MONOGRAPH

Posaconazole 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]

Posaconazole is a High Risk Medicine.

INDICATIONS AND RESTRICTIONS

- Posaconazole is used in the treatment of invasive fungal infections (such as invasive aspergillosis and mucomycosis) and in the prevention of invasive fungal infections in certain patients at risk (e.g. prolonged neutropenia).[1, 2]

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.

IV: Restricted (red) antifungal

ChAMP approval is required prior to prescription.

CONTRAINDICATIONS

- Hypersensitivity to posaconazole, other azole antifungals or any component of the formulation.[3]
- Posaconazole is contraindicated in patients being treated with ergometrine (and other ergot alkaloids), cisapride, atorvastatin, fluvastatin, simvastatin and other agents that can prolong the QT interval.[1, 3, 4]

PRECAUTIONS

- Posaconazole has been shown to prolong the QT interval; it should be used with caution in patients with an increased risk of arrythmias.[3]
- The intravenous solution contains 20 mmol of sodium per 300 mg.[5]
- Long term use of posaconazole may cause or worsen peripheral neuropathy. [1]
- Concurrent use of proton pump inhibitors (e.g. omeprazole) or conditions predisposing patients to malabsorption may result in reduced absorption of the oral suspension.[1]

FORMULATIONS

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

- 40 mg/mL oral suspension.
- 100 mg modified release tablets
- 300 mg/16.7 mL solution for IV infusion vial

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Check the dose carefully
The oral liquid and modified release tablets are NOT interchangeable. ALL prescriptions should state the formulation required.

Neonates and children less than 5 months of age:
Not routinely used in neonates or children less than 5 months of age, contact Infectious Disease or Microbiology consultants for advice.

Dosing in Overweight and Obese Children:

Obese patients may have a significantly reduced exposure to posaconazole due to an increased volume of distribution and increased clearance. Patients should be monitored for breakthrough fungal infections.[3]

Prophylaxis:

Oral modified release tablets (preferred over suspension if able to swallow tablets):

- **Children 7 to 12 years old AND < 40 kg AND able to swallow whole tablets:**

  5-7 mg/kg/dose (to a maximum of 300 mg) 12 hourly on day one, followed by 5-7 mg/kg (to a maximum of 300 mg) 24 hourly thereafter.[4, 6]

  Suggested dose bands[6]:

Weight	Dose
≥ 15 kg to < 22 kg	100 mg 12 hourly on day one, followed by 100 mg once daily thereafter
≥ 22 kg to < 31 kg	150 mg 12 hourly on day one, followed by 150 mg once daily thereafter
≥ 31 kg to < 36 kg	200 mg 12 hourly on day one, followed by 200 mg once daily thereafter
≥ 36 kg to < 40 kg	250 mg 12 hourly on day one, followed by 250 mg once daily thereafter

  Note: there is limited information available regarding halving posaconazole modified release tablets. Case reports have demonstrated target drug levels can be achieved.[7-9]

- **Children ≥ 2 years old AND weighing ≥ 40kg:** 300 mg 12 hourly on day one, followed by 300 mg 24 hourly thereafter.[3]

Oral suspension (use only if tablets not suitable):

- **Children ≥ 6 months to 12 years old:** 4 to 6 mg/kg/dose (to a maximum of 400 mg) given 8 hourly.[3]
- **Children ≥ 13 years old:** 200 mg per dose, given 8 hourly.[1, 3, 4]

Treatment:

Note: Loading doses are not required when switching between IV and oral delayed release tablet formulations.[3]

Oral modified release tablets (preferred over suspension if able to swallow tablets):

- **Children ≥ 10 kg to < 20 kg:** 200 mg 12 hourly on day one, followed by 200 mg 24 hourly thereafter.[10]
- **Children ≥ 20 kg to < 30 kg:** 300 mg 12 hourly on day one, followed by an alternating daily dose of 300 mg once daily and 200 mg once daily.[10]
- **Children ≥ 30 kg:** 300 mg 12 hourly on day one, followed by 300 mg 24 hourly thereafter.[10]

Oral suspension (use only if tablets not suitable):

- **Children ≥ 5 months:**
  - **< 34 kg:** 4.5 to 6 mg/kg/dose (to a maximum of 200 mg) given 6 hourly. [3]
  - **≥ 34 kg:** 200 mg given 6 hourly.[3] 400 mg twice daily can be given if there is adequate food intake (during or after a high-fat meal). [1, 3, 11]

IV Infusion:

- **Children < 30 kg:** 7 to 12 mg/kg/dose (to a maximum of 300mg) 12 hourly on day one, followed by 7 to 12 mg/kg/dose 24 hourly thereafter.[3, 4]

- **Children ≥ 30 kg**: 300 mg 12 hourly on day one, followed by 300 mg 24 hourly thereafter.[3, 4]

Renal impairment:

- eGFR calculator
- No dosage adjustments are required in renal impairment.
- The IV formulation should be avoided in patients with a eGFR of < 50 mL/minute due to the cyclodextran used as a solvent.[1, 3]
- Patients with eGFR < 20 mL/minute should be monitored for breakthrough fungal infections due to the variability in area under the curve ranges with severe renal impairment.[1]

Hepatic impairment:

- No dosage adjustments are required in hepatic impairment. Posaconazole should be used with caution in severe hepatic impairment as the half-life is doubled.[1, 4]

ADMINISTRATION

Oral suspension:

- Shake the bottle well before measuring out the required dose.[12]
- Absorption is very variable and is affected by the presence of food.[1, 12]
- It is important to ensure that posaconazole is administered during or after a high-fat meal for best absorption.[1]
- If this is not possible, administration with any meal or food supplement (the larger the volume of food supplement, the better the absorption) or an acidic, carbonated drink will improve absorption.[1, 12]
- Proton pump inhibitors should be avoided due to the reduction in absorption.[1]
- The oral suspension should be administered via the oral route when possible. Absorption is reduced by approximately 20% when administered via a nasogastric tube. If administering via an enteral tube, the suspension should be diluted with an equal amount of water to ensure it is able to pass through the tube.[13]
- For oncology patients, posaconazole suspension should be administered with oral Calogen® (nutritional supplement) as per the doses below:

≥ 10 years of age:

- 30 mL of Calogen® with each posaconazole dose

<10 years of age:

- ≥8 kg to < 16 kg: 10 mL of Calogen® with each posaconazole dose
- ≥16 kg to < 30 kg: 20 mL of Calogen® with each posaconazole dose
- ≥ 30 kg: 30 mL of Calogen® with each posaconazole dose

Modified release tablets:

- Posaconazole tablets should be swallowed whole (not crushed or chewed) and taken with food.[1, 7-9, 13]
- **Note:** there is limited information available regarding halving posaconazole modified release tablets. Case reports have demonstrated target drug levels can be achieved.[7-9]

IV infusion:

- Dilute to a final concentration of 1 to 2 mg/mL and infuse over 90 minutes via a Central Venous Access Device (CVAD).[5]
- Peripheral lines are not recommended due to the high incidence of thromboplebitis when administered peripherally.[5]

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

- Glucose 5%
- Sodium Chloride 0.9% and 0.45%
- Glucose 5% and sodium chloride 0.45%
- Glucose 5% and sodium chloride 0.9%[5]

Compatible at Y-site:

Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.

MONITORING

- Liver function should be measured at baseline and regularly throughout therapy.[1]
- Renal function and serum electrolytes should be measured weekly with prolonged therapy (longer than 7 days). Monitor serum creatinine closely if IV route must be used due to the cyclodextrin content of the IV solution which accumulates if eGFR < 50 mL/minute.[1, 3]
- Therapeutic drug monitoring is required. It takes approximately 10 days to reach steady state levels using the liquid formulation and 5 days to reach steady state with the extended release tablets or IV formulation.[1]
- Trough levels should be maintained above 0.7 mg/L for prophylaxis and between 1 mg/L and 1.8 mg/L for treatment.[1]
    - Once target level has been achieved, trough level monitoring should be performed monthly.
    - For patients taking the suspension, if levels are subtherapeutic, divide the total daily dose in 4 equal portions to improve absorption and recheck levels after 10 days.[13]
    - It is unclear if toxicity is concentration dependent.[1]
    - Increasing the oral dose of posaconazole above 800mg per day does not result in increased plasma concentrations.[1]
- ECG should be monitored in patients with risk factors for QT prolongation.[3]
- Monitor for signs and symptoms of pseudohyperaldosteronism as clinically appropriate.[3]

ADVERSE EFFECTS

Common: neutropenia, fever, diarrhoea, nausea, vomiting, abdominal pain, thrombophlebitis (with IV use), hypertension or hypotension, elevated liver function enzymes, headache, rash and dizziness.[1, 4]

Infrequent: hypokalaemia, respiratory insufficiency, oedema, constipation.[1]

Rare: prolonged QT interval (more common in patients on other causative medications) , torsades de pointes, cholestasis, liver failure or hepatotoxicity, tongue or facial oedema, anaphylaxis, adrenal insufficiency, blood dyscrasias, alopecia, peripheral neuropathy (more common with long-term use), pseudohyperaldosteronism, neurotoxicity (with high concentrations).[1, 4]

STORAGE

Oral suspension:

- Store below 25 °C[3, 12]

Modified release tablets:

- Store below 30 °C.[12].

IV Infusion:

- Store between 2 to 8° C[3, 5, 12]

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 **posaconazole**. 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

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