MONOGRAPH

Itraconazole Monograph - Paediatric

Scope (Staff):	Medical, Pharmacy, Nursing
Scope (Area):	All Clinical Areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

QUICKLINKS

DRUG CLASS

Azole antifungal.[1]

Itraconazole is a High Risk Medicine.

INDICATIONS AND RESTRICTIONS

Itraconazole is indicated for the treatment of cutaneous and systemic fungal infections due to susceptible fungi (including yeasts, some Aspergillus species and *Sporothrix schenckii* [sporotrichosis]) [1, 2]

Itraconazole can also be used as prophylaxis for the above conditions in children and adolescents with specific immune deficiencies.[1]

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.

CONTRAINDICATIONS

- Hypersensitivity to itraconazole or any component of the formulation.[3-5]
- Itraconazole is a strong cytochrome CYP3A4 inhibitor. Potential drug interactions should be investigated for commencing treatment and before any changes to the medication profile of the patient.[1, 3-5].

PRECAUTIONS

The three available itraconazole formulations (Sporanox® and Lozanoc® capsules) and oral solution (Sporanox® oral solution) are NOT interchangeable.

ALL prescriptions should state the formulation and brand required.

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

Sporanox® oral solution is the only available oral solution.

- Itraconazole should be used cautiously in patients with:
  - A history of hepatic dysfunction or failure
  - High risk of heart failure (including those with cardiac disease)
  - Chronic lung disease associated with pulmonary hypertension
  - Receiving treatment with negative ionotropic drugs (e.g. calcium channel blockers)

Contact Pharmacy or refer to literature for further information.[1, 4]

FORMULATIONS

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required:

- 50mg capsules (Lozanoc®)
- 10mg/mL oral solution (Sporanox® oral solution)

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Neonates: 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.[5]

Dose equivalence: One 50 mg Lozanoc® (suprabioavailable itraconazole) capsule is equivalent to one 100 mg Sporanox® (conventional itraconazole) capsule.[1, 6]

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. Dose should be adjusted based on therapeutic drug monitoring.[6, 7]

The dose should be rounded to the nearest 50mg to facilitate administration.[7]

- **Severe infections and Acute BronchoPulmonary Aspergillosis (ABPA) in Cystic Fibrosis:** 5mg/kg/dose (to a maximum initial dose of 150mg per dose) given twice daily.[7, 8]

Dose should be adjusted based on therapeutic drug monitoring.

- **Prophylaxis:** 2.5mg/kg/dose given once daily (to a maximum initial dose of 200mg daily) Dose should be adjusted based on therapeutic drug monitoring.[7]

Oral liquid:

Note: Bioavailability of the oral liquid in the fasting state is 60% higher than from the conventional itraconazole capsule taken with food.[1]

- **Usual dose:** 5mg/kg/DAY (to a maximum initial dose of 400mg daily) given in 1 or 2 divided doses. Dose should be adjusted based on therapeutic drug monitoring [1, 7]
- **Severe infections and ABPA in cystic fibrosis:** 5mg/kg/dose twice daily (to a maximum initial dose of 300mg per dose). Dose should be adjusted based on therapeutic drug monitoring [1, 7]
- **Prophylaxis:** 2.5mg/kg/dose (to a maximum initial dose of 200mg daily) given twice daily. Dose should be adjusted based on therapeutic drug monitoring.[6, 7]

Dosing in Overweight and Obese Children: No information currently available

Renal impairment:

- 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.[2, 4, 5]
- Large variations in plasma concentrations have been observed in adult patients with uraemia or receiving peritoneal dialysis or haemodialysis.[5]

Hepatic impairment:

- Itraconazole should be used with caution in patients with hepatic impairment.
- Dose reduction and close monitoring of liver function is required.[4, 5]

ADMINISTRATION

- **Lozanoc® 50mg capsules:** May be taken with or without food.[6]
- **Sporanox® oral solution:** The oral solution 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.[6]

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Not applicable

MONITORING

- Therapeutic drug monitoring is required due to the large variation in plasma concentrations with both formulations. Due to the long half-life of itraconazole levels should be taken at least 5 to 7 days (if loading doses are used) or 10 to 14 days (if no loading doses are used) after starting treatment or after any dose change or if there is a change in formulation.[1, 2, 9, 10]
- **Target trough levels:**
  - Prophylaxis 0.5-4mg/L
  - Treatment: 1-4mg/L.[2, 9, 10]

- **Collection tube:**
  - **Paediatric:** Serum, no gel (RED) or Lithium heparin, No gel (DKGNLITH) [9]
  - **Minimum volume required:** 1mL[9]
- 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, 3, 4, 6]
- Patients should be counselled to contact the prescriber if they experience any signs or peripheral neuropathy or symptoms suggestive of hepatitis including anorexia, nausea, vomiting, fatigue, abdominal pain or dark urine.[3, 6, 11]

ADVERSE EFFECTS

Common: dyspepsia, anorexia, fatigue, itch, dizziness, rash, headache, nausea, vomiting, abdominal pain, dyspnoea, diarrhoea, constipation, elevated lever enzymes.[1, 6, 11]

Infrequent: altered taste, hearing loss, insomnia, somnolence, gynaecomastia, impotence, flatulence [1, 6, 11]

Rare: hypertension (with high dose), peripheral oedema, pulmonary oedema, heart failure, severe cutaneous adverse reactions (SCARs) , hypokalaemia (more common with high dose), reversible adrenal insufficiency, thrombocytopenia and other blood dyscrasias, serious hepatotoxicity including hepatic failure, anaphylaxis, alopecia, peripheral neuropathy, menstrual disorder, pancreatitis, urinary frequency, visual disturbances, tinnitus.[1, 6, 11]

STORAGE

All formulations of itraconazole should be stored below 25°C[6]

INTERACTIONS

This medication may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

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

Related CAHS internal policies, procedures and guidelines
Antimicrobial Stewardship Policy
ChAMP Empiric Guidelines and Monographs
KEMH Neonatal Medication Protocols

References

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File Path:	W:\Safety & Quality\CAHS\CLOVERS MEDICAL Pharmacy\Procedures Protocols and Guidelines\ChAMP\Word\Monographs\PCH Templated (ED Guidelines)		
Document Owner:	Head of Department – Infectious Diseases		
Reviewer / Team:	Children's Antimicrobial Management Program Pharmacist		
Date First Issued:	September 2015	**Last Reviewed:**	February 2022
Amendment Dates:	March 2019	**Next Review Date:**	February 2025
Approved by:	Medication Safety Committee	**Date:**	February 2022
Endorsed by:	Drugs and Therapeutics Committee	**Date:**	February 2022
Standards Applicable:	NSQHS Standards: NSMHS: N/A Child Safe Standards: N/A		

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