

ANNEX 3

**SUMMARY OF THE CHARACTERISTICS OF COMMON ANTIMALARIAL DRUGS
THAT SHOULD BE CONSIDERED IN DRUG SELECTION**

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Option	Effective against		Cross-resistance	Dosage and regimen	Cost (US\$) per adult treatment course	Adverse effects
	P. vivax	P. falcip. resist. to				
Chloroquine	Yes		Hydroxy-chloroquine, Possibly amodiaquine, pyrimethamine, quinine	25 mg/kg chloroquine base 100 mg base is equivalent to 123 mg chloroquine hydrochloride and 136 mg sulfate) over 3 days	Tablets: 0.072 (0.062-0.08) Syrup: 0.85 (0.21-2.37) Injection: 0.54 (0.49-0.63)	Visual disturbances, GI disturbances, vomiting, anorexia, cutaneous reactions transient head-aches, neuropsychiatric effects, fatigue, seizures, rinitis (in dark-skinned people), acute porphyria Rare: haematological effects, neurological disorders, some cardiovascular effects, otic effects, myotoxicity, severe cutaneous reactions Long-term use may result in irreversible visual impairment with keratopathy and retinopathy Overdosage: cardiac arrest
Amodiaquine	Yes	CQ (partially)	Chloroquine	30 mg/kg amodiaquine base over 3 days	0.15	Nausea, vomiting, abdominal pain, bradycardia, diarrhoea, pruritis, toxic hepatitis, agranulocytosis
Sulfadoxine-pyrimethamine	No	CQ	Antifolates	Adults: 1500 mg sulfadoxine + 75 mg pyrimethamine (single dose)	0.082 (0.065-0.098)	Anorexia, GI disorders, ataxia, tremor Rare: headache, light-headedness, malaise, fatigue, irritability, insomnia, serious cutaneous reactions Very rare: Stevens-Johnson syndrome, toxic epidermal necrolysis after prophylactic administration, hepatotoxicity, vasculitis, agranulocytosis, erythroderma, thrombocytopenia, megaloblastic anaemia, leukopenia, methaemoglobinemia
Sulfalene-pyrimethamine	No	CQ	Antifolates	Adults: 1500 mg sulfalene + 75 mg pyrimethamine (single dose) Children: sulfalene 25 mg/kg + pyrimethamine 1.25 mg/kg	0.28	As for sulfadoxine-pyrimethamine
Quinine	Active against sexual & asexual erythrocytic forms	CQ and SP (sometimes cross-resistance with CQ)	Mefloquine (rare: with 4-amino quinolines); quinine is generally effective against CQ and SP resist.	24 mg/kg daily in three divided doses for 3, 7 or 10 days, depending on area and whether used alone or in combination: usually given for 7 days when given alone	Tablets: 1.35 (1.22-1.63) Injection: 2.57 (2.21-3.0) (7 days)	CNS, GI and cardiovascular disorders related to dose, thrombocytopenia, leukopenia, agranulocytosis, pancytopenia, coagulopathy, hepatic toxicity, haemolytic-uraemic syndrome, renal failure, ventricular tachycardia, anginal symptoms, severe hypotension, hypoglycaemia, cinchonism, metallic taste, dizziness, tinnitus
Quinimax (a combination of quinine, quinidine, cinchonine and cinchonidine)	As for quinine	CQ and SP	Mefloquine	As for quinine	Price not available	As for quinine
Quinidine	As for quinine	CQ and SP (sometimes cross-resistance with CQ)	Mefloquine	As for quinine	8.82	Cinchonism (tinnitus, muffled hearing, vertigo, dizziness, headache, blurred vision, GI effects) pruritis, erythematous rashes, subcutaneous or submucous haemorrhage, cardiosuppressant effect (more important than with quinine), CNS effects (dose related) severe hypotension, hypoglycaemia
Mefloquine (15 mg/kg)	Yes	4-amino-quinolones and SP combinations	Halofantrine, reduced sensitivity to quinine	Adults and children: 15 mg/kg (single dose)	2.14 (1.55-3.18)	GI effects, disturbed balance, blurred vision abnormal coordination, anxiety, dermatological events, affective disorders, CNS effects (overt psychosis, toxic encephalopathy, convulsions, hallucinations, cardiovascular effects) Rare: headache, bradycardia, rash, pruritis weakness, vertigo, sleep disturbances, nightmares cardiopulmonary arrest, transient AV block, pericarditis, cardiovascular collapse, myocardial infarction, agranulocytosis

Drug interactions	Half-life	Contraindications	Reported resistance	Formulations	Comments
Antacids or kaolin (should be given at least 4 h apart), cimetidine, rabies vaccine, metronidazole, ampicillin. Increased risk of convulsions in combination with mefloquine. May be antagonistic when used with quinine	10 days (depending on sensitivity of assay method) up to 2 months	History of epilepsy, persons with retinal or visual field changes, patients with porphyria (unless benefits outweigh potential hazard), psoriasis	Yes: <i>P. falciparum</i> resistant in many areas of South-East Asia, Africa, South America and Oceania <i>P. vivax</i> is resistant in Indonesia and Papua New Guinea	Tablets, 50 mg, 100 mg, 150 mg 300 mg base (as phosphate or sulfate) Syrup, 50 mg base (as phosphate or sulfate) in 5 ml Injection, 50 mg, 100 mg base (as phosphate or sulfate) per ml in 2-ml ampoule	Oral chloroquine phosphate is drug of choice for the treatment of uncomplicated malaria caused by <i>P. malaria</i> , <i>P. ovale</i> , susceptible strains of <i>P. falciparum</i> , but chloroquine-resistant strains of <i>P. falciparum</i> have been reported in all areas where malaria occurs except Haiti and Central America
No adverse drug interactions have been observed	10 h	Chemoprophylaxis, persons with hepatic disorders	Yes in many areas in Asia, East Africa, Papua New Guinea and the Amazon Basin	Tablets, 153.1 mg, 200 mg, (amodiaquine base as hydrochloride) Suspension (10 mg/ml amodiaquine base as HCl)	Some reports of hepatotoxicity and agranulocytosis; however, there is no conclusive evidence on toxicity when used in therapeutic doses. Concern about its cross-resistance with CQ
Drugs that interfere with folic acid metabolism, p-amino benzoic acid, other sulfonamides, cotrimoxazole, lorazepam, zidovudine, folic acid	180 h (sulfadoxine) 95 h (pyrimethamine)	Chemoprophylaxis, severe hepatic or renal dysfunction (except where benefits exceed the risk), megaloblastic anaemia caused by folate deficiency Infants < 2 months	Resistance reported in South-East Asia, Amazon Basin, East and South Africa, Bangladesh, Central & South America, Oceania and India	Tablets, 500 mg sulfadoxine, 25 mg pyrimethamine Injection 500 mg sulfadoxine, 25 mg pyrimethamine in 2.5-ml ampoule	Single-dose therapy, therefore adherence is high but risk of resistance developing rapidly owing to long half-life. Used in CQ-resistant areas
Drugs that interfere with folic acid metabolism, p-amino benzoic acid, other sulfonamides, cotrimoxazole, lorazepam, folic acid	65 h (sulfalene) 95 h (pyrimethamine)	Chemoprophylaxis, severe hepatic or renal dysfunction (except where benefits exceed the risk), megaloblastic anaemia caused by folate deficiency Infants < 2 months	Resistance reported in South-East Asia, Amazon Basin, sub-Saharan Africa, Bangladesh, Oceania	Tablets, 500 mg sulfalene, 25 mg pyrimethamine	Single-dose therapy, therefore high adherence but high risk of resistance developing rapidly owing to long half-life. Used in CQ-resistant areas
Mefloquine, cardiac glycosides, astemizole, flecainide, terfenadine, antacids containing aluminium, cimetidine used with chloroquine may be antagonistic, neuromuscular blocking agents, anticoagulants, drugs that increase urinary pH	10-12 h	Studies found no evidence of oxytocic effects when used for falciparum malaria in 1st trimester of pregnancy	Countries in southern Asia east of Bangladesh, several African countries on the Gulf of Guinea, some reports in E. Africa	Tablets 200 mg, 300 mg base (as sulfate), Injection 150 mg, 300 mg base (as dihydrochloride) per ml in 2-ml ampoule	Used for uncomplicated malaria in multidrug-resistant areas where <i>P. falciparum</i> does not respond to CQ, SP combinations and mefloquine: travellers returning to non-endemic areas who develop malaria; patients with uncom. malaria repeatedly vomiting; 2nd-line treatment for 1st line treatment failures or in hypersensitivity to sulfonamides (used in combination)
As for quinine	As for quinine	As for quinine	As for quinine	Tablets 125 mg, 500 mg (100 mg: 59.3 mg quinine, 1.6 mg quinidine, 0.4 mg cinchonine, 0.4 mg cinchonidine base) Injection, 100 mg, 200 mg,	Limited studies show no significant difference between therapeutic efficacy of quinimax and quinine
Neuromuscular blocking agents, cholinergic and anticholinergic agents, alkalizing agents, thiazide diuretics, some antacids, cimetidine, coumarin anticoagulants, anticonvulsants, phenothiazines, reserpine, cardiovascular drugs, other antiarrhythmic agents	10-12 h	Patients with AV junctional or idioventricular pacemaker, left bundle branch marked widening of the QRS complex, patients with ectopic impulses and rhythms due to escape mechanisms, cardiac glycoside-induced AV conduction disorders. Not recommended for use in pregnancy. Use with extreme caution in nursing women	Rarely reported in falciparum malaria	400 mg per ml Tablets 200 mg base (as sulfate)	Not recommended for routine treatment of uncomplicated malaria. Useful for treatment of parenteral treatment of severe and complicated malaria and may be used instead of quinine in patients with uncomplicated malaria requiring an initial dose of parenteral therapy
Cardioactive agents, antidepressants, quinine, quinidine, primaquine, halofantrine, ampicillin, tetracycline, metoclopramide, valproic acid. Human diploid cell rabies vaccine (HDCV) should be administered by intramuscular not intradermal route	10-40 days (shorter in children and pregnant women)	Cardioactive drugs, activities requiring fine coordination, history of neurological or psychiatric disease, treatment with mefloquine in previous 4 weeks. Studies show that use for treatment or prevention in 2nd or 3rd trimester is not associated with adverse outcome	Yes, Thai-Cambodian and Thai-Myanmar borders (sporadic reports in South America (Brazil, Guyana and French Guyana), Asia, Africa and Middle East)	Tablets 250 g base (as hydrochloride)	Used for <i>P. falciparum</i> infection resistant to CQ or SP combinations, recommended for chemoprophylaxis for travellers to areas with risk of CQ-resistant falciparum malaria

Option	Effective against		Cross-resistance	Dosage and regimen	Cost (US\$) per adult treatment course	Adverse effects
	P. vivax	P. falcip. resist. to				
Mefloquine (25 mg/kg)	Yes	As for mefloquine (15 mg/kg)	As for mefloquine (15 mg/kg)	25 mg/kg in two divided doses given 12 h apart	3.22 (2.33-4.77)	As for mefloquine (15 mg/kg)
Halofantrine	Yes	CQ, SP quinine	Mefloquine	Adults and children > 1 year: 24 mg/kg base in three divided doses at 6-h intervals (manufacturer recommends a second course of therapy one week after first treatment)	Tablets: 4.75 Syrup: 0.28	Nausea, abdominal pain, diarrhoea, pruritis, skin rashes, prolongation of PR and QT interval, serious ventricular dysrhythmias, individual report of cardiac arrest and torsades de pointes, intravascular haemolysis, convulsive seizures, compromising renal function
Artemether	Yes	CQ, SP quinine		4 mg/kg loading dose on day 1, then 2 mg/kg once daily for 6 days	Tablets: 4.20 (China) Injection: 8.8 (China)	GI effects, itching, drug fever rare: abnormal bleeding and dark urine, minor cardiac changes cardiotoxicity, neurotoxicity in animals (in vitro studies have shown that dihydroartemisinin is neurotoxic)
Artemisinin	Yes	CQ, SP quinine		20 mg/kg in divided dose on day 1, then 10 mg/kg once daily for 6 days	Tablets: 2.10 (Viet Nam)	As for artemether
Artesunate	Yes	CQ, SP quinine		4 mg/kg loading dose on day 1, then 2 mg/kg once daily for 6 days	2.16 (1.98-2.33) Injection: 11.2	As for artemether
Dihydroartemisinin	Yes	CQ, SP quinine		Adults: 4 mg/kg on day 1 followed by 2 mg/kg daily for 6 days	Price not available	As for artemether
Artelinic acid	No data available					
Primaquine	Yes			Radical treatment of P. vivax and P. ovale: 0.25 mg/kg daily for 14 days (outside SE Asia & Oceania); 0.50 mg/kg daily for 14 days or 0.75 mg/kg weekly for 8 weeks (SE Asia & Oceania); gametocytocidal: 0.75 mg/kg single dose	Antirelapse: 0.06-0.24 0.04-3.15)	GI effects, cramps, weakness, haematological disorders, suppression of myeloid activity, methaemoglobinaemia, haemoglobinaemia, agranulocytosis, granulocytopenia, hypertension and cardiac arrhythmia intravascular haemolysis, haemoglobinaemia Rare: headache, interference with visual accommodation and pruritis
Doxycycline	No	Used in combination with quinine in areas of reduced quinine susceptibility		Treatment in adults: 100 mg/day with quinine (3/7 days); 200 mg/day with mefloquine or artesunate (5 days); not used alone for treatment	0.08-0.11 (0.06-0.21)	GI effects, anorexia, phototoxic reactions, transient depression of bone growth discoloration of teeth and enamel hypoplasia (permanent), hypersensitivity reactions (rare), pre-existing renal insufficiency may be aggravated, acute renal failure, hepatic and haematologic effects (rare), oesophageal ulceration (rare: stomatitis, glossitis, dysphagi sore throat, pancreatitis, anogenital inflammation, black hairy tongue, cardiac overgrowth)
Tetracycline	Yes	Used in combination with quinine in areas of reduced quinine susceptibility		Adults and children > 8 years: 250 mg 4 times daily in combination with quinine; not used alone for treatment	0.14-0.20 (0.12-0.25)	GI effects, depletion of normal bowel flora phototoxic reactions, porphyria-like skin changes, pigmentation of nails
Proguanil	Yes		Pyrimethamine	Not used alone for treatment		Mouth ulceration
Dapsone	No			Not used alone for treatment		Fever, convulsions, anaemia, GI effects, headache, mouth ulcers, anorexia, neuropathy allergic dermatitis, severe anaemia, leukopenia
Atovaquone-proguanil	No	CQ, SP, halofantrine, mefloquine, amodiaquine		Adults: 1 g atovaquone + 400 mg proguanil (4 tablets) as a single dose for 3 days Children 11-20 kg: 62.5/25 mg daily (1 paediatric tablet); 21-30 kg: 2 tablets; 31-40 kg: 3 tablets; >40 kg: 1 adult tablet daily	42	Headache, abdominal effects, anorexia, coughing

Drug interactions	Half-life	Contraindications	Reported resistance	Formulations	Comments
As for mefloquine (15 mg/kg)	10-40 days	As for mefloquine (15 mg/kg)	As above	Tablets, 250 g base (as hydrochloride)	As above
Quinine (increased risk of cardiac effects), mefloquine (increased risk of cardiac effects), sparfloxacin	1-6 days	Pre-existing cardiac disease, history of or use of drugs that prolong QT interval, age < 1 year, pregnancy treatment with mefloquine during preceding 3 weeks, breastfeeding, family history of prolongation of QT intervals.	No	Tablets, 250 mg (hydrochloride) Paediatric suspension, 100 mg/5 ml	Restricted to the treatment of acute multidrug-resistant falciparum infections; not recommended for standby treatment
No pharmacological interactions with other drugs have been identified	4-11 h (11-12 h for dihydro-artemisinin following artemether administration)	Not recommended during first trimester. Can be used during the 2nd or 3rd trimester	There have been no reports of clinical resistance to artemisinin drugs	Oily solution for injection 80 mg in 1-ml ampoule, 40 mg/ml (paed) Capsules, 40 mg Composite tablets, 50 mg	Uncomplicated multidrug-resistant falciparum malaria. WHO recommends that artemisinin compounds should be administered in combination with mefloquine for a minimum of 3 days. If used alone, treatment should be for a minimum of 7 days. Main advantage is speed of action. Caution with prolonged repetitive doses owing to neurotoxicity
As for artemether	4-11 h (11-12 h for dihydro-artemisinin following artemether administration)	As for artemether	There have been no reports of clinical resistance to artemisinin drugs	Tablets, 250 mg Suppository 100 mg, 200 mg 300 mg, 400 mg, 500 mg	As for artemether
As for artemether	4-11 h (11-12 h for dihydro-artemisinin following artemether administration)	As for artemether	There have been no reports of clinical resistance to artemisinin	Tablets, 50 mg, 200 mg Powder for injection 60 mg of anhydrous artesunate in 1 ml Suppository 100 mg Rectocap 200 mg	As for artemether
As for artemether	40 min	As for artemether	As for artemether	Tablets, 20 mg, 60 mg, 80 mg Suppositories, 80 mg	As for artemether
	No data available	No data available	No data available	-	-
Any other drugs that may induce haematological disorders, quinacrine, quinine (reduces plasma concentrations of primaquine)	5 h (3.7-9.6 h)	Children < 4 years (risk of haemolysis) active rheumatoid arthritis, lupus erythematosus, conditions that predispose to granulocytopenia, patients with G6PD deficiency. Contraindicated in pregnancy owing to risk of haemolysis in fetus	Resistance occasionally reported to primaquine only. Vivax malaria resistant to primaquine mainly due to sub-therapeutic doses.	Tablets, 5.0 mg, 7.5 mg, 15.0 mg base as diphosphate	Used in antirelapse treatment in P. viva and P. ovale infections. Used as a gametocytocidal drug with an effective blood schizonticidal drug
Oral anticoagulants, halogenated agents, drugs affecting GI pH, anti-infective agents, products containing kaolin, pectin or bismuth, barbiturates, phenytoin, carbamazepine, oral contraceptives (caution: drugs with divalent or trivalent cations, antacids with Ca, Mg, Al)	14-24 h	Known hypersensitivity, age < 8 years, pregnancy, persons with hepatic dysfunctions.	Only used in combination	Capsule or tablet, 100 mg as hyclate	Used only in combination with quinine mefloquine or artesunate for treatment. Also used for chemoprophylaxis
As for doxycycline	8 h	Pre-existing severe hepatic or renal damage, age < 8 years. Not recommended for use in pregnancy	Only used in combination	Capsule or tablet, 250 mg as hydrochloride	Never used alone. Used in combination with quinine in treatment of falciparum malaria when resistance to quinine has been reported and in patients in whom SP is contraindicated
Warfarin	16 h	Areas with known resistance	Only used in combination	Tablet, 100 mg as hydrochloride	Used in combination with chloroquine for chemoprophylaxis. Used in new combinations for treatment (see below)
No adverse drug interactions have been observed		Patients with liver failure Not recommended for use in pregnancy	Only used in combination	Tablets, 50 mg, 100 mg	Used in new combinations under development (see below)
Tetracycline, metoclopramide, rifampicin, rifabutin (associated with decreased plasma concentration of atovaquone)	2-3 days (atovaquone) 12-21 h (proguanil)	Chemoprophylaxis in patients with severe renal impairment. Safety not yet established in pregnancy. Used with caution in nursing women.	No	Tablets (250 mg atovaquone/ 100 mg proguanil hydrochloride) Paediatric tablets (68.5 mg atovaquone/ 25 mg proguanil hydrochloride)	Used for treatment of acute falciparum malaria in areas resistant to CQ, SP, mefloquine, halofantrine, amodaquine (also used for prevention in some countries). Co-formulated tablet

Option	Effective against		Cross-resistance	Dosage and regimen	Cost (US\$) per adult treatment course	Adverse effects
	P. vivax	P. falcip. resist. to				
Pyronaridine	No			In new combination under development (see below)		Headache, dizziness, GI disorders transient ECG changes Rare: palpitations, skin rash, epigastric distress
Quinine + doxycycline	Yes	Q alone	As for quinine and doxycycline	Quinine-sensitive areas: quinine 8 mg/kg daily (3 days), doxycycline 100 mg daily (7 days) High level of resistance: quinine and doxycycline as above for 7 days (usually 7-day treatment is given)	Q sensitive areas, Q-3 + D-3 0.63 (0.55-0.84) Q-resistant areas, Q-7 + D-7 1.47 (1.3-1.66)	As for quinine and doxycycline
Quinine + tetracycline	Yes	Q alone	As for quinine and tetracycline	Quinine-sensitive areas: quinine 8 mg/kg daily (3 days), tetracycline 250 mg four times/day (5 days) High level of resistance: quinine and tetracycline as above for 7 days	Q-sensitive areas, Q-3 + T-5 0.79 (0.66-1.16) Q-resistant areas, Q-7 + T-7 1.65 (1.42-2.27)	As for quinine and tetracycline
Quinine + sulfadoxine-pyrimethamine	Yes	Q alone	As for quinine and SP	Quinine 8 mg/kg daily (3 days) 1500 mg sulfadoxine or sulfalene, 75 mg pyrimethamine on first day only	0.66 (0.59-0.8)	As for quinine and SP
Artesunate + mefloquine	Yes	CQ, SP, mefloquine	As for mefloquine	Single dose of 4 mg/kg for 3 days (ASU) and 15-25 mg/kg (MQ)	5.38 (4.06-7.04)	As for artesunate and mefloquine
Artemisinin + mefloquine	Almost no data		As for mefloquine	20 mg/kg in divided dose, then 10 mg/kg for 2 more days (ART) and 15-25 mg/kg (MQ)		
Artesunate + sulfadoxine-pyrimethamine	Yes	CQ	As for SP above	Single dose of 4 mg/kg (ASU) for 3 days and single dose of SP	2.24 (2.05-2.43)	As for artesunate and SP
Chloroquine + sulfadoxine-pyrimethamine	Yes	CQ		CQ 25 mg/kg over 3 days, SP 25 mg/kg (S) single dose	0.154 (0.127-0.18)	As for CQ and SP
Chloroquine + sulfalene-pyrimethamine	Yes	CQ		CQ 25 mg/kg over 3 days SP: 25 mg/kg (S) single dose	0.35 (0.34-0.36)	As for CQ and SP
Artemether-lumefantrine	No	CQ, SP	As for artemether	Adults: four tablets initially then again after 8 h, then twice daily for 2 days Children: 10-14 kg, one tablet as above; 15-25 kg, two tablets as above; 25-30 kg, three tablets as above	2.5	Headache, dizziness, sleep disorders, palpitation GI disorders, skin disorders, cough, asthenia, fatigue, arthralgia, myalgia

Combinations under development

Option	Effective against		Cross-resistance	Dosage and regimen	Cost (US\$) per adult treatment course	Adverse effects
	P. vivax	P. falcip. resist. to				
Dapsone-chlorproguanil	No	CQ, SP	Possibly other antifolates	Chlorproguanil 2 mg/kg, Dapsone 2.5 mg/kg	Not known (possibly < 0.50)	Fever, convulsions, anaemia, GI effects headache, mouth ulcers, anorexia, neuropathy allergic dermatitis, dapsone syndrome (rash with fever), severe anaemia, leukopenia
Dapsone-chlorproguanil + artesunate	Yes	CQ, SP		Single daily dose for 3 days	Not known	As for dapsone-proguanil and artesunate
Pyronaridine + artesunate	Yes	CQ, SP		Single daily dose for 3 days	Not known	As for pyronaridine and artesunate

Drug interactions	Half-life	Contraindications	Reported resistance	Formulations	Comments
No adverse drug interactions have been observed	60-90 h	Not recommended for use in pregnancy or lactating women (until further studies establish safety), children < 11 kg	No	Tablets	In combination under development. Only available as single drug in China
Mefloquine, halofantrine, cardioactive agents	16 h (quinine) 15-25 h (doxycycline)	Children < 8 years Not recommended for use in pregnancy	No	As for quinine and doxycycline	Used in areas where resistance to quinine has been reported. Non-fixed dose combination.
Mefloquine, halofantrine, cardioactive agents	16 h (quinine) 8-10 h (tetracycline)	Children < 8 years. Not recommended for use in pregnancy	No	As for quinine and tetracycline	Used in areas where resistance to quinine has been reported. Non-fixed dose combination.
As for quinine and SP	See quinine and SP	As for quinine and SP	No	As for quinine and SP	For use in areas where parasites are SP and quinine resistant and adherence may be a problem. Non-fixed dose combination
As for artesunate and mefloquine	See artesunate and mefloquine	As for artesunate and mefloquine. Not recommended for use in 1st trimester of pregnancy	No	As for artesunate and mefloquine	Used in mefloquine-resistant areas. Non-fixed dose combination
As for artemisinin and mefloquine	See artemisinin	Not recommended for use in 1st trimester of pregnancy	No	As for artemisinin and mefloquine	Used in mefloquine resistant areas. Non-fixed dose combination
As for artesunate and SP	See artesunate and SP	As for artesunate and SP	No	As for artesunate and SP	Used in multidrug-resistant areas Non-fixed dose combination
As for CQ and SP	See CQ and SP	As for CQ and SP	No	As for CQ and SP	Used for mixed chloroquine-resistant and chloroquine-sensitive <i>P. falciparum</i>
As for CQ and SP above	See CQ and SP	As for CQ and SP		As for CQ and SMP	Non-fixed dose combination
No specific drug interactions have been studied	2 h (artemether) lumefantrine: 2-3 days 4-6 days (patients with malaria)	Safe use in pregnancy not yet established		Tablets, 20 mg artemether 120 mg lumefantrine	Not evaluated for treatment of severe malaria. Better absorbed in the presence of food. Fixed-dose combination

Combinations under development

Drug interactions	Half-life	Contraindications	Reported resistance	Formulations	Comments
No specific adverse drug interactions have been studied	17-33 h (dap) 20 h (chloroguanil)	Patients with liver failure, history of G6PD deficiency or intravascular haemolysis. Adequate data on pregnancy not available	Not in use yet	None yet	New fixed-dose combination for use in Africa, Middle-East and Indian sub continent. Selects parasites less readily than SP. Presence of quadruple dhfr may render it ineffective. Expected to be available in 2001
No specific adverse drug interactions have been studied	17-33 h (dap) 20 h chloroguanil 4-11 h (artesunate)	Adequate data on pregnancy not Available	Not in use yet	None yet	Triple combination expected to be available in 2003
No specific adverse drug interactions have been studied	60-90 h (pyronaridine) 4-11 h (artesunate)	Not recommended for use in pregnant or lactating women until further studies establish safety	Not in use yet	None yet	New fixed-dose combination with adherence advantages, limited use thus less likelihood of early resistance. Expected to be available in 2003