**Trimethoprim with Sulfamethoxazole (cotrimoxazole) Monograph – Paediatric**

<table>
<thead>
<tr>
<th>Scope (Staff):</th>
<th>Medical, Nursing, Pharmacy</th>
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<tr>
<td>Scope (Area):</td>
<td>Perth Children’s Hospital (PCH)</td>
</tr>
</tbody>
</table>

**Child Safe Organisation Statement of Commitment**

The Child and Adolescent Health Service (CAHS) commits to being a child safe organisation by meeting the National Child Safe Principles and National Child Safe Standards. This is a commitment to a strong culture supported by robust policies and procedures to ensure the safety and wellbeing of children at CAHS.

**This document should be read in conjunction with this DISCLAIMER**

**DESCRIPTION**

Cotrimoxazole is a combination product containing both trimethoprim and sulfamethoxazole. They competitively inhibit bacterial folate production essential for bacterial growth and are bacteriostatic.\(^1\)

**INDICATIONS AND RESTRICTIONS**

- Cotrimoxazole is the drug of choice in the prophylaxis and treatment of *Pneumocystis jirovecii* (*Pneumocystis carinii*) pneumonia; it is also often indicated for the treatment of *Nocardia* spp, *Melioidosis*, *Listeria monocytogenes* infection, *Stenotrophomonas maltophilia* infection and toxoplasmosis.\(^1,2\)
- Cotrimoxazole is used in the treatment of infections due to community associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) and sometimes for the treatment of uncomplicated Gram Negative infections, such as urinary tract infection.\(^1,2\)

**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**

- Oral cotrimoxazole is not a restricted agent. Follow standard ChAMP guidelines where appropriate.
### CONTRAINDICATIONS
- Cotrimoxazole should not be used in patients with a history of severe allergy to sulfonamides as cross reactivity may occur.\(^{(1)}\) If no alternative agent exists, desensitisation may be considered. Contact Immunology for advice.

### PRECAUTIONS
- Avoid in patients with G6PD deficiency due to the risk of haemolytic anaemia.\(^{(1,3)}\)
- IV cotrimoxazole ampoules contain sodium metabisulfite which may cause allergic reactions in susceptible people.\(^{(4)}\)
- Patients requiring high doses or long term therapy may require supplementation with folic acid.\(^{(4)}\) Folic acid should not be prescribed in oncology patients without discussion with the patient's primary oncology consultant.

### FORMULATIONS
**Available at PCH:**
- 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 for intravenous administration

**Other formulations available:**
- Nil

### DOSAGE
The doses listed below fall within the standard range. Higher doses may be prescribed for certain situations in consultation with an infectious diseases or clinical microbiology consultant.

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

**Neonates (< 1 month of age):** Cotrimoxazole is generally avoided in pre-term infants and those <6 weeks of age due to the theoretical increased risk of kernicterus secondary to sulfonamides displacing bilirubin from plasma albumin.\(^{(1,2)}\)

Please refer to [KEMH Neonatal Medication Protocols](#).

**IV:**
- **Usual dose:** 5mg/kg/dose (to a maximum of 320mg) given 12 hourly.\(^{(1,5)}\)
- **Severe infections:** 5mg/kg/dose (to a maximum of 320mg) given 6 hourly.\(^{(1,5)}\)

**Oral:**
- **Treatment dose:** 4mg/kg/dose (to a maximum of 160mg) 12 hourly OR 0.5mL/kg/dose (to a maximum of 20mL) 12 hourly.
- **Severe infections:** 5mg/kg/dose (to a maximum of 320mg) 6 hourly.\(^{(1,5)}\)
MRSA Bone and Joint Infections: 8mg/kg/dose (to a maximum of 320mg/dose of trimethoprim component) every 12 hours.\(^6\) Plus folic acid 0.1mg/kg up to 5mg orally daily while prescribed high dose co-trimoxazole.\(^2\)

**UTI Prophylaxis:** 2mg/kg/dose (to a maximum of 80mg) at night OR 0.25mL/kg/dose (to a maximum of 10mL) at night.\(^1,5\)

**Impetigo:** 4mg/kg/dose (to a maximum of 160mg) given 12 hourly for 3 days OR 8mg/kg/dose (to a maximum of 320mg) given once daily for 5 days.\(^2\)

**Pneumocystis jiroveci [carinii] pneumonia:**

Prophylaxis (oncology patients): 2.5mg/kg/dose (to a maximum of 160mg) 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).\(^1\)

**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** (given 12 hourly on 3 days per week):

<table>
<thead>
<tr>
<th>Body surface area (m(^2))</th>
<th>80mg/4000mg tablets</th>
<th>Liquid (40mg/200mg per 5mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.5</td>
<td>N/A</td>
<td>0.3mL/kg/dose BD</td>
</tr>
<tr>
<td>0.5-0.75</td>
<td>0.5 tablet BD</td>
<td>5mL BD</td>
</tr>
<tr>
<td>0.76-0.99</td>
<td>1 tablet morning, 0.5 tablet at night</td>
<td>7.5mL BD</td>
</tr>
<tr>
<td>1-1.49</td>
<td>1 tablet BD</td>
<td>10mL BD</td>
</tr>
<tr>
<td>&gt;1.5</td>
<td>2 tablets BD</td>
<td>20mL BD</td>
</tr>
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</table>

In non-oncology patients, an alternative dosage option is: 5mg/kg/dose (to a maximum of 320mg) once daily on 3 days per week.\(^1,5\)

**Treatment:** As for treatment of severe infections (see above).\(^1\)

**DOSAGE ADJUSTMENT**

Dosage adjustment required in renal impairment:

Dosage adjustment may be required in cases of impaired renal function (with creatinine clearance of less than 50mL/min). \(^2\)

To calculate the estimated glomerular filtration rate (eGFR) in infants > 1 year and children, use the following formula:\(^2\)

\[
eGFR (\text{mL/min/1.73m}^2) = \frac{36.5 \times \text{height (in cm)}}{\text{Serum creatinine (micromol/L)}}
\]
**Dosing for standard treatment in association with renal impairment:**
CrCl > 50mL/minute : normal dosing
CrCl 26 – 50mL/minute : normal dosing for 14 days, then 50% dose at a normal dosing interval
CrCl 15 – 25mL/minute : normal dosing for 3 days, then 100% dose 24-hourly
CrCl <15mL/minute : avoid use, if essential, normal dosing for 3 days, then 100% dose 24-hourly.\(^{(2)}\)

**Dosing for Pneumocystis jiroveci [carinii] pneumonia and serious infections in association with renal impairment:**
CrCl > 25mL/minute : normal dosing
CrCl 15 – 25mL/minute : 100% at normal dosing interval for 2 days, then 100% dose 12-hourly
CrCl < 15mL/minute: 100% dose 12-24 hourly.\(^{(2)}\)
Contact Pharmacy for further advice.

**Dosage adjustment required in hepatic impairment:**
Cotrimoxazole should be avoided in cases of severe liver disease.\(^{(3)}\)

**RECONSTITUTION**
Not applicable – further dilution is required before administration (see below for further information).

**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.\(^{(4, 7)}\)
- If fluid restricted, 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.\(^{(4)}\)
- Discard the solution if there is any crystallisation or any visible turbidity during preparation or administration of the infusion.\(^{(4)}\)

**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.\(^{(8)}\)
- Advise patients on long term treatment to drink sufficient amounts of water to maintain an adequate urine output and avoid crystalluria.\(^{(1)}\)

**MONITORING**

- Monitor haematological function (full blood picture) and folate status during prolonged or high dose treatment.\(^{(1)}\)
- Urinalysis and renal function should be monitored monthly during prolonged treatment.\(^{(1, 3, 7, 9)}\)
- Patients with renal impairment should have their potassium levels regularly assessed.\(^{(1)}\)

**ADVERSE EFFECTS**

**Common:** fever, nausea, vomiting, diarrhoea, anorexia, rash, itch, sore mouth, hyperkalaemia, thrombocytopenia.\(^{(1, 3)}\)

**Rare:** headache, drowsiness, photosensitivity, blood dyscrasias (e.g. neutropenia), megaloblastic anaemia, methaemoglobinemia, bone marrow suppression, agranulocytosis, erythema, hypoglycaemia, hepatitis, crystalluria, urinary obstruction with anuria/oliguria, lowered mental acuity, depression, tremor, *Clostridium difficile*-associated disease, aseptic meningitis, Stevens-Johnson syndrome, toxic epidermal necrolysis.\(^{(1, 3)}\)

**COMPATIBLE FLUIDS**

- Glucose 5% (preferred due to improved stability)
- Glucose 10%
- Sodium chloride 0.9%
- Glucose/sodium chloride solutions
- Hartmann’s\(^{(4)}\)

**STORAGE**

- **Ampoules:** Store below 30°C. Do NOT refrigerate. Protect from light.
- **Tablets and suspension:** Store below 30°C\(^{(8)}\)

**INTERACTIONS**

- **Cotrimoxazole may interact with other medications; please consult PCH approved references (e.g. Clinical Pharmacology), your ward pharmacist or Pharmacy on extension 63546 for more information**

- Trimethoprim with sulfamethoxazole has antifolate activity (additive to that of methotrexate). Sulfamethoxazole may reduce renal excretion of methotrexate and increase its concentration and toxicity (bone marrow suppression). Use alternative antibacterial if possible, otherwise monitor for haematological toxicity and other adverse effects.\(^{(1, 3)}\)

- **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).

- The use of cotrimoxazole and mercaptopurine or
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<table>
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<tr>
<th>azathioprine can increase the risk of haematological toxicity – frequent monitoring is required.(^1,,3)</th>
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<tr>
<td>The use of cotrimoxazole with ciclosporin or tacrolimus can increase the risk of nephrotoxicity – monitoring of renal function is required.(^3)</td>
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<tr>
<td>Methenamine hippurate (hexamine hippurate) should not be used in conjunction with cotrimoxazole due to the increased risk of crystalluria.(^1,,3)</td>
</tr>
<tr>
<td>Rifampicin can decrease the concentration of cotrimoxazole; an increase in the cotrimoxazole dose may be required.(^1,,3)</td>
</tr>
<tr>
<td>Cotrimoxazole can enhance the anticoagulant effect of warfarin, increasing the risk of bleeding. An alternative antibiotic should be used whenever possible.(^1,,3)</td>
</tr>
<tr>
<td>There is an increased risk of hyperkalaemia when cotrimoxazole is given with medications that cause potassium retention (e.g. ACE inhibitors &amp; angiotensin-II receptor antagonists). Potassium levels should be monitored.(^1)</td>
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**COMMENTS**

| Patients should be instructed the avoid sunlight exposure, wear protective clothing and sunscreen to reduce the incidence of rash.\(^1\) |
| Cotrimoxazole has good oral bioavailability – consider switching to oral dosing as soon as clinically appropriate.\(^7,\,9\) |
| Cotrimoxazole distributes well into the central nervous system (CNS), joint fluid, sputum, bile and middle ear fluid.\(^9\) |

**MANUFACTURER SAFETY DATA SHEET (SDS)**

To access to the Manufacturer SDS for this product, use the following link to ChemAlert.

**Please note: The information contained in this guideline is to assist with the preparation and administration of trimethoprim with sulfamethoxazole (cotrimoxazole). Any variations to the doses recommended should be clarified with the prescriber prior to administration**

**Related internal policies, procedures and guidelines**

- Antimicrobial Stewardship Policy (Medication Management Manual)
- ChAMP Empiric Guidelines (ChAMP Manual)
- KEMH Neonatal Medication Protocols (KEMH)
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<td>7. Micromedex 2.0 [Internet]. Truven Health Analytics. 2019 [cited 2/12/2019].</td>
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