MONOGRAPH

Artemether with Lumefantrine (Riamet®) 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			
Dosage/Dosage Adjustments	Administration	Compatibility	Monitoring

DRUG CLASS

Antiprotozoal.(1)

INDICATIONS AND RESTRICTIONS

- Artemether with lumefantrine is used as monotherapy in the treatment of uncomplicated malaria and in severe malaria following treatment using an IV antimalarial agent.(1-3)

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 artemether, lumefantrine or any component of the formulation.[4]
- Artemether with lumefantrine may only be used in the first trimester of pregnancy if there are no other suitable options. Contact infectious diseases for alternative options as malaria in pregnancy is a medical emergency and treatment with artesunate may be required.[1-3]
- Artemether with lumefantrine is contraindicated in patients with a history of arrhythmias, bradycardia and congestive heart failure with reduced left ventricular ejection fraction, family history of sudden death or of congenital QT interval prolongation.[2, 5, 6]
- The use of artemether with lumefantrine is contraindicated in combination with strong CYP3A4 inducers (e.g. rifampicin, carbamazepine and phenytoin) as it may result in a marked reduction in the concentration of both agents and a loss of antimalarial activity.[2-4, 6]

PRECAUTIONS

- Care should be taken when using artemether with lumefantrine in patients taking other medications that may prolong the QT interval.[6]
- Electrolyte imbalance increases the risk of QT prolongation.[5]

FORMULATIONS

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

- Artemether 20 mg with lumefantrine 120 mg tablets (Riamet®)

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Neonates: Not routinely used in neonates and children < 5 kg. Contact Infectious Disease or Clinical Microbiology service for advice.[1]

Oral treatment comprises a 6-dose course.
A dose is taken at hour 0, 8, 24, 36, 48 and 60.
Doses must be taken with a fatty meal or full-fat milk to aid absorption.[1-3, 5]

Children ≥ 2 months:

- Weight ≥ 5 kg to < 15 kg: 1 tablet per dose (total of 6 tablets)
- Weight ≥ 15 kg to < 25 kg: 2 tablets per dose (total of 12 tablets)
- Weight ≥ 25 kg to < 35 kg: 3 tablets per dose (total of 18 tablets)
- Weight ≥ 35 kg: 4 tablets per dose (total of 24 tablets)

Discuss patients with malaria acquired in the Greater Mekong subregion (Thailand, Vietnam, Cambodia, Laos and Myanmar) who are slow to respond with Infectious Diseases. Treatment may be extended with additional doses given at hour 72, 84, 96 and 108 (i.e. 2 additional days of treatment).[7]

Primaquine should be added for treatment of *P. vivax* or *P. ovale* malaria as artemether-lumefantrine only treats the blood stage of malaria. *P. ovale* and *P. vivax* can exist as dormant parasites in the liver which can reactivate to cause relapsed malaria if primaquine is not prescribed.[1, 6]

Dosing in Overweight and Obese Children: There is limited information regarding dosage adjustment in overweight or obese children. It appears that no dose adjustment is required, however close follow-up of obese patients is required as some studies have demonstrated a lower cure rate in patients over 65kg.[6, 8, 9]

Renal impairment:

- eGFR calculator
- There is limited information regarding the use of artemether with lumefantrine in patients with renal impairment. No dosage adjustments are recommended however care should be taken in this population.[2-4, 6]
- Patients with a creatinine clearance of less than 10 mL/minute/1.73m^2 should have electrocardiogram (ECG) monitoring and potassium levels should be closely monitored.[5]

Hepatic impairment:

- There is limited information regarding the use of artemether with lumefantrine in patients with hepatic impairment. No dosage adjustments are recommended in patients with mild to moderate hepatic impairment, care should be taken in patients with severe impairment.[3, 4]
- Patients with severe hepatic impairment should have electrocardiogram (ECG) monitoring and potassium levels should be closely monitored.[5]

ADMINISTRATION

- Artemether with lumefantrine should be taken with a fatty meal or full-fat milk food to enhance absorption and improve tolerability.[1-4, 6, 10]
- The tablets may be crushed and mixed with 5 - 10 mL of water to enable administration to those patients unable to swallow tablets.[3, 4, 10]

MONITORING

- Clinicians should be alert to possible QT prolongation with treatment, and high-risk patients (including those with hypokalaemia or hypomagnesaemia) should have ECG and potassium levels monitored throughout treatment.[2, 3, 6]
- Patients requiring concurrent use of other QT prolonging medications should have routine ECG throughout treatment.[6]
- Fever, parasitaemia and clinical improvement should be assessed, especially in patients who are vomiting or unable to take each dose with food due to the increased risk of treatment failure.[4, 6]
- Patients with severe malaria with hyperparasitaemia should be checked for haemolysis for 4 to 6 weeks.[1]

ADVERSE EFFECTS

The adverse effects of artemether with lumefantrine are similar to the symptoms of malaria and may be difficult to distinguish.[1]

Common: headache, dizziness, sleep disorder, anorexia, nausea, vomiting, diarrhoea, myalgia, arthralgia, weakness, fatigue, palpitations, itch, rash, abdominal pain, prolonged QT interval, cough, fever, asthenia.[1, 5, 6]

Infrequent: paraesthesia, ataxia, urticaria, hepatitis, clonus, drowsiness[1, 5, 6]

Rare: hypersensitivity, angioedema, severe haemolysis may occur 2 to 4 weeks after the treatment of severe malaria with hyperparasitaemia.[1, 5, 6]

STORAGE

- Tablets should be stored below 30˚C.[2]

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 **artemether with lumefantrine**. 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
Emergency Department Guidelines - Malaria

References

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File Path:	W:\Paediatrics\PMH\ChAMP\Monographs\FINALISED\00 Current version 00		
Document Owner:	Head of Department – Infectious Diseases		
Reviewer / Team:	Children's Antimicrobial Management Program Pharmacist		
Date First Issued:	October 2013	**Last Reviewed:**	June 2023
Amendment Dates:	March 2020, June 2023	**Next Review Date:**	July 2026
Approved by:	Medication Safety Committee	**Date:**	June 2023
Endorsed by:	Drugs and Therapeutics Committee	**Date:**	July 2023
Standards Applicable:	NSQHS Standards:  NSMHS: N/A Child Safe Standards: N/A		

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