## MONOGRAPH

### Itraconazole Monograph - Paediatric

<table>
<thead>
<tr>
<th>Scope (Staff):</th>
<th>Clinical Staff – 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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This document should be read in conjunction with this [DISCLAIMER](#).

### DESCRIPTION

<table>
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<th>High Risk Drug</th>
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Itraconazole is a broad spectrum azole antifungal. It impairs ergosterol synthesis in fungal cell membranes resulting in their breakdown.\(^{(1,2)}\)

Itraconazole is a **High Risk Medicine**

### INDICATIONS AND RESTRICTIONS

Itraconazole is indicated for the treatment of cutaneous and systemic fungal infections due to Dermatophytes (*Trichophyton spp.*, *Epidermophyton fluccosum* and *Microsporum spp.*), yeasts (*Candida* and *Cryptococcus*), *Aspergillus* species, *Sporothrix schenckii* (sporotrichosis) and *Histoplasma capsulatum* (histoplasmosis).\(^{(1)}\)

Itraconazole can also be used as prophylaxis for the above conditions in children and adolescents with specific immune deficiencies.

**Oral**: **Monitored (orange) antifungal**

- 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.

**DTC restrictions:**

Lozanoc\(^{®}\) capsules also require an IPA for all non-PBS indications.

### CONTRAINDICATIONS

- Itraconazole is contraindicated in patients with a known hypersensitivity to it or any of its excipients.\(^{(2-4)}\)
- Itraconazole has a number of clinically significant drug interactions that may contraindicate its use. Refer to interactions section below.\(^{(1-4)}\)

### PRECAUTIONS

The two available capsule brands (Sporanox\(^{®}\) and Lozanoc\(^{®}\)) and oral liquid (Sporanox liquid\(^{®}\)) are NOT interchangeable.
ALL prescriptions should state the formulation and brand required. 

PCH stocks only the Lozanoc® brand in the capsule formulation.

Sporanox® is the only available oral solution. 

One 50 mg Lozanoc® capsule is equivalent to one 100 mg Sporanox® capsule.

The recommended dose for Lozanoc® is therefore half the recommended dose for conventional (Sporanox®) itraconazole capsules.\(^{(1,5)}\)

Itraconazole should be used cautiously in patients with a history of hepatic dysfunction or failure and in those with a high risk of heart failure including patients with cardiac disease, patients with chronic lung disease associated with pulmonary hypertension, patients receiving treatment with negative ionotropic drugs (e.g. calcium channel blockers). Contact Pharmacy or refer to literature for further information.\(^{(2-4,6)}\)

### FORMULATIONS

Available at PCH:
- 50mg capsules (Lozanoc®)
- 10mg/mL oral solution (Sporanox®)

Other formulations available:
- 100mg capsules (Sporanox® and additional generic brands)

Sporanox® capsules are no longer available at PCH.

Any patients currently on Sporanox® capsules, should be converted to the equivalent dose of the Lozanoc® capsules and have therapeutic drug monitoring conducted to ensure the appropriate levels are being achieved.

### DOSAGE

The doses listed below fall within the standard range. Higher doses may be prescribed for certain situations (e.g. based on therapeutic drug monitoring) in consultation with an infectious diseases or clinical microbiology consultant.

**Neonates (less than 30 days of age):**

Not routinely used in neonates, contact Infectious Disease or Microbiology consultants for advice. Care should be taken in neonates due to the propylene glycol content of the oral solution.

**Dose equivalence:** One 50 mg Lozanoc® capsule is equivalent to one 100 mg Sporanox® (conventional itraconazole) capsule.\(^{(1,5)}\)

**Lozanoc® capsules:**

Note: Doses below refer to the Lozanoc® brand of itraconazole only

**Usual dose:** 2.5 - 3.75mg/kg/DAY (to a maximum initial dose of 200mg daily) given in 1 or 2 doses.
**DOSAGE ADJUSTMENT**

<table>
<thead>
<tr>
<th>Item</th>
<th>Details</th>
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<tbody>
<tr>
<td><strong>Dose adjustment required in hepatic impairment:</strong></td>
<td>Itraconazole should be used with caution in patients with hepatic impairment.</td>
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<tr>
<td></td>
<td>Dose reduction and close monitoring of liver function is required, contact Pharmacy or Infectious Diseases for advice.</td>
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<tr>
<td><strong>Dose adjustment required in renal impairment:</strong></td>
<td>Dosage reduction is generally not required in cases of significant renal impairment. However, there is a possibility of a reduced oral bioavailability. Contact Pharmacy for advice.</td>
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**RECONSTITUTION**

<table>
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<tr>
<th>Item</th>
<th>Details</th>
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<tbody>
<tr>
<td><strong>Not applicable</strong></td>
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**ADMINISTRATION**

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<tr>
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<tr>
<td><strong>Lozanoc® 50mg capsules:</strong></td>
<td>May be taken with or without food.</td>
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<tr>
<td><strong>Sporanox® oral liquid:</strong></td>
<td>The oral liquid should be administered on an empty stomach approximately 1 hour before food or 2 hours after food. Absorption may be reduced if administered via a feeding tube.</td>
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**MONITORING**

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<tr>
<td><strong>Therapeutic drug monitoring is required due to the large variation in plasma concentrations with both capsules and oral liquid. Due to the long half-life of itraconazole levels should be taken at least 7 to 14 days after starting treatment or after any dose change or if there is a change in formulation.</strong></td>
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<td><strong>Trough levels of greater than 0.5mg/L for prophylaxis and between 1-2mg/L for treatment should be achieved.</strong></td>
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### Collection tube:
**Paediatric:** Lithium Heparin (Dark green top) 1mL (no gel) or Serum (red top) 1mL (no gel)

**Minimum volume required:** 1mL\(^{(10)}\)

Renal and hepatic function and potassium levels should be monitored in patients taking itraconazole for 1 month or longer and in all patients with risk factors for hepatotoxicity regardless of duration of therapy.\(^{(1-4)}\)

### ADVERSE EFFECTS

**Common:** dyspepsia, anorexia, fatigue, itch, dizziness, rash, headache, nausea, vomiting, taste disturbance, abdominal pain, dyspnoea, diarrhoea, constipation, elevated liver enzymes,\(^{(1, 6)}\)

**Rare:** insomnia, somnolence, gynaecomastia, impotence, hypertension (with high dose), peripheral oedema, pulmonary oedema, heart failure, Stevens-Johnson syndrome, hypokalaemia (more common with high dose), reversible adrenal insufficiency, thrombocytopenia and other blood dyscrasias, serious hepatotoxicity including hepatic failure, anaphylaxis, alopecia, peripheral neuropathy, , flatulence, constipation, menstrual disorder, pancreatitis, , urinary frequency, visual disturbances, tinnitus.\(^{(1, 6)}\)

### COMPATIBLE FLUIDS

Not applicable

### STORAGE

All formulations of itraconazole should be stored below 25°C\(^{(5)}\)

### INTERACTIONS

Itraconazole interacts with other medications; please consult PCH approved references (such as Clinical Pharmacology), your ward pharmacist or Pharmacy on extension 60190 for more information.

- Itraconazole is a strong CYP3A4 inhibitor and potential drug interactions, should be investigated before commencing treatment and with any change in the medication profile of the patient.\(^{(1, 2, 5)}\)

- Itraconazole should be used with caution in patients taking a calcium channel blocker (e.g. verapamil, diltiazem). There is an increased risk of heart failure due to the combined negative inotropic effect.\(^{(1)}\)

- Itraconazole requires an acidic environment for absorption. It should not be taken in conjunction with antacids, H\(_2\) receptor antagonists or proton pump inhibitors. If these medications cannot be ceased during itraconazole therapy, itraconazole can be taken with an acidic beverage (e.g. cola) to assist in absorption.\(^{(2, 3)}\)

- Itraconazole should be avoided wherever possible in patients also requiring vincristine and other vinca alkaloids.\(^{(1)}\)
- Itraconazole should be used with caution in patients undergoing therapy with cyclophosphamide or ifosfamide. A change in anti-fungal agent for the duration of cyclophosphamide/ifosfamide administration, or a change or delay in the chemotherapy dose may be required. (1)

- Itraconazole is a strong CYP3A4 inhibitor and significantly increases the concentration of ivacaftor. A reduction in dose of ivacaftor to one tablet (or sachet) twice WEEKLY. (5)

- Orkambi® (lumecaftor/ ivacaftor) may require dose adjustment when used in conjunction with itraconazole, please refer to PCH approved references.

**COMMENTS**

Patients should be counselled to report feeling unusually tired, nauseous or not eating, any dark urine, pale stools or yellowing of the whites of the eyes or skin. (1)

**MANUFACTURER SAFETY DATA SHEET (SDS)**

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

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

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**Related internal policies, procedures and guidelines**

- Antimicrobial Stewardship Policy
- ChAMP Empiric Guidelines
References


This document can be made available in alternative formats on request for a person with a disability.