Guidelines for Treatment of Malaria in the United States

(Based on drugs currently available for use in the United States — October 1, 2019)

CDC Malaria Hotline: (770) 488-7788 or (855) 856-4713 (toll free) Monday–Friday, 9 am to 5 pm EST; (770) 488-7100 after hours, weekends, and holidays

Clinical Diagnosis/ *Plasmodium* Species	Drug Susceptibility (Based on Region Infection Was Acquired)	Recommended Regimen and Adult Dose[1]	Recommended Regimen and Pediatric Dose[1] *Pediatric dose should NEVER exceed adult dose*
Uncomplicated malaria/ *P. falciparum,* or **s**pecies not identified If "species not identified" is later diagnosed as *P. vivax* or *P. ovale*, please see *P. vivax* and *P. ovale* (below) re: treatment with primaquine or tafenoquine	**Chloroquine resistance or unknown resistance[2]** All malarious regions except those specified as chloroquine sensitive listed in the box below	**A. Artemether-lumefantrine (Coartem™)[3,4]** **Tablet=20mg artemether/ 120 mg lumefantrine** A 3-day treatment schedule with a total of 6 oral doses is recommended for both adult and pediatric patients based on weight. The patient should receive the initial dose, followed by the second dose 8 hours later, then 1 dose bid for the following 2 days. Dosing as follows: 5–<15 kg: 1 tablet per dose 15–<25 kg: 2 tablets per dose 25–<35 kg: 3 tablets per dose ≥35 kg: 4 tablets per dose	
		B. Atovaquone-proguanil (Malarone™)[4,5] **Adult tablet= 250 mg atovaquone/ 100 mg proguanil** 4 adult tabs po qd x 3 days	**B. Atovaquone-proguanil (Malarone™)[4,5]** **Adult tab=250 mg atovaquone/ 100 mg proguanil** **Peds tab=62.5 mg atovaquone/ 25 mg proguanil** 5–<8 kg: 2 peds tabs po qd x 3 days 8–<10 kg: 3 peds tabs po qd x 3 days 10–<20 kg: 1 adult tab po qd x 3 days 20–<30 kg: 2 adult tabs po qd x 3 days 30–<40 kg: 3 adult tabs po qd x 3 days ≥40 kg: 4 adult tabs po qd x 3 days
		C. Quinine sulfate[6] plus one of the following: doxycycline[7], tetracycline[7], or clindamycin **Quinine sulfate:** 542 mg base (=650 mg salt) po tid x 3 or 7 days[8] **Doxycycline:** 100 mg po bid x 7 days **Tetracycline:** 250 mg po qid x 7 days **Clindamycin:** 20 mg/kg/day po divided tid x 7 days	**C. Quinine sulfate[6] plus one of the following: doxycycline[7], tetracycline[7], or clindamycin** **Quinine sulfate:** 8.3 mg base/kg (=10 mg salt/kg) po tid x 3 or 7 days[8] **Doxycycline:** 2.2 mg/kg/dose po q12 h x 7 days **Tetracycline:** 25 mg/kg/day po divided qid x 7 days **Clindamycin:** 20 mg /kg/day po divided tid x 7 days

[1] If a person develops malaria while taking chemoprophylaxis, that particular drug should not be used as a part of their treatment regimen. Use one of the other options instead.

[2] Options A is the preferred option, but options B and C are adequate alternatives and should not be withheld if more readily available than Option A. Because of a higher risk of severe neuropsychiatric reactions, we do not recommend option D (mefloquine) unless the other options cannot be used. For option C, because there is more data on the efficacy of quinine in combination with doxycycline or tetracycline, these treatment combinations are preferred to combination with clindamycin.

[3] Can be used in second and third trimesters of pregnancy. Can be used in first trimester of pregnancy if no other drug options are available. Not recommended in infants <5 kg.

[4] Take with food or whole milk. If patient vomits within 30 minutes of taking a dose, then repeat the dose.

[5] Not recommended in pregnancy or in infants weighing <5 kg. However, may be used if other treatment options are not available or are not being tolerated, and if the potential benefit is judged to outweigh potential risks.

[6] Quinine manufactured in the US contains 324 mg (salt) per capsule; therefore, 2 capsules should be sufficient for adult dosing. Pediatric dosing may be difficult due to unavailability of non-capsule forms of quinine.

[7] Not recommended during pregnancy or in children <8 years old. However, doxycycline or tetracycline may be used in combination with quinine (as recommended for non-pregnant adults) if other treatment options are not available or are not tolerated, and the benefit outweighs the risks.

[8] Quinine should be given for 3 days, except for infections acquired in Southeast Asia where 7 days of treatment is required.

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		D. Mefloquine[9] 684 mg base (=750 mg salt) po as initial dose, followed by 456 mg base (=500 mg salt) po given 6-12 hours after initial dose. Total dose: 1,250 mg salt	**D. Mefloquine[9]** 13.7 mg base/kg (=15 mg salt/kg) po as initial dose, followed by 9.1 mg base/kg (=10 mg salt/kg) po given 6–12 hours after initial dose Total dose: 25 mg salt/kg
Uncomplicated malaria/ ***P. falciparum*** or species not identified	**Chloroquine sensitivity[10]** Central America west of Panama Canal, Haiti, and the Dominican Republic	**Chloroquine phosphate (Aralen™ and generics)** 600 mg base (=1,000 mg salt) po immediately, followed by 300 mg base (=500 mg salt) po at 6, 24, and 48 hours Total dose: 1,500 mg base (=2,500 mg salt); **OR** **Hydroxychloroquine (Plaquenil™ and generics)** 620 mg base (=800 mg salt) po immediately, followed by 310 mg base (=400 mg salt) po at 6, 24, and 48 hours Total dose: 1,550 mg base (=2,000 mg salt)	**Chloroquine phosphate (Aralen™ and generics)** 10 mg base/kg po immediately, followed by 5mg base/kg po at 6, 24, and 48 hours Total dose: 25 mg base/kg; **OR** **Hydroxychloroquine (Plaquenil™ and generics)** 10 mg base/kg po immediately, followed by 5 mg base/kg po at 6, 24, and 48 hours Total dose: 25 mg base/kg
Uncomplicated malaria/ ***P. malariae or P. knowlesi***	**All regions[10]**	**Chloroquine phosphate:** Treatment as above; **OR** **Hydroxychloroquine:** Treatment as above	**Chloroquine phosphate:** Treatment as above; **OR** **Hydroxychloroquine:** Treatment as above
Uncomplicated malaria/ ***P. vivax*** *or* ***P. ovale***	**All regions[10]** In case of suspected chloroquine-resistant *P. vivax,* see row below	**Chloroquine phosphate plus either primaquine phosphate or tafenoquine (Krintafel™)[11,12]** **Chloroquine phosphate:** Treatment as above **Primaquine phosphate:** 30 mg base po qd x 14 days[13] **Tafenoquine:** 300 mg po x 1 dose; **OR** **Hydroxychloroquine plus either primaquine phosphate or tafenoquine (Krintafel™)[11,12]** **Hydroxychloroquine:** Treatment as above **Primaquine phosphate:** 30 mg base po qd x 14 days[13] **Tafenoquine:** 300 mg po x 1 dose	**Chloroquine phosphate plus primaquine phosphate[11,12]** **Chloroquine phosphate:** Treatment as above **Primaquine phosphate:** 0.5 mg base/kg po qd x 14 days; **OR** **Hydroxychloroquine plus primaquine phosphate[11,12]** **Hydroxychloroquine:** Treatment as above **Primaquine phosphate:** 0.5 mg base/kg po qd x 14 days **Tafenoquine (Krintafel™)[11,12]** can be used instead of primaquine in children ≥16 years: 300 mg po x 1 dose
Uncomplicated malaria/ ***P. vivax***		**A. Artemether-lumefantrine (Coartem™)[3, 4] plus either primaquine phosphate or tafenoquine (Krintafel™)[11,12]** **Artemether-lumefantrine (Coartem™):** Treatment as above **Primaquine phosphate or tafenoquine:** Treatment as above **Tafenoquine (Krintafel™)[11,12]** can be used instead of primaquine in children ≥16 years: 300 mg po x 1 dose	

[9] Mefloquine is not recommended in persons who have acquired infections from Southeast Asia due to drug resistance.

[10] Regimens used to treat chloroquine-resistant infections may also be used if chloroquine and hydroxychloroquine are not available. Note that if treating *P. vivax* or *P. ovale* infections, primaquine or tafenoquine (after quantitative testing to rule out G6PD deficiency) should also be given.

[11] Primaquine and tafenoquine eradicate hypnozoites in the liver, thus preventing relapses of *P. vivax* and *P. ovale* infections. Because primaquine and tafenoquine can cause hemolytic anemia in G6PD-deficient persons, quantitative G6PD testing must occur prior to starting treatment with these drugs. For persons with intermediate G6PD deficiency, primaquine may be given 45 mg orally once a week for 8 weeks with close monitoring for hemolysis after consultation with an expert in infectious disease and/or tropical medicine.

[12] Primaquine and tafenoquine must not be used during pregnancy; pregnant patients with *P. vivax* and *P. ovale* infections should receive chloroquine prophylaxis (300 mg [base] po once a week) during pregnancy. After delivery, patients with normal G6PD activity should be treated with primaquine or tafenoquine or continue with chloroquine prophylaxis for a total of 1 year. Primaquine can be used during breastfeeding if the infant is found to have normal G6PD activity. Tafenoquine is not recommended during breastfeeding.

[13] Total dose of primaquine in patients ≥70 kg should be adjusted to a total dose of 6 mg/kg, given in daily doses of 30 mg/day times the number of days to complete the total dose.

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	Chloroquine resistance[14] Papua New Guinea and Indonesia	**B. Atovaquone-proguanil plus either primaquine phosphate or tafenoquine (Krintafel™)**[11,12] **Atovaquone-proguanil:** Treatment as above **Primaquine phosphate or tafenoquine:** Treatment as above	**B. Atovaquone-proguanil plus primaquine phosphate**[11,12] **Atovaquone-proguanil:** Treatment as above **Primaquine phosphate:** Treatment as above **Tafenoquine (Krintafel™)**[11,12] can be used instead of primaquine in children ≥16 years: 300 mg po x 1 dose
		C. Quinine sulfate plus either doxycycline[7] **or tetracycline**[7] **plus either primaquine phosphate or tafenoquine (Krintafel™)**[11,12] **Quinine sulfate:** Treatment as above for 3 days **Doxycycline or tetracycline: Treatment as above** **Clindamycin:** Treatment as above **Primaquine phosphate or tafenoquine:** Treatment as above	**B. Quinine sulfate plus either doxycycline**[7] **or tetracycline**[7]**, plus primaquine phosphate**[11,12] **Quinine sulfate:** Treatment as above for 3 days **Doxycycline or tetracycline:** Treatment as above **Clindamycin:** Treatment as above **Primaquine phosphate:** Treatment as above **Tafenoquine (Krintafel™)**[11,12] can be used instead of primaquine in children ≥16 years: 300 mg po x 1 dose
		D. Mefloquine plus either primaquine phosphate or tafenoquine (Krintafel™)[11,12] **Mefloquine:** Treatment as above **Primaquine phosphate or tafenoquine:** Treatment as above	**C. Mefloquine plus primaquine phosphate**[11,12] **Mefloquine:** Treatment as above **Primaquine phosphate:** Treatment as above **Tafenoquine (Krintafel™)**[11,12] can be used instead of primaquine in children ≥16 years: 300 mg po x 1 dose
Uncomplicated malaria treatment for pregnant women If *P. vivax* or *P. ovale* infections, please see footnote 12	**Chloroquine sensitivity** See sections above for regions with chloroquine-sensitive malaria species	**Chloroquine phosphate:** Treatment as above; **OR** **Hydroxychloroquine:** Treatment as above	Not applicable
	Chloroquine resistance See sections above for regions with chloroquine-resistant malaria species	**Artemether-lumefantrine (Coartem™):** Treatment as above (second or third trimesters); **OR** **Quinine sulfate plus clindamycin:** Treatment as above (all trimesters); **OR** **Mefloquine:** Treatment as above (all trimesters)	Not applicable
Severe malaria[15,16,17] If *P. vivax* or *P. ovale* infections, please see footnote 12	**All regions**	**Intravenous (IV) artesunate available under an expanded access investigational new drug (IND) protocol *(Call CDC hotline).*** Give 2.4 mg/kg per dose: doses at 0, 12, and 24 hours for a total of three doses; **AND**	**Intravenous (IV) artesunate available under an expanded access investigational new drug (IND) protocol *(Call CDC).*** For children ≥20 kg: Give 2.4 mg/kg per dose: doses at 0, 12, and 24 hours for a total of three doses;

[14] Options A, B, and C are equally recommended. Option D, due to increased risk of severe neuropsychiatric side effects, should be used only when other options are not available. Chloroquine-resistant *P. vivax* have been well documented in Papua New Guinea and Indonesia. Rare case reports of chloroquine-resistant *P. vivax* have also been documented in Burma (Myanmar), India, and Central and South America. *P. vivax* infections outside of Papua New Guinea or Indonesia should be treated with chloroquine, if patient does not respond, treatment should be changed to cover chloroquine-resistant *P. vivax* and CDC should be notified immediately (Malaria Hotline number listed above).

[15] Laboratory-confirmed of suspected malaria cases who have one or more of the clinical criteria for severe disease [impaired consciousness/convulsions/coma, severe anemia, acute kidney injury, acute respiratory distress syndrome, circulatory shock, disseminated intravascular coagulation, spontaneous bleeding, acidosis, jaundice (along with at least one other sign)] and/or parasitemia of ≥5%. Information on how to estimate parasite density is available at www.dpd.cdc.gov/dpdx; and it should be repeated every 12 hours until negative parasitemia. Severe malaria is most often caused by *P. falciparum.*

[16] All patients with severe malaria should be treated with IV artesunate. Call CDC Malaria hotline for IV artesunate.

[17] Exchange transfusion is no longer recommended based on a systematic review of the literature and analysis of US malaria surveillance data showing no added benefit.

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		If, after 24 hours of artesunate, parasitemia ≤1% and patient able to tolerate oral medications, administer one of the following oral drug regimens, starting at least four hours after the last dose of artesunate: **Artemether-lumefantrine (Coartem™) (preferred):** Treatment as above **Atovaquone-proguanil (Malarone™):** Treatment as above **Quinine plus doxycycline:** Treatment as above **Quinine plus clindamycin:** Treatment as above **Mefloquine:** Treatment as above **If parasitemia >1% after 24 hours of artesunate,** continue IV artesunate at same daily dose above until parasitemia ≤1% for a maximum of 7 days. Doses given at 0, 12, and 24 hours count as 1 day, which means up to 6 additional days. Proceed with full-dose oral follow-on treatment as above as soon as parasitemia ≤1% and patient able to tolerate oral medications. Call CDC Malaria hotline if additional artesunate is needed and/or advice on treatment **If parasitemia ≤1% but patient not able to take oral medication,** continue IV artesunate at same daily dose above for a maximum of 7 days, or switch to IV treatment with doxycycline (up to 7 days) or clindamycin (up to 7 days), dosing as above. Artesunate doses given at 0, 12, and 24 hours count as 1 day, which means up to 6 additional days. Proceed with full-dose oral follow-on treatment as above as soon as patient is able to tolerate oral medications. Call CDC Malaria hotline if additional artesunate is needed and/or advice on treatment **If needed, give interim treatment until IV artesunate arrives.** If oral medications are not tolerated, consider administration via nasogastric tube or after an antiemetic **Artemether-lumefantrine (Coartem™) (preferred):** Treatment as above **Atovaquone-proguanil (Malarone™):** Treatment as above **Quinine sulfate:** Treatment as above **Mefloquine:** Only if other options not available, treatment as above	For children <20 kg: Give 3.0 mg/kg per dose: doses at 0, 12, and 24 hours for a total of three doses; **AND** **If, after 24 hours of artesunate, parasitemia ≤1% and patient able to tolerate oral medications,** administer one of the following oral drug regimens, starting at least four hours after the last dose of artesunate: **Artemether-lumefantrine (Coartem™) (preferred):** Treatment as above **Atovaquone-proguanil (Malarone™):** Treatment as above **Quinine plus doxycycline:** Treatment as above. **Quinine plus clindamycin:** Treatment as above. **Mefloquine:** Treatment as above. **If parasitemia >1% after 24 hours of artesunate,** continue IV artesunate at same daily dose above until parasitemia ≤1% for a maximum of 7 days. Doses given at 0, 12, and 24 hours count as 1 day, which means up to 6 additional days. Proceed with full-dose oral follow-on treatment as above as soon as parasitemia ≤1% and patient able to tolerate oral medications. Call CDC Malaria hotline if additional artesunate is needed and/or advice on treatment **If parasitemia ≤1% but patient not able to take oral medication,** continue IV artesunate at same daily dose above for a maximum of 7 days, or switch to IV treatment with doxycycline (up to 7 days) or clindamycin (up to 7 days), dosing as above. Artesunate doses given at 0, 12, and 24 hours count as 1 day, which means up to 6 additional days. Proceed with full-dose oral follow-on treatment as above as soon as patient is able to tolerate oral medications. Call CDC Malaria hotline if additional artesunate is needed and/or advice on treatment **If needed, give interim treatment until IV artesunate arrives.** If oral medications are not tolerated, consider administration via nasogastric tube or after an antiemetic **Artemether-lumefantrine (Coartem™) (preferred):** Treatment as above **Atovaquone-proguanil (Malarone™):** Treatment as above **Quinine sulfate:** Treatment as above **Mefloquine:** Only if other options not available, treatment as above