Program (ChAMP)

#### **MONOGRAPH**

## **Primaquine 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**

	QUICK	LINKS	
Dosage/Dosage Adjustments	Administration	Compatibility	<u>Monitoring</u>

#### **DRUG CLASS**

Antimalarial.(1)

## **INDICATIONS AND RESTRICTIONS**

- Primaquine is used to eradicate the intrahepatic forms (hypnozoites) of *Plasmodium vivax* and *Plasmodium ovale*. It is also used to eliminate the transmissible stage of *Plasmodium falciparum* in malaria receptive regions of Australia (just south of Broome, Tennant Creek to above Townsville north of 19°S latitude). (2, 3)
- Primaquine is also used as a second line agent in the treatment of *Pneumocystis jiroveci* pneumonia in combination with clindamycin, however this combination is associated with considerable toxicity.<sup>(1, 3)</sup>

## Oral: Monitored (orange) antiprotozoal

- 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 primaquine, 8-aminoquinolines or any component of the formulation. (4, 5)
- Primaquine is contraindicated in patients with severe glucose-6-phosphate dehydrogenase (G6PD) deficiency. (1, 4-7)
- Primaquine is contraindicated in acutely unwell patients who have a tendency to develop granulocytopenia (e.g. rheumatoid arthritis or systemic lupus erythematosus). (1, 3, 4, 7, 8)
- Primaquine is contraindicated in patients currently receiving medications that may depress bone marrow or agents that may cause haemolytic anaemia due to the increased risk of myelosuppression.<sup>(4)</sup>
- Primaguine is contraindicated in pregnancy. (3-5)
- Primaquine must not be given concurrently with quinacrine, or to patients who have recently taken quinacrine due to the significant increased risk of toxicity. (3, 4)

#### **PRECAUTIONS**

- Primaquine is associated with a definite risk of haemolysis in individuals with mild to moderate G6PD deficiency and should be avoided. In cases of mild to moderate G6PD deficiency a weekly dosage regimen may be tolerated. Discuss with the Infectious Diseases team. (1, 3-6)
- Patients with nicotinamide adenine dinucleotide (NADH) methemoglobin reductase deficiency have reported methaemoglobinaemia with primaquine use. (3, 4)
- Use primaquine with caution in patients with conditions that may increase the risk of QT prolongation.<sup>(4, 5, 7)</sup>
- Primaquine should be avoided in children less than 6 months old due to the risk of methaemoglobinaemia.<sup>(1)</sup>
- Discontinue primaquine promptly if signs of haemolytic anaemia occur (e.g. darkening urine, marked fall in haemoglobin).<sup>(5)</sup>
- 7.5 mg of primaguine base is equivalent to 13.2 mg of primaguine phosphate. (1, 3)

#### **FORMULATIONS**

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

7.5mg (primaquine base) oral tablet.

Imprest location: Formulary One

#### **DOSAGE & DOSAGE ADJUSTMENTS**

Children MUST be screened for G6PD deficiency before commencing therapy. (1-4, 7, 8)
All doses are expressed as primaguine base.

## Neonates and children less than 6 months of age:

- Not routinely used in neonates or infants less than 6 months of age due to the risk of methaemoglobinaemia. Contact Infectious Diseases consultants for advice.<sup>(1)</sup>
- For children > 4 weeks of age doses of 0.5 mg/kg/dose once daily for 14 days have been given for radical cure / prevention of relapse.<sup>(4)</sup>

#### Oral:

#### Children ≥ 6 months of age:

#### Radical cure of P. vivax or P. ovale infection:

Should be used in conjunction a standard course of malaria therapy. (1, 3, 9)

#### P. vivax

- ≥ 6 months of age and ≥ 70kg: 30 mg once daily, until a total dose equalling 6 mg/kg is given.<sup>(3, 6)</sup>
- ≥ 6 months of age and < 70kg: 0.5 mg/kg/dose (to a maximum of 30 mg) once daily for 14 days. (3, 4, 9) 0.25 mg/kg/dose (to a maximum of 15 mg) can be given twice daily for 14 days in patients with nausea. (2)</li>

#### P. ovale:

≥ 6 months all weights: 0.25 mg/kg/dose (to a maximum of 15 mg) once daily for 14 days.<sup>(2, 4, 8)</sup>

#### Elimination of transmissible stage of *P. falciparum*:

- A single dose of primaquine should be given in addition to standard malaria therapy to eliminate the transmissible stage of *Plasmodium falciparum* in malaria receptive regions / low transmission areas of Australia just south of Broome, Tennant Creek to above Townsville – north of 19°S latitude).<sup>(2, 3)</sup>
- This dose is best given with the initial treatment to ensure transmission is blocked as soon as possible. (6)
- 0.25 mg/kg as a single dose (to a maximum of 15 mg).<sup>(3, 4, 9)</sup>

**Pneumocystis jiroveci [carinii] pneumonia:** 0.25 mg/kg (to a maximum of 15 mg) once daily for 21 days in conjunction with oral clindamycin. This combination is associated with considerable toxicity and is not considered first line.<sup>(6)</sup>

#### **Dosing in Overweight and Obese Children:**

 There is limited information regarding the optimal dosing of malaria therapies in obese patients. Discuss dosing for obese or overweight children with the Infectious Diseases team.

#### **Renal impairment:**

- eGFR calculator
- No dosage adjustment appears to be necessary in renal impairment, however use with caution in patients with severe renal impairment. (3, 4)

### **Hepatic impairment:**

 As primaquine is metabolised by the liver, it should be used with caution in patients with hepatic impairment and liver function tests should be checked weekly.<sup>(3, 4)</sup>

#### **ADMINISTRATION**

- Tablets should be given with food to mask the bitter taste and reduce gastrointestinal symptoms.<sup>(3, 4, 6)</sup>
- When being used for the treatment of malaria, an additional dose should be given if the patient vomits within 1 hour of oral administration.<sup>(1)</sup>

#### **MONITORING**

- G6PD deficiency must be excluded before commencing treatment courses. Exclusion of G6PD deficiency is not necessary for single doses.<sup>(1, 3, 7, 8)</sup>
- Full blood count (FBC) should be conducted before commencing treatment and regularly with ongoing treatment. (1, 3, 4)
- Visual colour check of urine should be conducted periodically during treatment as an indicator
  of haemolytic anaemia.<sup>(3, 4)</sup>
- If primaquine is used in patients with cardiac disease or other QT prolonging drugs, ECG should be conducted.<sup>(3, 7)</sup>

#### **ADVERSE EFFECTS**

**Common:** abdominal pain, dose related nausea and vomiting (generally less if taken with food), epigastric distress, dizziness, headache, leucocytosis.<sup>(1, 4)</sup>

Infrequent: methaemoglobinaemia, haemolytic anaemia in G6PD deficiency. (1, 8)

**Rare:** skin reactions, hypertension, arrhythmias, anaemia, leucopenia, granulocytopenia and agranulocytosis, cardiac arrhythmias, prolonged QT interval. (1, 3, 4, 8)

#### **STORAGE**

Store tablets below 25°C.(3, 5)

#### **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 **primaquine**. 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

PCH Emergency Department Guidelines - Malaria

#### References

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