MONOGRAPH

Trimethoprim with Sulfamethoxazole (co-trimoxazole) Monograph - Paediatric

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

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

Combination antibacterial: trimethoprim is a dihydrofolate reductase inhibitor and sulfamethoxazole is a sulphonamide.[1, 2]

INDICATIONS AND RESTRICTIONS

- Co-trimoxazole is used in the treatment of:
  - Community associated methicillin-resistant *Staphylococcus aureus* infections (CA-MRSA)
  - Uncomplicated Gram Negative infections, such as urinary tract infections.[2]
  - *Pneumocystis jirovecii* (*Pneumocystis carinii*) pneumonia;
  - *Nocardia* spp. infection
  - Melioidosis, (in combination with other agents)
  - *Listeria monocytogenes* infection,
  - *Stenotrophomonas maltophilia* infection and
  - Toxoplasmosis. [3]

IV: Monitored (orange) antibiotic

- 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.

Oral: Unrestricted (green) antibiotic

This is not a restricted agent. Follow standard ChAMP guidelines where appropriate.

CONTRAINDICATIONS

- Hypersensitivity to trimethoprim, sulfamethoxazole, sulfonamides or any component of the formulation.[2, 4]
- Co-trimoxazole is contraindicated in patients with *folate deficiency megaloblastic anaemia* since either component could exacerbate this condition.[4]
- If no alternative agent exists, desensitisation may be considered. Contact Immunology for advice.[2, 3]

PRECAUTIONS

- Avoid in patients with G6PD deficiency due to the risk of haemolytic anaemia.[3-5]
- IV co-trimoxazole ampoules contain sodium metabisulfite which may cause allergic reactions in susceptible people.[6]
- Caution should be taken in patients with mild folate deficiency.[4]
- Patients requiring high doses or long term therapy may benefit from folic acid supplementation to reduce the risk of haematological adverse effects.[7] Folic acid should not be prescribed in oncology patients without discussion with the patient's primary Oncology consultant.
- The IV formulation contains propylene glycol. If using high IV doses, consider the propylene glycol content of all concurrent medications as toxicity may occur (e.g. kidney injury, CNS toxicity or organ failure).[4]
- Care should be taken in neonates and infants <6 weeks of age theoretical increased risk of kernicterus secondary to sulfonamides displacing bilirubin from plasma albumin.[4, 5]
- There have been reports of fatal gasping syndrome in neonates (less than 1 month of age) after the administration of parenteral solutions containing the preservative benzyl alcohol, consider the combined daily metabolic load of benzyl alcohol from all sources if using sulfamethoxazole.[4]

FORMULATIONS

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

- Trimethoprim 40mg / sulfamethoxazole 200mg per 5mL oral suspension
- Trimethoprim 80mg / sulfamethoxazole 400mg tablets
- Trimethoprim 160mg / sulfamethoxazole 800mg tablets (double strength preparation)
- Trimethoprim 80mg / sulfamethoxazole 400mg per 5mL ampoule

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

ALL doses are expressed in and should be prescribed as the trimethoprim component.

Neonates (< 1 month of age): Co-trimoxazole is generally avoided in pre-term infants due to the theoretical increased risk of kernicterus secondary to sulfonamides displacing bilirubin from plasma albumin.[3-5]

Refer to Neonatal Medication Protocols for dosing

Treatment

Children ≥4 weeks to 18 years:

IV Treatment:

- **Usual dose:** 5mg/kg/dose (to a maximum of 320mg trimethoprim component) given 12 hourly. [2, 8]
- ***Pneumocystis jiroveci [carinii]* pneumonia or other severe infections:** 5mg/kg/dose (to a maximum of 320mg trimethoprim component) given 8 hourly.[3, 9]
- Dose may be increased to 5mg/kg/dose (to a maximum of 320mg trimethoprim component) 6 hourly in critically ill patients.[3]
- Co-trimoxazole has good oral bioavailability – consider switching to oral dosing as soon as clinically appropriate.[10]

Oral Treatment:

- **Usual dose:** 4mg/kg/dose (to a maximum of 160mg trimethoprim component) 12 hourly. E**quivalent to** 0.5mL/kg/dose (to a maximum of 20mL) 12 hourly.[2, 8]
- **Impetigo:** 4mg/kg/dose (to a maximum of 160mg trimethoprim component) given 12 hourly for 3 days. Equivalent to 0.5mL/kg/dose (to a maximum of 20mL) 12 hourly for 3 days

  OR

  8mg/kg/dose (to a maximum of 320mg) given once daily for 5 days.[3] Equivalent to 1mL/kg/dose (to a maximum of 40mL) once daily for for 5 days
- **Severe infections: (e.g. *Pneumocystis jiroveci [carinii]* pneumonia or MRSA Bone and Joint Infection):** 5mg/kg/dose (to a maximum of 480mg trimethoprim component) 8 hourly. [3, 9] Plus folic acid 2.5mg to 10mg orally once daily while prescribed high dose co-trimoxazole.[11]

Prophylaxis

Children ≥4 weeks to 18 years:

- **UTI Prophylaxis:** 2mg/kg/dose (to a maximum of 80mg trimethoprim component) at night. **Equivalent** to 0.25mL/kg/dose (to a maximum of 10mL) at night.[2, 8]

***Pneumocystis jiroveci [carinii]* pneumonia prophylaxis:**

- **Prophylaxis (oncology patients):** 2.5mg/kg/dose (to a maximum of 160mg trimethoprim component) 12 hourly on 3 consecutive days per week (Friday, Saturday, Sunday). Equivalent to 0.3mL/kg/dose 12 hourly on 3 consecutive days per week (Friday, Saturday, Sunday).[2, 4]

- Oncology patients should have co-trimoxazole withheld 24 hours prior to HIGH DOSE methotrexate (> 1g/m^2) until calcium folinate and post hydration fluids discontinued (as per methotrexate levels and protocol requirements).
- **Alternative prophylaxis dosing based on a patient's body surface area** (75mg/m^2/dose (to a maximum of 160mg trimethoprim component) given 12 hourly on 3 days per week:[4]

Body surface area (m^2)	80mg/400mg tablets	Liquid (40mg/200mg per 5mL)
<0.5	N/A	0.3mL/kg/dose BD
0.5-0.75	HALF a tablet BD	5mL BD
0.76-0.99	1 tablet morning and HALF a tablet at night	7.5mL BD
1-1.49	1 tablet BD	10mL BD
≥1.5	2 tablets BD	20mL BD

- **Prophylaxis (non-oncology patients) :** 5mg/kg/dose (to a maximum of 320mg) once daily on 3 days per week.[2, 4]

Dosing in Overweight and Obese Children: Dose based on measured body weight.

Renal impairment:

- eGFR calculator

Dosing adjustment required for standard twice daily dosing in association with renal impairment:

- eGFR > 50mL/minute : normal dosing
- eGFR 26 – 50mL/minute : normal dosing for 14 days, then 50% dose at a normal dosing interval
- eGFR 15 – 25mL/minute : normal dosing for 3 days, then 100% dose 24-hourly
- eGFR <15mL/minute : avoid use, if essential, normal dosing for 3 days, then 100% dose 24hourly.[3]

Dosing adjustment required for *Pneumocystis jiroveci [carinii]* pneumonia and serious infections in association with renal impairment:

- eGFR > 25mL/minute : normal dosing
- eGFR 15 – 25mL/minute : 100% at normal dosing interval for 2 days, then 100% dose 12-hourly
- eGFR < 15mL/minute: 100% dose 12 to 24 hourly.[3]

Contact Pharmacy for further advice.

Hepatic impairment:

- Co-trimoxazole should be avoided in cases of severe liver disease. Patients are at a higher risk of adverse effects.[2, 5, 12]

ADMINISTRATION

IV infusion:

- Dilute to 1 in 25 (i.e. 0.64mg/mL trimethoprim component) with a compatible fluid, mix well and infuse over 60 to 90 minutes. The infusion should be commenced within half an hour of preparation due to reduced stability of the solution.[5, 6]
- In fluid restricted patients, it may be diluted 1 in 15 with glucose 5% to a concentration of 1.07mg/mL (trimethoprim component) and infused over 60 minutes. In this case, the infusion must be mixed well and commenced immediately as the stability is significantly reduced. At this higher concentration, the solution should be checked periodically throughout the infusion for precipitation.[4-6]
- In critical care settings (ICU) co-trimoxazole may be administered undiluted via a central venous access device (CVAD).[5, 6]
- Discard the solution if there is any crystallisation or any visible turbidity during preparation or administration of the infusion.[6]

Oral:

- Give each dose with or soon after food to reduce stomach upset.[2, 4]
- When using the suspension, shake the bottle well before measuring each dose.[4]
- Advise patients on long term treatment to drink sufficient amounts of water to maintain an adequate urine output and avoid crystalluria.[2]

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

- Glucose 5% (preferred due to improved stability)
- Glucose 10%
- Sodium chloride 0.45%
- Sodium chloride 0.9%
- Glucose/sodium chloride solutions
- Hartmann's[6]

Compatible at Y-site:

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

MONITORING

- Monitor haematological function (full blood picture) and folate status during prolonged or high dose treatment. [2, 4]
- Urinalysis and renal function should be monitored monthly during prolonged treatment, especially in patients with pre-existing renal impairment.[2, 4]
- Check potassium levels in patients with renal impairment, on concurrent medications that increase potassium levels or taking a high dose.[2]
- Patients should be instructed to contact the prescriber if they experience sore throat, fever, troublesome rash, cough, joint pain, difficulty breathing, dark urine or pale stools.[2]

- Patients should be instructed the avoid sunlight exposure, wear protective clothing and sunscreen to reduce the incidence of rash.[2]

ADVERSE EFFECTS

Common: fever, nausea, vomiting, diarrhoea, anorexia, rash, itch, sore mouth, hyperkalaemia, thrombocytopenia.[2]

Infrequent: headache, drowsiness, photosensitivity, blood dyscrasias (e.g. neutropenia).[2]

Rare: megaloblastic anaemia, ataxia (IV use in HIV patients), methaemoglobinaemia, blood disorders (leucopenia, eoisinophilia), agranulocytosis, erythema, hypoglycaemia, hyponatraemia, hepatitis, crystalluria, urinary obstruction with anuria/oliguria, lowered mental acuity, depression, tremor, *Clostridium difficile*-associated disease, aseptic meningitis, Stevens-Johnson syndrome, toxic epidermal necrolysis.[2, 5]

STORAGE

Ampoules: Store below 30˚C. Do NOT refrigerate as precipitation may occur at low temperatures. Protect from light.[1, 6]

Tablets and suspension: Store below 30˚C. Protect from light.[1]

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 **trimethoprim with sulfamethoxazole (co-trimoxazole)**. 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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