MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

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

Severe malaria:

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	*P. malariae* or *P. knowlesi*
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	
Footnotes & References	

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

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

Plasmodium Spp.	Treatment Regimen	Duration	Comments
Uncomplicated malaria with <u>chloroquine resistant</u> *P. vivax* or *P. ovale*	*Preferred* **Artemether 20 mg-lumefantrine 120 mg (Coartem™)** = 1 tablet 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 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. *AND* **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) *Alternative for chloroquine-resistant organisms:* **Atovaquone 62.5 mg-proguanil 25 mg (Malarone™)** = 1 peds tablet 5 - <8 kg: 2 peds tablets PO daily 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* **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)	Coartem™: 3 days Primaquine: 14 days Malarone™: 3 days Primaquine: 14 days	Please see CDC guidelines for management during Pregnancy CDC Malaria Treatment Table Treatment of *P. vivax* or *P. ovale* requires addition of second agent to eliminate dormant hepatic hypnozoites There may be a role for chloroquine prophylaxis for patients unable to take primaquine, consult with ID/CDC for further guidance Coartem™ clears parasites more quickly than chloroquine Regimens used for chloroquine-resistant species of malaria can also be substituted for chloroquine-sensitive species of malaria as needed based on drug availability. Coartem™ and Malarone™ should be taken with food, and are OK to crush

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

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

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.

Antimicrobial Subcommittee Approval: 06/2020; 03/2021	Originated: 06/2020
P&T Approval: 07/2020; 04/2021	Last Revised: 04/2021
Revision History: 04/2021: Removed IND artesunate information	