Whittington Health NHS

Malaria Investigation and Treatment Guideline for Adults

Subject:	Malaria Investigation and Treatment for Adults
Policy Number	IPC/Micro 34
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Version:	3
Policy Executive Owner:	Dr Richard Jennings, Medical Director
Name and Designation of Author:	Dr Ben Killingley, Acute Medicine Consultant Dr Laura Maynard-Smith, Microbiology
Name of Assurance Committee:	Infection Prevention & Control Committee
Date Issued:	November 2015
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Target Audience:	All physicians, microbiologists, haematologists, haematology, laboratory staff, nurses
Key Words:	Malaria, fever, tropical, imported, travel, falciparum, vivax, ovale, malariae, quinine, chloroquine, malarone, artesunate, artemether-lumefantrine

Version Control Sheet

Version	Date	Author	Status	Comment
1	March 2012	Dr Richard Jennings	In-active	
2	November 2015	Dr Ben Killingley Dr Laura Maynard-Smith	Active	• New trust template • Intravenous artesunate replaces intravenous quinine as first line treatment of severe malaria and uncomplicated falciparum malaria if not able to tolerate oral therapy in adults and 2nd and 3rd trimesters of pregnancy • Intravenous artesunate replaces intravenous quinine in the treatment of severe malaria from SE Asia in all stages of pregnancy • Artemether-lumefantrine replaces quinine and doxycycline or clindamycin as first line treatment of uncomplicated falciparum malaria except in pregnancy • Artemether-lumefantrine replaces chloroquine for the treatment of *Plasmodium vivax* malaria from regions of known chloroquine resistance except in pregnancy • Advice can be sought from Dr Ben Killingley and Dr Richard Jennings, Consultants in Acute Medicine and Infectious Diseases, at the Whittington Hospital

➢ Criteria for use

This guideline applies to all adult patients known to have malaria or suspected of having malaria.

➢ Background/ introduction

There are 1500-2000 cases imported malaria in the UK each year, of which approximately half are diagnosed in London. Three quarters are caused by *Plasmodium falciparum*, and there are an average of 6 deaths from malaria in the UK each year. Patients returning from West Africa, predominantly Nigeria and Ghana, are most commonly represented [1]. Untreated, falciparum malaria can cause the rapid onset of coma, severe anaemia, hypoglycaemia, acute renal injury or pulmonary oedema [2]. The remainder of malaria cases are caused by *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae*, or mixed infections in which *Plasmodium falciparum* is usually one of the two species present.

The presentation of malaria can be very non-specific and diagnosis is not possible on routine blood tests. With travel to malaria-endemic countries increasing, a thorough travel history and high degree of clinical awareness is essential.

Over the past decade, the choice of therapy for both severe and uncomplicated malaria has changed considerably with the introduction of artemisinin derivatives (see Appendix 1 for drug information). WHO guidelines now recommend use of IV artesunate for adults with severe falciparum malaria [3]. Two large clinical trials, the SEAQUAMAT (2005) and AQUAMAT (2010) trials demonstrated clear survival advantages with intravenous artesunate compared to quinine for severe falciparum malaria in adults and children respectively [4,5]. Infections where the species is not known, or there is a mixed infection, should be treated as for falciparum malaria. WHO guidelines also recommend use of artemisinin combination therapy for treatment of uncomplicated falciparum malaria and non-falciparum malaria in areas of chloroquine resistance [3]. Chloroquine resistance is increasing in *Plasmodium vivax* species in Indonesia, Papua New Guinea, East Timor and the Solomon Islands. Recent studies on drug resistance in Indonesia have suggested that more than 65% cases vivax malaria in the region are chloroquine-resistant [6, 7].

In the Whittington Hospital, all cases of malaria must be managed with the involvement of the Whittington microbiology department and/or Dr Ben Killingley or Dr Richard Jennings (Consultant Infectious Diseases Physicians). Cases of severe malaria must always be managed in conjunction with the Hospital for Tropical Diseases (HTD) at University College London Hospitals.

➢ Inclusion/ exclusion criteria

Inclusion criteria: All adult patients known to have malaria or suspected of having malaria.

Exclusion criteria: None.

➢ Clinical management

1. Who to test for malaria

Malaria should be suspected and tested for if:

- The patient has recently returned from the tropics AND has any of the following:
- Fever
- Recent history of fever
- Systemic illness otherwise unexplained (symptoms are often very non-specific)

Patients with falciparum malaria will usually present within a month of returning from the tropics, but some can present up to 3 months after travel.
Patients infected with other species of malaria can present many months later.

We recommend malaria is considered **up to one year** after travel.

Anti-malarial prophylaxis is not 100% protective and adherence is often poor. A history of prophylaxis should not lower your index of suspicion.

2. How to test for malaria

Send a 5ml EDTA (full blood count) bottle to haematology for a Malaria Parasite Screen as soon as the suspicion of malaria is raised. The timing of the blood sample does not need to coincide with fever.

Mark the first sample as URGENT and state the countries and dates visited by the patient on the request.

All first samples will be processed by the haematology laboratory with a thick and thin blood film and antigen test regardless of the time of day. The antigen test will be able to differentiate between *Plasmodium falciparum* malaria and/or 'other' malarias, though not with further species differentiation between *P. vivax*, *P. ovale* or *P. malariae*. This can only be determined using microscopy on blood film.

The report will include the following:

1. The species – *Plasmodium falciparum*, *P. vivax*, *P. ovale*, *P. malariae* or whether there is a mixed infection.

Then, for falciparum malaria only:

2. Parasite stage – Ring forms, schizonts, gametocytes
3. Percentage parasitaemia (percentage of red cells parasitized with ring form parasites)

The presence of schizonts may mean that a further replication cycle is imminent and the percentage parasitaemia will rise.

Percentage parasitaemias are not given for non-falciparum malaria because this does not influence treatment.

Patients whose initial malaria test is positive should be treated IMMEDIATELY (see below).

Patients whose initial malaria test is negative with ongoing fever, should have daily malaria tests until three tests have been negative on three consecutive days. If the fever resolves, further testing is not required.

Patients whose initial malaria test shows a negative blood film but a positive antigen test should be discussed with the Whittington Microbiology Department and/or Dr Ben Killingley / Dr Richard Jennings. If these people are not available then discuss with the on call ID registrar at UCLH.

Empirical therapy despite a negative malaria test should not be initiated without specialist advice (ID/microbiology department at Whittington or ID on call registrar at UCLH).

3. Assessment of severity in falciparum malaria

Patients with falciparum malaria can deteriorate rapidly because of the impact of parasitized red cells sequestered in small vessels. Even patients who might be assumed to have a degree of natural immunity are at risk of severe deterioration. Left untreated, severe malaria is fatal in the majority of cases.

UNCOMPLICATED = parasitaemia <2% with no evidence organ dysfunction and able to take oral therapy.

SEVERE = parasitaemia >2% *or*
parasitaemia <2% and **any of the following**:

- Any reduction in GCS
- Seizures
- Raised respiratory rate, hypoxia, evidence of pulmonary oedema on CXR
- Shock (BP <90/60 mmHg)
- Acidosis (pH <7.3 or lactate >4.0)
- Hypoglycaemia (BM <2.2 mmol/L)
- Anaemia (Hb <8.0 g/dL)
- Renal impairment (oliguria or elevated creatinine)
- Haemoglobinuria
- Jaundice
- Spontaneous bleeding or lab evidence of disseminated intravascular coagulation (DIC)

4. Treatment of uncomplicated falciparum malaria

Use oral treatment unless the patient is vomiting, in which case treat as severe falciparum malaria (below).

Do not use a drug for treatment if the patient has been using it for prophylaxis (e.g. Malarone).

1st line: Artemether-lumefantrine (Riamet®)

4 tablets PO at 0, 8, 24, 36, 48 and 60 hours.

Take with milk or fatty food as this aids absorption.

NB. There are a number of drugs which interact with Riamet® – see Appendix 1 for list.

Contraindicated in pregnancy – for treatment in pregnancy, see section 7.

2nd line: Quinine plus Doxycycline *or* Quinine plus Clindamycin

Quinine 10mg/kg (max 700mg) PO every 8 hours (reduce to 12 hourly regimen if patient develops tinnitus and deafness)
plus
Doxycycline 200mg PO daily (**contraindicated in pregnancy –** for treatment in pregnancy see section 7)

Or

Quinine 10mg/kg (max 700mg) PO every 8 hours (reduce to 12 hourly regimen if patient develops tinnitus and deafness)
plus

Clindamycin 450mg PO every 8 hours (**safe in pregnancy** – for treatment in pregnancy see section 7)

Duration: 7 days

5. Treatment of severe falciparum malaria

THIS IS A MEDICAL EMERGENCY.

Effective anti-malarial drug therapy should be started immediately, either with IV quinine or artesunate. Use the parenteral therapy most readily available, and if there is any delay administer oral treatment until pharmacy can provide an IV preparation.

In addition, the following people must be notified immediately:

- Duty medical registrar
- ED consultant
- Acute medicine consultant/consultant physician on-call
- ITU consultant
- Whittington Infectious Disease consultant or Microbiology Consultant during normal working hours Monday-Friday, and the on-call ID physician at UCLH outside of normal working hours

Patients with severe malaria should be managed on a **High Dependency Unit** with frequent medical review.

1st line: Artesunate

This has fewer side effects than IV quinine and has been shown to reduce mortality compared to quinine in clinical trials [4, 5]. There is no need to adjust for renal impairment or to monitor for cardiac toxicity.

Dosage regimen for IV artesunate:

2.4mg/kg IV bolus at 0, 12 and 24 hours, and then every 24 hours thereafter.

Continue above regimen until patient is improving and can reliably swallow, then switch to oral artemether-lumefantrine (Riamet®) full course of six doses over three days (4 tablets at 0, 8, 24, 36, 48 and 60 hours).

2nd line: Quinine

Dosage regimen for IV quinine:

Loading dose 20mg/kg (max 1400mg) IV in 250ml Normal Saline (0.9% Sodium Chloride) infused over 4 hours.

Then, 8 hours after loading dose – maintenance dose of 10mg/kg (max 700mg) IV every 8 hours – in 250ml Normal Saline (0.9% Sodium Chloride) infused over 4 hours.

If the patient received mefloquine in the preceding 3 days, a loading dose is NOT required.

Continue above regimen until patient is improving and can reliably swallow to complete a total 7 day course with oral quinine and doxycycline, or quinine and clindamycin as outlined above under 'treatment for uncomplicated falciparum malaria'.

CAUTIONS

- Cardiac: Quinine is a class 1 anti-arrhythmic drug. It interacts with other class 1 agents to lengthen the QT interval, predisposing patients to Torsade de Pointes. Always check an ECG prior to starting IV quinine for QT interval. In patients with underlying cardiac disease, use cardiac monitoring and consider withholding regular anti-arrhythmic medication.
- Monitor blood sugar: Careful monitoring of patient's BM monitoring every 2-4 hours. IV quinine induces endogenous secretion of insulin, promoting hypoglycaemia.

6. Treatment of non-falciparum malaria

Plasmodium vivax and *ovale* require combination treatment with chloroquine and primaquine to control both the active infection and destroy the liver hypozoite stages which can lead to relapse. *Plasmodium malariae* has no hypozoite stage and can be treated with chloroquine alone. In patients returning from **Indonesia, Papua New Guinea, East Timor and the Pacific Islands**, chloroquine resistant *P. vivax* should be strongly suspected.

Chloroquine

In patients weighing 40-80kg:

Chloroquine (as base): 620mg PO at 0 hours, then 310mg PO at 6, 24 and 48 hours.

In patients weighing <40kg or >80kg:

Chloroquine (as base): 25mg/kg PO in divided doses over two days.

2/5 x total dose at 0 hours, then 1/5 x total dose at 6, 24 and 48 hours.

Itching with chloroquine should not be considered a contraindication.

Primaquine

Primaquine should not be given to pregnant patients or those with a G6PD deficiency. Normal G6PD levels range 5.9 – 11.7 U/g Hb and primaquine in patients who are G6PD deficient can cause severe haemolysis.

Dosing:

P.vivax – Primaquine PO 15mg BD for 14 days.

P.ovale – Primaquine PO 15mg OD for 14 days.

Patients who are G6PD deficient should be discussed with the ID consultant in conjunction with the haematology consultant.

For relapse prevention in pregnancy, see section 7.

Suspected chloroquine resistance

There is evidence of increasing resistance to chloroquine in Plasmodium vivax in Indonesia, Papua New Guinea, East Timor and the Pacific Islands (for full list of countries where chloroquine resistance has been reported, see http://www.who.int/malaria/areas/drug_resistance/drug_efficacy_database/en/) [9].

In patients returning from these countries, or in patients where there is recrudescence of symptoms within 28 days, patients should be treated with:

> PO artemether-lumefantrine (Riamet®) as per dosing above for uncomplicated *Plasmodium falciparum* infections **and** primaquine.

7. Treatment in pregnancy

FALCIPARUM MALARIA

Falciparum malaria is likely to be more severe in pregnancy than the blood film suggests, due to placental sequestration of parasites. Under-treatment of the infection may lead to placental insufficiency and, occasionally, still birth [10]. Always admit pregnant patients with malaria initially and work closely with the obstetric team.

Quinine is safe and effective in all stages of pregnancy.

With oral quinine, additional clindamycin should be used, not doxycycline.

WHO guidelines recommend IV artesunate is not used in the first trimester of pregnancy, but evidence that it is safe is accumulating.

In pregnant patients with severe falciparum malaria returning from South East Asia, IV artesunate should be used at all stages of pregnancy, due to increasing rates of resistance.

NON-FALCIPARUM MALARIA

Chloroquine is safe in pregnancy or while breastfeeding, as per above regimen.

Do not give primaquine in pregnancy or while breastfeeding. Relapse should instead be prevented by giving weekly chloroquine 300mg PO or proguanil 100mg daily until delivery.

After delivery and breast feeding, primaquine can be given as normal.

8. Quinine ‘allergy’

Genuine allergic (anaphylactic) reactions to quinine are extremely rare. In contrast, itching is a very common reaction to chloroquine, particularly in people of West African origin, and is often mis-reported by the patient as an “allergy”. Chloroquine itch is readily prevented or treated with antihistamines, and is not a contraindication to the use of chloroquine or quinine. If there is a clear history of a previous severe allergic reaction to quinine, and there is no alternative treatment available, the case must be discussed immediately with the Infectious Diseases consultant or the on-call ID physician at UCLH.

9. Continuing Care

The decision to discharge a patient should be based on a combination of clinical response and declining percentage parasitaemia. Patients completing treatment for falciparum malaria as an outpatient should return to hospital at least every 24 hours for a repeat malaria film until the parasite count is documented to be falling.

NB. Late haemolysis (10-28 days after treatment) has been observed occasionally in patients treated for severe malaria with artesunate and other artemisinins. Haemoglobin should be checked after 2 weeks.

Patients with uncomplicated falciparum malaria and patients with non-falciparum malaria do not require routine outpatient follow up. All patients should be advised to re-attend ED to request a malaria test if a fever recurs within 12 months following discharge.

All patients should be offered advice on future prevention, which should include the following:

- Avoidance of mosquito bites through insect repellents and wearing of long sleeves and trousers at dawn and dusk
- Use of an insecticide-treated mosquito net
- Use of appropriate chemoprophylaxis

➢ Contacts (inside and outside the Trust including out-of-hours contacts)

- Microbiology SpR – bleep 3069 or x5085 in working hours; on mobile via switch out of hours
- ID consultants – Drs Ben Killingley & Richard Jennings via switchboard
- Dr Michael Kelsey, Consultant Microbiologist – x 5082
- Dr Julie Andrews, Consultant Microbiologist – x 3894
- Haematology laboratory scientist on call – x 5767 in working hours and Saturday until midday; bleep 2686 out of hours
- Haematology SpR – bleep 3060 or x5756 in working hours; on mobile via switch out of hours
- Obstetric SpR – bleep 2838, 24 hours a day
- UCLH – 020 3456 7890 and request to speak to on-call ID registrar

➢ References (evidence upon which the guideline is based)

1. Public Health England. Malaria imported into the United Kingdom: 2014. PHE, London 2015.
2. Lalloo DG, Shingadia D, Pasvol G, Chiodini PL, Whitty CJ, Beeching NJ, et al. UK malaria treatment guidelines. J Infect. 2007 Feb;54(2):111-21.
3. World Health Organization. Guidelines for the treatment of malaria, 3rd ed, WHO, Geneva 2015. http://www.who.int/malaria/publications/atoz/9789241549127/en/ (Accessed on September 18th 2015)

4. Dondorp A, Nosten F, Stepniewska K, Day N, White N; South East Asian Quinine Artesunate Malaria Trial (SEAQUAMAT) group. Artesunate versus quinine for treatment of severe falciparum malaria: a randomised trial. Lancet. 2005;366(9487):717-25

5. Dondorp AM, Fanello CI, Hendriksen IC, et al. Artesunate versus quinine in the treatment of severe falciparum malaria in African children. (AQUAMAT): an open-label, randomised trial. Lancet 2010; 376:1647-57

6. Price RN, von Seidlein L, Valecha N, Nosten F, Baird JK, White NJ. Global extent of chloroquine-resistant Plasmodium vivax: a systematic review and meta-analysis. Lancet Inf Dis. 2014;14:982-91

7. Tjitra E, Anstey N, Sugiarto P, Warikar N, Kenangalem E, Karyana M, et al. Multidrug-resistant Plasmodium vivax associated with severe and fatal malaria: a prospective study in Papua, Indonesia. PLOS Med 2008;5(6): e128 doi:10.1371/journal.pmed.0050128

8. Sinclair D, Zani B, Donegan S, Olliaro P, Garner P. Artemisinin-based combination therapy for treating uncomplicated malaria. Cochrane Database Systematic Review 2009, Issue 3. Art. No.: CD007483. DOI:10.1002/14651858.CD007483.pub2.

9. Gogtay N, Kannan S, Thatte UM, Olliaro PL, Sinclair D. Artemisinin-based combination therapy for treating uncomplicated Plasmodium vivax malaria. Cochrane Database Systematic Review 2013, Issue 10. Art. No.: CD008492. DOI:10.1002/14651858.CD008492.pub3.

10. McGready R, Lee SJ, Wiladphaingern J, Ashley EA, Rijken MJ, Boel M, et al. Adverse effects of falciparum and vivax malaria and the safety of antimalarial treatment in early pregnancy: a population-based study. Lancet Inf Dis. 2012;12:388-96

To be completed and attached to any procedural document when submitted to the appropriate committee for consideration and approval

		Yes/No	Comments
1.	**Does the procedural document affect one group less or more favourably than another on the basis of:**		
	• Race	No	
	• Ethnic origins (including gypsies and travellers)	No	
	• Nationality	No	
	• Gender	No	
	• Culture	No	
	• Religion or belief	No	
	• Sexual orientation including lesbian, gay and bisexual people	No	
	• Age	No	
	• Disability - learning disabilities, physical disability, sensory impairment and mental health problems	No	
2.	**Is there any evidence that some groups are affected differently?**	No	
3.	**If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?**	No	
4.	**Is the impact of the procedural document likely to be negative?**	No	
5.	**If so can the impact be avoided?**	N/A	
6.	**What alternatives are there to achieving the procedural document without the impact?**	N/A	
7.	**Can we reduce the impact by taking different action?**	N/A	

If you have identified a potential discriminatory impact of this procedural document, please refer it to the Director of Human Resources, together with any suggestions as to the action required to avoid/reduce this impact.

For advice in respect of answering the above questions, please contact the Director of Human Resources.

Checklist for the Review and Approval of Procedural Document

To be completed and attached to any procedural document when submitted to the relevant committee for consideration and approval.

	Title of document being reviewed:	Yes/No	Comments
1.	**Title**		
	Is the title clear and unambiguous?	Yes	
	Is it clear whether the document is a guideline, policy, protocol or standard?	Yes	
2.	**Rationale**		
	Are reasons for development of the document stated?	Yes	
3.	**Development Process**		
	Is it clear that the relevant people/groups have been involved in the development of the document?	Yes	
	Are people involved in the development?	Yes	
	Is there evidence of consultation with stakeholders and users?	Yes	
4.	**Content**		
	Is the objective of the document clear?	Yes	
	Is the target population clear and unambiguous?	Yes	
	Are the intended outcomes described?	Yes	
5.	**Evidence Base**		
	Are key references cited in full?	N/A	
	Are supporting documents referenced?	N/A	
6.	**Approval**		
	Does the document identify which committee/ group will approve it?	Yes	
7.	**Dissemination and Implementation**		
	Is there an outline/plan to identify how this will be done?	Yes	
8.	**Document Control**		
	Does the document identify where it will be held?	Yes	
9.	**Process to Monitor Compliance and Effectiveness**		
	Are there measurable standards or KPIs to support the monitoring of compliance with and	Yes	

	Title of document being reviewed:	Yes/No	Comments
	effectiveness of the document?		
	Is there a plan to review or audit compliance with the document?	Yes	
10.	**Review Date**		
	Is the review date identified?	Yes	
	Is the frequency of review identified? If so is it acceptable?	Yes	
11.	**Overall Responsibility for the Document**		
	Is it clear who will be responsible for co-ordinating the dissemination, implementation and review of the document?	Yes	

Executive Sponsor Approval			
If you approve the document, please sign and date it and forward to the author. Procedural documents will not be forwarded for ratification without Executive Sponsor Approval			
Name		Date	
Signature			
Relevant Committee Approval			
The Director of Nursing and Patient Experience's signature below confirms that this procedural document was ratified by the appropriate Governance Committee.			
Name		Date	
Signature			
Responsible Committee Approval – only applies to reviewed procedural documents with minor changes			
The Committee Chair's signature below confirms that this procedural document was ratified by the responsible Committee			
Name		Date	
Name of Committee		Name & role of Committee Chair	
Signature			

Tool to Develop Monitoring Arrangements for Policies and guidelines

What key element(s) need(s) monitoring as per local approved policy or guidance?	Who will lead on this aspect of monitoring? Name the lead and what is the role of the multidisciplinary team or others if any.	What tool will be used to monitor/check/observe/Assess/inspect/ authenticate that everything is working according to this key element from the approved policy?	How often is the need to monitor each element? How often is the need complete a report? How often is the need to share the report?	What committee will the completed report go to?
Element to be monitored	**Lead**	**Tool**	**Frequency**	**Reporting arrangements**
Appropriate assessment of severity based on guideline	Dr M C Kelsey	Audit	Annual	Pathology Audit Meeting
Appropriate management according to severity	Dr M C Kelsey	Audit	Annual	Pathology Audit Meeting

Appendix 1: Artemisinin derivatives used in this guideline

Artemisinin derivatives, including artesunate and artemether, undergo conversion to dihydroartemesinin, the active metabolite, after injection or ingestion. Dihydroartemesinin has a broad spectrum of activity against the blood stage asexual *Plasmodium* parasites.

Artesunate is a water soluble intravenous drug used for the treatment of severe malaria (any species) and uncomplicated falciparum malaria if unable to tolerate oral medication.

Riamet® (artemether-lumefantrine) is an oral agent used for follow-on treatment of severe malaria (any species), uncomplicated falciparum malaria and for *P. vivax* from regions with known chloroquine resistance.

	IV artesunate	**PO artemether- lumefantrine (Riamet®)**
Dose	• Adults: 2.4 mg/kg IV bolus at 0, 12 and 24 hours, then every 24 hours thereafter	1 tablet = 20mg artemether / 120mg lumefantrine • Adults: 4 tablets PO at 0, 8, 24, 36, 48 and 60 hours Riamet® should be taken with fatty foods or milk.
Adjustment in renal impairment	None	None NB: In severe renal impairment monitor ECG and plasma potassium concentration.
Adjustment in liver impairment	None	None
Pregnancy and breast-feeding	• Use for all stages of pregnancy if returning from SE Asia • NOT recommended for first trimester if returning from other countries (use IV quinine) • Minimal data on use in breastfeeding but benefit thought to outweigh theoretical concerns	• In pregnancy, animal studies have also shown adverse effects on the early development of the fetus, but the artemisinin derivatives have not been fully evaluated during early pregnancy in humans • Avoid breast-feeding for at least 1 week after last dose (due to long half-life of lumefantrine; present in milk in animal studies)
Side effects	• Common: o Nausea o Vomiting o Anorexia o Dizziness • Rare: o Neutropenia o Anaemia o Delayed haemolysis o Elevated liver enzymes o Hypersensitivity	• Common: o Vomiting o Diarrhoea o Abdominal pain o Anorexia o Cough o Headache • Uncommon: o Sleep disturbances o Dizziness o Prolonged QT interval

	reactions (1:3000) o ECG abnormalities	o Elevated liver enzymes • Rare: o Myalgia o Arthralgia o Hypersensitivity reactions (1:3000)
Interactions	• Avoid drugs that prolong QT interval if possible • Increased plasma concentration with nevirapine	• Drugs metabolised by CYP2D6 and CYP3A4 (e.g. rifampicin) • Drugs known to prolong the QTc intervals • Anti-retroviral drugs • Other antimalarials • Grapefruit juice
Contraindications	Known hypersensitivity to artesunate or artemisinin derivatives	• Known hypersensitivity to artemether or lumefantrine • Family history of congenital QT interval prolongation • Family history of sudden death • History of arrhythmias • History of clinically relevant bradycardia • History of congestive heart failure accompanied by reduced left ventricular ejection fraction • Acute porphyrias