## Sulfamethoxazole with trimethoprim (cotrimoxazole) Monograph – Paediatric

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

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.\(^1\)

- 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 nocardiosis, melioidosis, *Listeria monocytogenes* infection, *Stenotrophomonas maltophilia* infection and toxoplasmosis.

- 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.\(^2\)

### INDICATIONS AND RESTRICTIONS

#### 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 a sulphur drug 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. Folic acid should not be prescribed in oncology patients without discussion with the patient's primary oncology consultant.

FORMULATIONS
Available at PCH:
- 40mg trimethoprim/200mg sulfamethoxazole per 5mL oral suspension (Bactrim®)
- 80mg trimethoprim /400mg sulfamethoxazole tablets (Resprim®)
- 80mg trimethoprim /400mg sulfamethoxazole per 5mL ampoule for intravenous administration

Other formulations available:
- 40mg trimethoprim/200mg sulfamethoxazole per 5mL oral suspension (multiple generic brands)
- 160mg trimethoprim /800mg sulfamethoxazole tablets (Double strength preparation – Bactrim DS®, Resprim Forte®, Septrin Forte®)

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 (<30 days postnatal life): Cotrimoxazole is generally avoided in pre-term infants and those <1 month of age due to the increased risk of kernicterus secondary to sulfonamindes 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
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
**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 3 days.\(^{(2)}\)

**Pneumocystis jiroveci [carinii] pneumonia:**

**Prophylaxis (oncology patients):** 2.5mg/kg/dose (to a maximum of 160mg) 12 hourly on 3 days per week. Equivalent to 0.3mL/kg/dose 12 hourly on 3 days per week.\(^{(1)}\)

**Alternative prophylaxis dosing based on a patients BSA (given 12 hourly on 3 days per week):**

<table>
<thead>
<tr>
<th>Body surface area ((m^2))</th>
<th>80mg/400mg 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>

**OR**

**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).\(^{(1)}\)

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**DOSAGE ADJUSTMENT**

**Dosing adjustment required in renal impairment:**

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

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

\[
\text{eGFR} \ (\text{mL/min/1.73m}^2) = \frac{36.5 \times \text{height (in cm)}}{\text{Serum creatinine (micromol/L)}}
\]

**Dosing for standard treatment in association with renal impairment:**

- **CrCl > 50mL/minute:** normal dosing
- **CrCl 25 – 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 < 15 mL/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 > 25 mL/minute: normal dosing

CrCl 15 – 25 mL/minute: 100% at normal dosing interval for 2 days, then 100% dose 12-hourly

CrCl < 15 mL/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.\(^{(3)}\)

<table>
<thead>
<tr>
<th>RECONSTITUTION</th>
<th>Not applicable – further dilution is required before administration (see below for further information).</th>
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<tbody>
<tr>
<td>ADMINISTRATION</td>
<td>IV infusion:</td>
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<tr>
<td></td>
<td>- 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.(^{(4, 6)})</td>
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<tr>
<td></td>
<td>- If fluid restricted, it may be diluted 1 in 10 with glucose 5% to a concentration of 1.6 mg/mL (trimethoprim component) and run over 60 minutes.</td>
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<td></td>
<td>- In this case, the infusion must be mixed well and commenced immediately as the stability is significantly reduced.</td>
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<td>- At this higher concentration, the solution should be checked periodically throughout the infusion for precipitation.(^{(4)})</td>
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<td></td>
<td>- Discard the solution if there is any crystallisation or any visible turbidity during preparation or administration of the infusion.(^{(4)})</td>
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<td>Oral:</td>
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<td>- Give each dose with or soon after food to reduce stomach upset.(^{(1)})</td>
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<td>- When using the suspension, shake the bottle well before measuring each dose.(^{(7)})</td>
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<td></td>
<td>- Advise patients on long term treatment to drink sufficient amounts of water to maintain an adequate urine output and avoid crystalluria.(^{(1)})</td>
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### MONITORING
- Monitor haematological function (full blood picture) and folate status during prolonged or high dose treatment.
- Urinalysis and renal function should be monitored monthly during prolonged treatment.\(^{(1, 3, 6, 8)}\)
- 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 and protect from light.
- **Tablets and suspension:** store below 30°C\(^{(7)}\)

### INTERACTIONS
**Cotrimoxazole has many drug interactions; please consult PCH approved references, your ward pharmacist or Pharmacy on 6456 0190 (option 1) for more information.**
- Cotrimoxazole has anti-folate activity and when used in conjunction with methotrexate can reduce methotrexate excretion and increase toxicity (predominantly haematological toxicity). Concomittant use should be avoided.\(^{(1, 3)}\)
- The use of cotrimoxazole and mercaptopurine or azathioprine can increase the risk of haematological toxicity – frequent monitoring is required.\(^{(1, 3)}\)
- The use of cotrimoxazole with ciclosporin or tacrolimus can increase the risk of nephrotoxicity – monitoring of renal function is required.\(^{(4)}\)
- Methenamine hippurate (hexamine hippurate) should not be used in conjunction with cotrimoxazole due to the increased risk of crystalluria.\(^{(1, 3)}\)
- Rifampicin can decrease the concentration of cotrimoxazole; an increase in the cotrimoxazole dose may be required.\(^{(1, 3)}\)
### Cotrimoxazole

- Cotrimoxazole can enhance the anticoagulant effect of warfarin, increasing the risk of bleeding. An alternative antibiotic should be used whenever possible.\(^{(1, 3)}\)
- There is an increased risk of hyperkalaemia when cotrimoxazole is given with medications that cause potassium retention (e.g., ACE inhibitors & angiotensin-II receptor antagonists). Potassium levels should be monitored.\(^{(1)}\)

### Comments

- Patients should be instructed to 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.\(^{(6, 8)}\)
- Cotrimoxazole distributes well into the CNS, joint fluid, sputum, bile, and middle ear fluid.\(^{(8)}\)

### Manufacturer Safety Data Sheet (SDS)

To access 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.**
References


6. Micromedex 2.0 [Internet]. Truven Health Analytics. 2016 [cited 12/10/2016].


Useful resources (including related forms)

Neonatal Medication Protocols (KEMH)

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