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. It is also known as co-trimoxazole.(1)

INDICATIONS AND RESTRICTIONS

- Co-trimoxazole should be reserved for indications where the combination is more effective than trimethoprim alone.(2) It is commonly used in the treatment of:
    - Community associated methicillin-resistant *Staphylococcus aureus* infections (CA-MRSA)
    - *Pneumocystis jirovecii* (*Pneumocystis carinii*) pneumonia (treatment and prophylaxis);
    - Infections caused by *Nocardia, Listeria monocytogenes, Stenotrophomonas maltophilia, or Burkholderia pseudomallei* (2)

IV: Monitored (orange) antibiotic

As per indications stipulated in Formulary One. For any other use, phone approval must be obtained from ChAMP before prescribing as per the Antimicrobial Stewardship Policy.

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. If no alternative agent exists, desensitisation may be considered. Contact Infectious Diseases and Immunology for advice.[1, 3-5]
- Co-trimoxazole is contraindicated in patients with folate deficiency megaloblastic anaemia since either component could exacerbate this condition.[1]
- A history of drug-induced immune thrombocytopenia from either trimethoprim or sulfamethoxazole.[1]

PRECAUTIONS

- Avoid in patients with Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency due to the risk of haemolytic anaemia. [1, 3, 4]
- IV co-trimoxazole ampoules contain sodium metabisulfite which may cause allergic reactions in susceptible people.[3, 6]
- Caution should be taken in patients with folate deficiency, as folate deficiency may worsen.[1, 4]
- 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).[7]
- Patients should be instructed to avoid excessive sun exposure due to the risk of photosensitivity.[1, 7]
- During high dose treatment, patients should increase their fluid intake to reduce the risk of crystalluria.[1]
- Care should be taken in neonates and infants <2 months of age;
    - There is a theoretical increased risk of kernicterus secondary to sulfonamides displacing bilirubin from plasma albumin, however there is no evidence this occurs with sulfamethoxazole.[1]
    - There have been reports of fatal gasping syndrome in neonates (less than 4 weeks old) 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 IV co-trimoxazole.[7]

FORMULATIONS

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

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

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

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

Oral suspension	Single strength tablet	Double strength tablets	IV
8 mg trimethoprim component in 1 mL	80 mg trimethoprim component per tablet	160 mg trimethoprim component per tablet	80 mg trimethoprim per 5 mL of IV solution

Neonates: **Refer to Neonatal Medication Protocols**

Treatment

Children ≥4 weeks to 18 years:

IV Treatment – reserved for severe infections:

- Co-trimoxazole has rapid and almost complete oral absorption – consider switching to oral dosing as soon as clinically appropriate.[3, 8]
- **Usual dose:** 5 mg/kg/dose (to a maximum of 320 mg trimethoprim component) given 12 hourly. [1, 9]
- ***Pneumocystis jiroveci [carinii]* pneumonia or other severe infections:** 5 mg/kg/dose (to a maximum of 320 mg trimethoprim component) given 8 hourly.[2, 10]
- Dose may be increased to 5 mg/kg/dose (to a maximum of 320 mg trimethoprim component) 6 hourly in critically ill patients.[1, 2, 9]

Oral Treatment:

- **Usual dose:** 4 mg/kg/dose (to a maximum of 160 mg trimethoprim component) 12 hourly. **Equivalent to** 0.5 mL/kg/dose (to a maximum of 20 mL) 12 hourly.[1, 9]
- **Impetigo:** 4 mg/kg/dose (to a maximum of 160 mg trimethoprim component) given 12 hourly for 3 days.[9, 11] Equivalent to 0.5 mL/kg/dose (to a maximum of 20 mL) 12 hourly for 3 days.
- **Severe infections: (e.g. *Pneumocystis jiroveci [carinii]* pneumonia or MRSA Bone and Joint Infection):** 5 mg/kg/dose (to a maximum of 480 mg trimethoprim component) 8 hourly. [2, 10] Plus folic acid 2.5 mg to 10 mg orally once daily while prescribed high dose co-trimoxazole.[12]

Prophylaxis

Children ≥4 weeks to 18 years:

- **UTI Prophylaxis:** 2 mg/kg/dose (to a maximum of 80 mg trimethoprim component) at night. Equivalent to 0.25 mL/kg/dose (to a maximum of 10 mL) at night.[1, 5, 9]

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

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

Equivalent to 0.3 mL/kg/dose 12 hourly on 3 consecutive days per week (Friday, Saturday, Sunday).[1, 5, 7]

- 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** (75 mg/m^2/dose (to a maximum of 160 mg trimethoprim component) given 12 hourly on 3 days per week.[5, 7]

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

- **Prophylaxis (non-oncology patients):** 5 mg/kg/dose (to a maximum of 320 mg) once daily on 3 days per week.[1, 7, 9]

Dosing in Overweight and Obese Children: Dose based on measured body weight.[13]

Renal impairment:

- eGFR calculator
- Co-trimoxazole should be used cautiously in patients with renal impairment. Adequate hydration is required to reduce the risk of crystalluria and additional monitoring (as per monitoring section) is recommended.[5]
- See table on the following page.

eGFR	Treatment[5]		Prophylaxis[5]	
	Usual dose 4 mg/kg/dose given 12 hourly	**Usual dose 5 mg/kg/dose given 6 to 8 hourly**	**Usual dose 2.5 mg/kg/dose given 12 hourly OR 5 mg/kg/dose given once daily on three days per week**	**Usual dose 2mg/kg/dose at night**
≥ 30mL/minute/1.73m^2	No dose adjustment required	No dose adjustment required	No dose adjustment required	No dose adjustment required
≥ 15 to < 30 mL/minute/1.73m^2	50% dose given 12 hourly	50% dose given 8 to 12 hourly	Cap the dose at 80 mg trimethoprim component per dose and give once daily on three days per week	There is limited information regarding prophylaxis dosing in renal impairment. Discuss with ChAMP or Pharmacy.
< 15mL/minute/1.73m^2	Use is not recommended – if required use cautiously with increased monitoring.			
	25% to 50% dose administered once or twice daily.	25% to 50% dose administered once or twice daily.	Cap the dose at 80 mg trimethoprim component per dose and give once daily on three days per week	

Hepatic impairment:

- Co-trimoxazole is contraindicated in cases of severe liver disease due to decreased metabolism. Specific dose adjustments are not available. Patients are at a higher risk of adverse effects.[1, 4, 5]

ADMINISTRATION

IV infusion:

- Dilute to 1 in 25 (i.e. 0.64 mg/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.[1, 3, 6]

- In fluid restricted patients, it may be diluted 1 in 15 with glucose 5% to a concentration of 1.07 mg/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 as this may occur within 1-2 hours.[6]
- In critical care settings (PCC) co-trimoxazole may be administered undiluted via a central venous access device (CVAD).[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.[1]
- When using the suspension, shake the bottle well before measuring each dose.[3]
- Advise patients on long term treatment to drink sufficient amounts of water to maintain an adequate urine output and avoid crystalluria.[5]

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 (DBL brand only)[3, 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. [1, 4, 5, 7]
- Urinalysis and renal function should be monitored monthly during prolonged treatment, especially in patients with pre-existing renal impairment.[1, 5, 7]
- Check sodium and potassium levels in patients with renal impairment, on concurrent medications that increase potassium levels or taking a high dose.[1, 3-5]
- 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.[1]

ADVERSE EFFECTS

Common: fever, nausea, vomiting, diarrhoea, anorexia, rash, itch, sore mouth, hyperkalaemia, thrombocytopenia.[1, 4]

Infrequent: headache, drowsiness, photosensitivity, blood dyscrasias (e.g. neutropenia).[1]

Rare: megaloblastic anaemia, ataxia, methaemoglobinaemia, blood disorders (leucopenia, eosinophilia), agranulocytosis, erythema, hypoglycaemia, hyponatraemia, hepatitis, crystalluria, urinary obstruction with anuria/oliguria, lowered mental acuity, depression, tremor, *Clostridioides difficile*-associated disease, aseptic meningitis, severe cutaneous adverse reactions (SCARs).[1, 4]

STORAGE

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

Tablets and suspension: Store below 25˚C. Protect from light.[3]

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

References

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