Guidelines for the prevention and treatment of *Pneumocystis jirovecii* pneumonia

1 PURPOSE & SCOPE

These guidelines were published in December 2014 and are concordant with Therapeutic Guidelines Antibiotic 15th ED.


The summary recommendations are shown below.

2 INTRODUCTION

Pneumocystis jirovecii infection (PJP) is a common cause of pneumonia in patients with cancer-related immunosuppression. There are well-defined patients who are at risk of PJP due to the status of their underlying malignancy, treatment-related immunosuppression and/or concomitant use of corticosteroids. Prophylaxis is highly effective and should be given to all patients at moderate to high risk of PJP. **Trimethoprim-sulfamethoxazole (TMP-SMX)** is the drug of choice for prophylaxis and treatment, although several alternative agents are available. Appropriate PJP prophylaxis can reduce the occurrence of PJP in high risk populations by up to 90% [2].

3 INVESTIGATIONS

CXR changes are variable. A bilateral diffuse interstitial infiltrate extending from the perihilar region is most often described. Atypical appearances include unilateral infiltrates, nodules, cavities, pneumothoraces or even apparently normal chest x-rays. HRCT may be useful to identify ‘ground glass’ changes not seen on chest x-ray. PET scan can also be useful in indeterminate clinical cases.

Bronchoscopy is the investigation of choice.

Quantitative PCR methods have largely replaced staining methods. Contact Infectious Diseases for clinical interpretation if the cycle threshold is high (ie low volume) despite high clinical risk.

4 PROPHYLAXIS DRUGS AND INDICATIONS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult</th>
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<tbody>
<tr>
<td><strong>TMP–SMX</strong></td>
<td>160 + 800 mg (one DS tablet) orally, daily</td>
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<td></td>
<td>(If concerned about neutropenia 80 + 400 mg (one SS tablet) orally, daily is equally efficacious)</td>
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<tr>
<td><strong>Dapsone</strong></td>
<td>100 mg orally, daily</td>
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<tr>
<td><strong>Pentamidine</strong></td>
<td>300 mg inhaled via nebuliser, every 4 weeks (administered via a jet-nebuliser producing a droplet size of 1–2 microns)</td>
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<tr>
<td></td>
<td>This cannot be administered at Peter Mac.</td>
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<tr>
<td><strong>Atovaquone</strong></td>
<td>1500 mg orally, daily with a high-fat meal</td>
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</tbody>
</table>

For paediatric dosing, refer to online consensus guideline.
### INDICATIONS FOR PROPHYLAXIS

#### Haematological malignancy (grade of recommendation)

*Note: Patients may have multiple or cumulative risk factors; consider underlying disease, disease status and treatment-related immunosuppression.*

**Known indications:**
- Allogeneic HSCT (all) (C)
- ALL (all) (A)
- AML or lymphoma regardless of treatment protocol (children only) (C)
- Autologous HSCT (all children and selected high-risk adults) (C)
- Regimens: R–CHOP14, high-dose methotrexate (C)
- Lymphocyte-depleting agents (e.g. alemtuzumab) or patients whose CD4 count <200 cells/μL before commencing chemotherapy (C)
- Corticosteroids: where 16–25 mg prednisolone or ≥4 mg dexamethasone for ≥1 month is planned (C)
- Regimens: FCR, ABVD, gemcitabine (single centre reports of higher risk for these regimens; consider prophylaxis) (D)

#### Solid tumours (grade of recommendation)

- Regimens where 16–25 mg prednisolone or ≥4 mg dexamethasone for ≥1 month is planned (C)
- Brain tumours, particularly if temozolomide or craniospinal irradiation is planned (B)
- Other solid tumours undergoing myelosuppressive chemotherapy (children only) (C)

**First-line prophylactic agent should be trimethoprim-sulfamethoxazole, unless:**

1. Previous allergy or hypersensitivity to sulfa-drugs  
   *Recommend: trimethoprim-sulfamethoxazole desensitisation (unless previous anaphylaxis)*
2. Planned methotrexate chemotherapy in adults  
   *Recommend: second-line prophylactic agent*

**A second-line prophylactic agent should be used if trimethoprim-sulfamethoxazole is contraindicated:**

1. Dapsone, OR
2. Pentamidine (nebulised, monthly), OR
3. Atovaquone

**Duration of Prophylaxis:**

Prophylaxis should continue for at least 6 weeks after steroid cessation. A longer period of prophylaxis may be required if ongoing chemotherapy (e.g. cytarabine, cyclophosphamide, fludarabine, fluorouracil, methotrexate) is planned. Life-long prophylaxis should be considered if the patient has had a previous episode of PJP and persisting immunosuppression.
### 5 TREATMENT OF SUSPECTED OR PROVEN PJP INFECTION

<table>
<thead>
<tr>
<th>Adult</th>
<th>Comments</th>
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<tbody>
<tr>
<td><strong>TMP–SMX</strong></td>
<td>$5 + 25 \text{ mg/kg oral or IV, 8-hourly for 21 days}$&lt;br&gt;<strong>In severe disease, increase to 6-hourly initially</strong></td>
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<tr>
<td><strong>Clindamycin plus primaquine</strong></td>
<td>$450 \text{ mg clindamycin orally, 8-hourly}$&lt;br&gt;<strong>PLUS</strong>&lt;br&gt;$15 \text{ mg primaquine orally, daily for 21 days}$&lt;br&gt;In severe disease, increase clindamycin to 900 mg IV initially then dose as above. Also, increase primaquine to 30 mg</td>
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<tr>
<td><strong>Pentamidine</strong></td>
<td><strong>In severe disease where TMP–SMX contraindicated:</strong>&lt;br&gt;$4 \text{ mg/kg IV, daily for 21 days}$</td>
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<tr>
<td><strong>Dapsone plus trimethoprim</strong></td>
<td>$100 \text{ mg dapsone orally, daily}$&lt;br&gt;<strong>PLUS</strong>&lt;br&gt;$5 \text{ mg/kg trimethoprim orally, 8-hourly for 21 days}$</td>
</tr>
<tr>
<td><strong>Atovaquone</strong></td>
<td><strong>For mild–moderate diseases:</strong>&lt;br&gt;$750 \text{ mg orally, 12-hourly for 21 days}$</td>
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For patients with PaO2 <70mmHg, concurrent therapy with prednisolone is recommended. This is usually given as 40mg 12-hourly for 5 days, then 40mg daily for 5 days then 20mg 12-hourly for 11 days.

Remember that secondary prophylaxis for PJP is likely to be required while this patient remains immunocompromised.

### 6 REFERENCES

Disclaimer: This Document has been developed for Peter Mac use and has been specifically designed for Peter Mac circumstances. Printed versions can only be considered up-to-date for a period of one month from printing date after which, the latest version should be downloaded from iPolicy.


10 VERSION AND APPROVAL HISTORY

<table>
<thead>
<tr>
<th>Date</th>
<th>Version #</th>
<th>Author; Owner and Authoriser</th>
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</thead>
<tbody>
<tr>
<td>Nov 2011</td>
<td>&lt;1 (if new)&gt;</td>
<td>Karin Thursky (Chair Antimicrobial Stewardship Committee)</td>
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<tr>
<td></td>
<td></td>
<td>Presented and approved at PTAC July 2011</td>
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<td>January 2015</td>
<td>2</td>
<td>New guideline with updated recommendations from National Consensus Guidelines</td>
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