosfomycin base as there are different salt formulations available which are NOT equivalent.[7, 8]

Oral - Children ≥ 4 weeks:

For the treatment of uncomplicated UTI's only

- **Children ≥ 4 weeks to < 1 year old:** 1 gram (of fosfomycin base) as a single dose.[11, 12]
- **Children ≥ 1 year to < 12 years old:** 2 grams (of fosfomycin base) as a single dose.[11, 13]
- **Children ≥ 12 years old:** 3 grams (of fosfomycin base) as a single dose.[11, 13]

Dose may be repeated after 2 to 3 days in patients on advice from Infectious Diseases.[14, 15]

IV: Children ≥ 4 weeks:

- **Weight < 10 kg:** 200-300 mg/kg/DAY (of fosfomycin base) in three divided doses.[2, 6, 15]
- **Weight ≥ 10 to < 40kg:** 200-400mg/kg/DAY (of fosfomycin base) in three or four divided doses.[2, 6, 15]
- **Weight ≥ 40kg:** 12-16 grams DAILY (of fosfomycin base) in two or three divided doses. Maximum individual dose is 8 grams. Doses of up to 24 grams per DAY may be used in cases of meningitis.[2, 6, 15]

Note: the higher end of the dose range should be used in cases of severe infection and/or when the suspected or known organism is less sensitive.[2]

Renal impairment:

eGFR calculator

Oral:

- Fosfomycin trometamol is contraindicated in severe renal insufficiency (creatinine clearance <10 mL/minute/1.73m^2).[1, 2, 5]

IV:

- There is minimal information regarding dose adjustment in children < 12 years of age, contact the ChAMP team for advice. The following dose adjustments are recommended for those ≥ 12 years of age.[6]

  (See table on following page)

eGFR[6, 15]	Recommended dose	First dose
≥ 80 mL/minute/1.73m^2	Normal dosing	N/A
> 40 to < 80 mL/minute/1.73m^2	Normal dosing, but use with caution	N/A
> 30 to ≤ 40 mL/minute/1.73m^2	70% of the recommended **daily** dose in 2-3 divided doses	First dose (loading dose) should be doubled to a maximum of 8 grams
> 20 to ≤ 30 mL/minute/1.73m^2	60% of the recommended **daily** dose in 2-3 divided doses	
> 10 to ≤ 20 mL/minute/1.73m^2	40% of the recommended **daily** dose in 2-3 divided doses	
≤ 10 mL/minute/1.73m^2	20% of the recommended **daily** dose in 1-2 divided doses	

Hepatic impairment:

- There is minimal information available regarding the use of IV or oral fosfomycin in paediatric patients with impaired hepatic function. It appears that no dosage adjustments are necessary.[6, 16]

Dosing in Overweight and Obese Children:

- There is limited information regarding dosing of oral and IV fosfomycin in overweight and obese children. Given the volume of distribution, dosing based on actual body weight should be used.[17, 18]

RECONSTITUTION & ADMINISTRATION

3 gram (fosfomycin base) sachet.

- Dissolve the contents of a single 3 gram sachet in 50 to 75 mL of cool water for reconstitution and stir to dissolve. Do not dissolve in hot water.[4, 6, 19, 20]
- If a part dose is required dissolve the contents of the 3 gram sachet in 60 mL of cool water for reconstitution. Each 20 mL of the resulting solution contains 1 gram. Discard any remaining solution.
- Fosfomycin may be taken without regard to food, however is best taken in the evening prior to bedtime after emptying the bladder.[4, 5]
- Once dissolved, the solution should be taken immediately.[4, 6]

IV - reconstitution:

- Reconstitute each vial with the volume of glucose 5% or water for injection in the table below. Further dilution is required prior to administration.[10]

Vial Strength (Fosfomycin base)	Volume of glucose 5% or water for injection required	Resulting concentration	Powder volume
2 gram	19 mL	100 mg/mL	1 mL
4 gram	18 mL	200 mg/mL	2 mL
8 gram	16 mL	400 mg/mL	4 mL

IV - administration:

- Flush the line before and after infusion with glucose 5% or 10%.[10]
- The required dose should be diluted with glucose 5% or glucose 10% to a final concentration of 40 mg/mL prior to infusion.[10]Infusion rate should NOT exceed 133 mg/minute. Refer to suggested infusion times below.[2]

Dose range	Minimum infusion time[2, 10]
≤ 2 grams	15 minutes
> 2 grams to ≤ 4 grams	30 minutes
> 4 grams to ≤ 8 grams	60 minutes

- In patients at risk of hypokalaemia, consider using extended infusion times up to 4 hours.[6]

COMPATIBILITY *(intravenous formulation)*

Compatible fluids:

- Glucose 5%
- Glucose 10%[10]

Compatible at Y-site:

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

INCOMPATIBLE drugs:

- IV fosfomycin is **INCOMPATIBLE** with sodium chloride solutions. IV lines should be flushed with glucose 5% or 10% prior to and immediately following administration.[10]

MONITORING

- Monitor electrolytes (in particular sodium, potassium and phosphate) and fluid balance.[2, 6]
- There have been reports of hepatic injury (including steatosis and hepatitis), agranulocytosis and neutropenia. Full blood count and hepatic function should be monitored whilst undergoing treatment with the IV formulation.[6]

ADVERSE EFFECTS

Common: asthenia, diarrhoea, dizziness, dyspepsia, headache, nausea and vomiting, rash, vulvovaginitis, abdominal pain, back pain, dysmenorrhoea, pharyngitis and rhinitis.[1, 2, 5, 16]

Infrequent: paraesthesia[1, 2, 5]

Rare: antibiotic associated colitis, hypersensitivity reaction s (e.g. anaphylaxis, angioedema, rash), taste disturbance, constipation.[1, 2]

IV use: decreased appetite, dyspnoea, electrolyte imbalance, fatigue, oedema, taste altered, vertigo, bone marrow disorders, eosinophilia, hepatic disorders, visual impairment, agranulocytosis, asthma, confusion, leucopenia, neutropenia, tachycardia, thrombocytopenia.[2, 5, 16]

STORAGE

Oral: Store below 25°C.[5]

IV: Store vials below 25°C and protect from light.[10]

- Products prepared by Pharmacy Compounding Service (PCS) should be stored between 2°C and 8°C and protected from light.[6]

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 **fosfomycin (IV and oral)**. 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

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