# Antifungal Prophylaxis

**Scope (Staff):** Medical, Nursing and Pharmacy

**Scope (Area):** PCH

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This document should be read in conjunction with this DISCLAIMER

**Prophylaxis** refers to antifungal therapy in a patient at risk of, but without clinical or microbiological evidence of fungal infection. This is distinct from empiric or targeted therapy in a child with clinical features or suspicion of invasive fungal infection.

<table>
<thead>
<tr>
<th>CLINICAL SCENARIO</th>
<th>Risk Factors</th>
<th>DRUGS/DOSES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neonates</strong></td>
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<tr>
<td>Preterm infants</td>
<td>All babies &lt; 34 weeks gestation or &lt;1500g</td>
<td>Oral or nasogastric <em>nystatin</em> 1mL three time a day</td>
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<tr>
<td>All infants with additional risk factors for invasive candida infections</td>
<td>Any babies with any risk factors for candidiasis including one or more of: i) endotracheal intubation; ii) total parental nutrition; iii) prolonged (&gt;7 days) or broad spectrum antibiotics(^a) iv) systemic steroids</td>
<td>Oral or nasogastric <em>nystatin</em> 1mL three times a day</td>
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</tbody>
</table>

The risk of invasive candidiasis is greatest in preterm and term babies with multiple risk factors including prematurity, low birth weight, endotracheal intubation, total parental nutrition or use of prolonged and/or broad spectrum antibiotics\(^a\)

In babies with multiple risk factors and/or who are unable to tolerate oral/nasogastric nystatin, **CONSIDER** changing to *IV fluconazole* prophylaxis (6mg/kg/dose twice weekly).

<table>
<thead>
<tr>
<th>Primary Immunodeficiency</th>
<th>Risk Factors</th>
<th>DRUGS/DOSES</th>
</tr>
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<tbody>
<tr>
<td>Chronic granulomatous disease</td>
<td>Other primary immunodeficiency with an increased risk of invasive fungal infection</td>
<td><strong>Oral itraconazole</strong> syrup 2.5mg/kg/dose (to a maximum starting dose of 200mg) 12 hourly with therapeutic drug monitoring(^b)</td>
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<tr>
<td>Other primary immunodeficiencies at increased risk of invasive fungal infection including: Wiskott Aldrich Syndrome, Severe combined immunodeficiency (SCID) and severe neutropenia</td>
<td><strong>Oral itraconazole</strong> syrup 2.5mg/kg/dose (to a maximum starting dose of 200mg) 12 hourly with therapeutic drug monitoring(^b)</td>
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<tr>
<td>Children with HIV infection</td>
<td>Prophylactic antifungals are not routinely recommended</td>
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<tr>
<td>CLINICAL SCENARIO</td>
<td>DRUGS/DOSES</td>
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<tr>
<td></td>
<td>Risk Factors</td>
<td>Standard Protocol</td>
</tr>
<tr>
<td>Solid organ transplantation</td>
<td>Liver Transplantation</td>
<td>Oral/nasogastric <strong>nystatin</strong> 1mL four times a day is recommended for the first three months post transplantation</td>
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<tr>
<td>Kidney Transplantation</td>
<td>Prophylactic antifungals are not routinely recommended</td>
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<tr>
<td>Other solid organ transplants</td>
<td>Antifungal prophylaxis is indicated. Discuss with interstate transplantation team, the infectious diseases or clinical microbiology service</td>
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<tr>
<td>Haematopoietic Stem Cell Transplantation</td>
<td>Allogeneic HSCT without risk factors for mould infection</td>
<td><strong>IV or oral fluconazole</strong> 6mg/kg/dose (to a maximum of 400mg) once daily from end of conditioning</td>
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<tr>
<td></td>
<td>Allogeneic HSCT with acute graft versus host disease (grade II-IV) or chronic extensive GVHD</td>
<td>Oral <strong>posaconazole</strong> liquid&lt;sup&gt;c,d,e,f&lt;/sup&gt; Aged ≥ 8 months: 4mg/kg/dose (to a maximum of 200mg) three times a day from end of conditioning with therapeutic drug monitoring (TDM) <strong>OR</strong> Oral <strong>posaconazole</strong> tablets&lt;sup&gt;d,e,f&lt;/sup&gt; If weighing at least 40kg: 300mg twice daily on day one, followed by 300mg once daily thereafter from end of conditioning <strong>OR</strong> If an intravenous agents is required due to intolerance or inadequate therapeutic levels, use: <strong>IV micafungin</strong>: 1mg/kg/dose (to a maximum of 50mg) once daily</td>
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<tr>
<td></td>
<td>Allogeneic HSCT at high risk of mould infection including children with: i) primary immunodeficiency ii) previous HSCT iii) expected delayed engraftment or graft failure iv) prior IFI</td>
<td><strong>IV or oral fluconazole</strong> 6 mg/kg/dose (to a maximum of 400mg) once daily</td>
</tr>
<tr>
<td></td>
<td>Autologous stem cell transplantation</td>
<td>Autologous HSCT in neutropenic phase</td>
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<tr>
<td>CLINICAL SCENARIO</td>
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</tbody>
</table>
| Haematological malignancies | Acute Myeloid Leukaemia or Myelodysplastic syndrome | Oral *posaconazole* liquid<sup>c,d,e,f</sup>
Aged ≥ 8 months: 4mg/kg/dose (to a maximum of 200mg) three times a day from end of conditioning with therapeutic drug monitoring (TDM)
OR
Oral *posaconazole* tablets<sup>d,e,f</sup>
If weighing at least 40kg: 300mg twice daily on day one, followed by 300mg once daily thereafter from end of conditioning
OR
If intravenous therapy required due to intolerance or inadequate therapeutic levels, use:
*IV* *micafungin*:
1mg/kg/dose (to a maximum of 50mg) once daily |
| | Relapse Acute Lymphocytic Leukaemia | During intensive phases, use:
*IV* *micafungin*:
1mg/kg/dose (to a maximum of 50mg) once daily, followed by
*IV or oral* *fluconazole*
6mg/kg/dose (to a maximum of 400mg) once daily |
| | Infant ALL | |
| | High risk ALL | During intensive phases, use:
*IV or oral* *fluconazole*
6mg/kg/dose (to a maximum of 400mg) once daily |
| | Standard risk ALL | **Antifungal prophylaxis is not routinely recommended.**
Oral *fluconazole* 6mg/kg/dose (to a maximum of 400mg) once daily may be considered in some children deemed to be at increased risk of mucocutaneous candidal infection |
| Other 3B patients | Stage 4 neuroblastoma | Antifungal prophylaxis is recommended during intensive phases of therapy
*IV or oral* *fluconazole*
6mg/kg/dose (to a maximum of 400mg) once daily |
| | HLH induction therapy | |
| | Aplastic Anaemia | Severe aplastic anaemic (ANC < 0.5 cells/uL)
Antifungal prophylaxis is recommended for children with severe aplastic anaemia
*IV or oral* *fluconazole*
6mg/kg/dose (to a maximum of 400mg) once daily
If neutropenia is prolonged (> 4 weeks) |
Based on a past history of fungal infection and exposure to specific chemotherapeutic and biological agents, specific children may be deemed to be at greater risk of invasive fungal infection (IFI).

Individual prophylaxis plans may be devised and documented in the notes for these children.

Discontinuation or modification of these individual plans are only to be made following discussion with the treating physician.

a. Broad-spectrum antibiotics include 3rd generation cephalosporins, beta-lactam/beta-lactamase inhibitors and carbapenems.

b. Doses given are for itraconazole syrup. This is preferred given the improved bioavailability. If capsules are deemed to be preferable, contact pharmacy for advice regarding dose adjustment. The target trough concentration for itraconazole prophylaxis is >500 microgram/L. Refer to the ChAMP monograph for further information.

c. Absorption of posaconazole syrup should be administered during or after a high-fat meal to optimise absorption. Proton pump inhibitors significantly reduce oral bioavailability and should be avoided.

d. Given the uncertain and unpredictable pharmacokinetics, therapeutic drug monitoring is recommended when using posaconazole. The target trough concentration for posaconazole prophylaxis is >700 microgram/L or 0.7 mg/L.

e. The liquid and tablet formulations of oral posaconazole are NOT interchangeable. The formulation must be specified on each drug order.

f. Due to the potential for significant drug interactions, specific drug-drug combinations should be avoided.
   - Bortezomib, Imatinib, Dasatinib, Sorafenib: avoid all azoles (flu-, itra-, vori- and posaconazole).
   - Vincristine, Cyclophosphamide, Ifosfamide: avoid all azoles except fluconazole.
   - Cyclosporin, tacrolimus, sirolimus: dose reduction of these specific immunosuppressive drugs is required when taking posaconazole. Seek advice from ChAMP Pharmacist.
Related internal policies, procedures and guidelines

Antimicrobial Stewardship Policy
ChAMP Empiric Guidelines

References