TREATMENT OF MALARIA IN ADULT AND PEDIATRIC PATIENTS

WHO recommendations are to treat uncomplicated malaria from all species with artemisinin-based combination therapy (such as Coartem™) based on safety and effectiveness of the drug, as well as to help streamline treatment recommendations for malaria. CDC and WHO treatment guidelines now concur with recommendations for Coartem™ as first line agent with known chloroquine resistance or species not identified. The CDC currently recommends chloroquine-containing regimens as first line therapy for chloroquine-susceptible species of malaria, which differs from WHO recommendations. We have elected to streamline institutional recommendations to be in line with WHO recommendations when there is discrepancy, given local drug availability and that Coartem™ clears parasitemia faster than chloroquine.

Definitions

Uncomplicated malaria:

Persons with a positive blood smear OR history of recent possible exposure and no other recognized pathology who do not meet severe criteria <u>Severe malaria</u>:

Persons with a positive blood smear OR history of recent possible exposure and no other recognized pathology who have one or more of the following clinical criteria:

- Parasitemia of >5%
- Impaired consciousness/coma
- Severe normocytic anemia
- Renal failure
- Pulmonary edema
- Acute respiratory distress syndrome
- Circulatory shock

- Disseminated intravascular coagulation
- Spontaneous bleeding
- Acidosis
- Hemoglobinuria

- Jaundice
- Repeated generalized convulsions

Chloroquine sensitivity:

- P. falciparum acquired in Central America (west of the Panama Canal), Haiti, and Dominican Republic
- All P. malariae, P. knowlesi, and P. ovale
- All P. vivax EXCEPT infections acquired in Papua New Guinea or Indonesia

| Uncomplicated malaria | | |
|--|--|--|
| P. falciparum or not identified | <u>P. malariae or P. knowlesi</u> | |
| P. vivax or P. ovale chloroquine sensitive | P. vivax or P. ovale chloroquine resistant | |
| Severe malaria | | |
| All species | | |
| Supply information | | |
| Pharmacy steps to obtaining Artesunate | | |
| <u>Footnotes & References</u> | | |





| Plasmodium Spp. | Treatment Regimen | Duration | Comments |
|-------------------|--|------------|--|
| Uncomplicated | Chloroquine resistant, unknown, or sensitive: | | WHO recommends treatment with artemisinin-based |
| malaria with P. | Preferred | | therapies (ACTs) for all <i>P. falciparum</i> |
| falciparum or | Artemether 20 mg-lumefantrine 120 mg (Coartem™) = 1 tablet | Coartem™: | |
| species not | 5 - <15 kg: 1 tablet/dose | 3 days | If patient used Malarone™ as chemoprophylaxis then use |
| identified | 15 - <25 kg: 2 tablets/dose | | another treatment option |
| | 25 - <35 kg: 3 tablets/dose | | |
| Recommend to | ≥35 kg: 4 tablets/dose | | Please see CDC guidelines for treatment of pregnant |
| empirically start | | | women during the first trimester CDC Malaria Treatment |
| malaria | The patient should receive the initial dose, followed by the second dose 8 | | <u>Table</u> |
| treatment for | hours later, then 1 dose PO BID for the following 2 days. | | |
| patients with | | | Coartem™ and Malarone™ should be taken with food, and |
| Ebola PUI | Alternative | | are OK to crush |
| | Atovaquone 62.5 mg-proguanil 25 mg (Malarone™) = 1 peds tablet | Malarone™: | |
| | 5 - <8 kg: 2 peds tablets PO daily | 3 days | |
| | 8 - <10 kg: 3 peds tablets PO daily | | |
| | Atovaquone 250 mg-proguanil 100 mg (Malarone™) = 1 adult tablet | | |
| | 10 - <20 kg: 1 adult tablet PO daily | | |
| | 20 - <30 kg: 2 adult tablets PO daily | | |
| | 30 - <40 kg: 3 adult tablets PO daily | | |
| | ≥40 kg: 4 adult tablets PO daily | | |
| | | | |





| Plasmodium Spp. | Treatment Regimen | Duration | Comments |
|--------------------|---|--------------|--|
| Uncomplicated | Preferred | | Please see CDC guidelines for management during |
| malaria with | Artemether 20 mg-lumefantrine 120 mg (Coartem™) = 1 tablet | Coartem™: | Pregnancy CDC Malaria Treatment Table |
| <u>chloroquine</u> | 5 - <15 kg: 1 tablet per dose | 3 days | |
| sensitive P. vivax | 15 - <25 kg: 2 tablets per dose | | Treatment of <i>P. vivax</i> or <i>P. ovale</i> requires addition of |
| or <i>P. ovale</i> | 25 - <35 kg: 3 tablets per dose | | second agent to eliminate dormant hepatic hypnozoites |
| | ≥35 kg: 4 tablets per dose | | |
| | | | There may be a role for chloroquine prophylaxis for |
| | The patient should receive the initial dose, followed by the second dose 8 | | patients unable to take primaquine, consult with ID/CDC |
| | hours later, then 1 dose PO BID for the following 2 days. | | for further guidance |
| | AND | | |
| | Primaquine (after confirmation that NOT G6PD deficient AND NOT pregnant) | Primaquine: | Coartem™ clears parasites more quickly than chloroquine |
| | Adults (≥18 years): | 14 days | |
| | 30 mg primaquine base PO daily | | Regimens used for chloroquine-resistant species of malaria |
| | Children (<18 years): | | can also be substituted for chloroquine-sensitive species of |
| | 0.5 mg/kg primaquine base PO daily (max: 30 mg/dose) | | malaria as needed based on drug availability. |
| | Alternative for chloroquine sensitive organisms: | | If chloroquine is being used, check EKG for QT interval prior |
| | Chloroquine phosphate (Aralen™) – dose based on chloroquine base | Chloroquine: | to dosing, given risk for QT prolongation |
| | Adults (≥18 years): | 48 hours | |
| | 600 mg base PO immediately, followed by 300 mg base PO at 6, 24, and | | Coartem™ and Malarone™ should be taken with food, and |
| | 48 hours (total dose: 1,500 mg base) | | are OK to crush |
| | Children: | | |
| | 10 mg/kg base (max: 600 mg) PO immediately, followed by 5 mg/kg base | | Chloroquine comes as a liquid formation, but if this cannot |
| | (max: 300 mg) PO at 6, 24, and 48 hours (total dose: 25 mg/kg base) | | be obtained, then crushing the tablet is acceptable. |
| | AND | | |
| | Primaquine (after confirmation that NOT G6PD deficient AND NOT pregnant) | | Chloroquine phosphate – 250 mg of chloroquine phosphate |
| | Adults (≥18 years): | | is equivalent to 150 mg of chloroquine base (600 mg |
| | 30 mg primaquine base PO daily | | chloroquine base = 1,000 mg salt; 300 mg chloroquine base |
| | Children (<18 years): | | = 500 mg salt) |
| | 0.5 mg/kg primaquine base PO daily (max: 30 mg/dose) | | |





| Uncomplicated malaria with chloroquine resistant P. vivaxPreferredCoartem™: 3 daysPregnancy CDC Malaria Treatment Table 3 days15 - <15 kg: 25 + <35 kg: 25 + <35 kg: 235 kg: 4 tablets per dose15 - <25 kg: 4 tablets per dose25 - <35 kg: 4 tablets per dose7 reatment of P. vivax or P. ovale requires additionable second agent to eliminate dormant hepatic hymans There may be a role for chloroquine prophylax | tion of pnozoites kis for |
|---|---------------------------------|
| chloroquine resistant P. vivax or P. ovale5 - <15 kg: 15 - <25 kg: 2 tablets per dose 25 - <35 kg: 3 tablets per dose3 daysTreatment of P. vivax or P. ovale requires additional second agent to eliminate dormant hepatic hype | pnozoites kis for |
| resistant P. vivax15 - <25 kg: 2 tablets per dose | pnozoites kis for |
| or P. ovale 25 - <35 kg: 3 tablets per dose ≥35 kg: 4 tablets per dose There may be a role for chloroquine prophylax | pnozoites kis for |
| ≥35 kg: 4 tablets per dose There may be a role for chloroquine prophylax | kis for |
| There may be a role for chloroquine prophylax | |
| | |
| | TH ID (CDC |
| The patient should receive the initial dose, followed by the second dose 8 patients unable to take primaquine, consult wi | ith ID/CDC |
| hours later, then 1 dose PO BID for the following 2 days. for further guidance | |
| AND | |
| Primaquine (after confirmation that NOT G6PD deficient AND NOT pregnant) Primaquine: Coartem™ clears parasites more quickly than c | hloroquine |
| Adults (≥18 years): | |
| 30 mg primaquine base PO daily Regimens used for chloroquine-resistant species | |
| Children (<18 years): can also be substituted for chloroquine-sensiti | ve species of |
| 0.5 mg/kg primaquine base PO daily (max: 30 mg/dose) malaria as needed based on drug availability. | |
| | |
| Alternative for chloroquine-resistant organisms: Coartem™ and Malarone™ should be taken with the should be taken with t | th food, and |
| Atovaquone 62.5 mg-proguanil 25 mg (Malarone™) = 1 peds tablet Malarone™: are OK to crush | |
| 5 - <8 kg: 2 peds tablets PO daily 3 days | |
| 8 - <10 kg: 3 peds tablets PO daily | |
| Atovaquone 250 mg-proguanil 100 mg (Malarone™) = 1 adult tablet 10 - <20 kg: 1 adult tablet PO daily | |
| 20 - <30 kg: 2 adult tablets PO daily | |
| 30 - <40 kg: 3 adult tablets PO daily | |
| ≥40 kg: 4 adult tablets PO daily | |
| AND | |
| Primaguine (after confirmation that NOT G6PD deficient AND NOT pregnant) Primaguine: | |
| Adults (≥18 years): | |
| 30 mg primaquine base PO daily | |
| Children (<18 years): | |
| 0.5 mg/kg primaquine base PO daily (max: 30 mg/dose) | |





| Plasmodium Spp. | Treatment Regimen | Duration | Comments |
|-----------------|--|--------------|---|
| Uncomplicated | Preferred | | These species have no known chloroquine resistance, but |
| malaria with P. | Artemether 20 mg-lumefantrine 120 mg (Coartem™) = 1 tablet | Coartem™: | Coartem™ clears parasites more quickly than chloroquine |
| malariae or P. | 5 - <15 kg: 1 tablet per dose | 3 days | |
| knowlesi | 15 - <25 kg: 2 tablets per dose | | If chloroquine is being used, check EKG for QT interval prior |
| | 25 - <35 kg: 3 tablets per dose | | to dosing, given risk for QT prolongation |
| | ≥35 kg: 4 tablets per dose | | |
| | | | Coartem™ should be taken with food, and are OK to crush |
| | The patient should receive the initial dose, followed by the second dose 8 | | |
| | hours later, then 1 dose PO BID for the following 2 days. | | Chloroquine comes as a liquid formation, but if this cannot |
| | | | be obtained, then crushing the tablet is acceptable. |
| | Alternative | | |
| | Chloroquine phosphate (Aralen™) – dose based on chloroquine base | Chloroquine: | Chloroquine phosphate – 250 mg of chloroquine phosphate |
| | Adults (≥18 years): | 48 hours | is equivalent to 150 mg of chloroquine base (600 mg |
| | 600 mg base PO immediately, followed by 300 mg base PO at 6, 24, and | | chloroquine base = 1,000 mg salt; 300 mg chloroquine base |
| | 48 hours (total dose: 1,500 mg base) | | = 500 mg salt) |
| | Children: | | |
| | 10 mg/kg base (max: 600 mg) PO immediately, followed by 5 mg/kg | | |
| | base (max: 300 mg) PO at 6, 24, and 48 hours (total dose: 25 mg/kg | | |
| | base) | | |





| Plasmodium Spp. | Treatment Regimen | Duration | Comments |
|---------------------|--|------------------------|--|
| Severe malaria | Artesunate (IV) is the first line recommended agent | Continue treatment | If patient used Malarone™ as chemoprophylaxis then use |
| (all spp) | Adults and children ≥20 kg: | with artensunate IV | an another treatment option |
| | 2.4 mg/kg/dose at 0, 12 hours, and 24 hours | q24h until | |
| Severe malaria is | Children <20 kg: | parasitemia is <1% | IV quinine is not available in the US. |
| most often | 3 mg/kg/dose at 0, 12 hours, and 24 hours | and able to tolerate | |
| caused by P. | | oral medications. | Delayed hemolysis can occur ~1 week after artesunate |
| falciparum, but is | Once parasitemia <1%, follow IV artesunate with a full 3-day follow-on course | | treatment in patients with hyperparsitemia. Recommend |
| also a risk with P. | of: | | follow up weekly CBCs for 28 days after initiation of |
| knowlesi | Artemether 20 mg-lumefantrine 120 mg (Coartem™) = 1 tablet | Maximum duration | Artesunate. (See page 11 of IND document) |
| | 5 - <15 kg: 1 tablet per dose | of IV artesunate: | |
| | 15 - <25 kg: 2 tablets per dose | 7 days | Monitor carefully for hypoglycemia during the course of |
| | 25 - <35 kg: 3 tablets per dose | | therapy |
| | ≥35 kg: 4 tablets per dose | | |
| | | If there is persistent | Blood smears should be repeated ever 12 to 24 hours, until |
| | The patient should receive the initial dose, followed by the second dose 8 hours later, then 1 dose PO BID for the following 2 days. | parasitemia at the | at least 2 consecutive blood smears are negative. Also, |
| | flours later, then I dose FO bib for the following 2 days. | end of the follow-on | blood smear should be repeated at the end of treatment. |
| | Alternative once parasitemia <1%, follow IV artesunate with a full 3-day | course, would | (See page 19 of IND document) |
| | follow-on course of: | warrant extension | |
| | Atovaquone 250 mg-proguanil 100 mg (Malarone™) = 1 adult tablet | of Coartem until | Coartem™ and Malarone™ should be taken with food, and |
| | 10 - <20 kg: 1 adult tablet PO daily | negative smears x2. | are OK to crush |
| | 20 - <30 kg: 2 adult tablets PO daily | | If delay in obtaining artesunate recommend and out |
| | 30 - <40 kg: 3 adult tablets PO daily | | If delay in obtaining artesunate, recommend oral anti- malarial drug (Artemether-lumefantrine) immediately |
| | ≥40 kg: 4 adult tablets PO daily | | while awaiting delivery of IV Artesunate. If oral medications |
| | Atovaquone 62.5 mg-proguanil 25 mg (Malarone™) = 1 peds tablet | | are not tolerated, consider administration via nasogastric |
| | 5 - <8 kg: 2 peds tablets PO daily | | tube or after an antiemetic |
| | 8 - <10 kg: 3 peds tablets PO daily | | tube of after an afficientetic |
| | *For patients with <i>P. vivax</i> and <i>P. ovale</i> please also provide | | |
| | Primaquine (after confirmation that NOT G6PD deficient AND NOT pregnant) | | |
| | Adults (≥18 years): | | |
| | 30 mg primaquine base PO daily | | |
| | Children (<18 years): | | |
| | 0.5 mg/kg primaquine base PO daily (max: 30 mg/dose) | | |



Footnotes:

https://www.cdc.gov/malaria/resources/pdf/Malaria Treatment Table 120419.pdf CDC MALARIA HOTLINE: 770-488-7788 (M-F, 9am to 5pm), 770-488-7100 (after hours)

References:

- Centers for Disease Control and Prevention. Malaria Treatment (United States). https://www.cdc.gov/malaria/diagnosis_treatment/clinicians1.html. May 26, 2020.
- World Health Organization. Guidelines for the treatment of malaria. 3rd edition. 2015. https://www.ncbi.nlm.nih.gov/books/NBK294440/. May 26, 2020.

| 1 Originated: 06/2020 |
|-------------------------|
| 1 Last Revised: 04/2021 |
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04/2021: Removed IND artesunate information

The recommendations in this guide are meant to serve as treatment guidelines for use at Michigan Medicine facilities. If you are an individual experiencing a medical emergency, call 911 immediately. These guidelines should not replace a provider's professional medical advice based on clinical judgment, or be used in lieu of an Infectious Diseases consultation when necessary. As a result of ongoing research, practice guidelines may from time to time change. The authors of these guidelines have made all attempts to ensure the accuracy based on current information, however, due to ongoing research, users of these guidelines are strongly encouraged to confirm the information contained within them through an independent source.

If obtained from a source other than med.umich.edu/asp, please visit the webpage for the most up-to-date document.