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SECTION 1: Preamble / Introduction

Malaria is a disease caused by infection with the *Plasmodium* parasite in the human host. It remains a major cause of morbidity and mortality in tropical climates and because of the ease of travel, the diagnosis of malaria is not restricted to individuals residing in the tropics. It should be suspected in any febrile patient who has come from, or has travelled to, an endemic area, especially within the previous 3 months. Please refer to the Canadian Malaria Guidelines (available at http://publications.gc.ca/collections/collection_2014/asp-c-phac/HP40-102-2014-eng.pdf) for information on geographic locations and maps of endemic areas.

Malaria parasites may be difficult to find on blood smear and even when identified, determining the species of *Plasmodium* can be difficult. Furthermore, mixed infections with two types of malaria are also possible. Malaria can be fatal, especially if due to *Plasmodium falciparum*, and not promptly recognised and treated. Malaria continues to be a major cause of death world-wide and is the principal life-threatening infection facing Canadian travellers in malaria-endemic areas. In Canada there are approximately 400-500 malaria cases annually. Unfortunately, due to misdiagnosis or delayed therapy, some of these cases result in severe disease and even death.

Severe *P. falciparum* malaria (see definition, Table I, page 7) infections may have a mortality rate of 20% or higher. Patients require immediate hospitalisation and urgent, intensive medical management, including parenteral malaria therapy.

This binder has been assembled with the goal of improving the recognition, diagnosis, and management of malaria in adult patients. It includes sections on when to suspect malaria, guidelines for treatment, drug dosing regimens and admission order forms to aid the clinician in initial management. This binder provides a synopsis of malaria management in adult patients, and is not intended to be all-inclusive. Appropriate references and specialists should be consulted when managing children, or when more in-depth information is required. Resources at The Ottawa Hospital include the Infectious Diseases Consultation Service (page through locating), as well as the Tropical Medicine and International Health Clinic (613-737-8856).

A. E. McCarthy, MD, FRCPC, DTM&H
Director Tropical Medicine and International Health Clinic
Division of Infectious Diseases
The Ottawa Hospital

Rosemary Zvonar, B.Sc.Phm, FCSHP
Antimicrobial Pharmacy Specialist
The Ottawa Hospital

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SECTION 2: Diagnosing Malaria

When to Suspect Malaria

A travel history must be obtained from all patients with a presentation or history of fever.

Malaria should be suspected in any traveller who presents with a febrile illness within 3 months of departure from a malaria-endemic area.

The disease is characterized by FEVER and “flu-like” symptoms such as myalgias, headache, abdominal pain, and malaise. Rigors and chills often occur. The classically described alternate-day fevers or other periodic fevers are often not present. Severe malaria due to P. falciparum may cause seizures, coma, and renal and respiratory failure, and may lead to death. Malaria deaths are frequently the result of delays in the diagnosis and treatment of the infection.

The clinical presentation of malaria is often non-specific and blood films are required for diagnosis. P. falciparum usually presents within 3 months of last exposure, but may be delayed if the patient has taken chemoprophylaxis. Other types of malaria may occur months or even years after travel in endemic areas.

Suspicion of malaria is a medical emergency and should be immediately investigated with thick and thin blood films, and a rapid diagnostic (antigen) test. (Blood films plus rapid diagnostic antigen testing for malaria are routinely performed at TOH). The diagnosis, speciation, and level of parasitemia must be determined by an experienced microscopist on an emergency (STAT) basis.

If initial blood films are negative, then blood films should be repeated within 12-24 hours if the patient remains symptomatic.

With P. falciparum, the progression from asymptomatic infection to severe and complicated malaria can be extremely rapid, with death occurring within 36 to 48 hours. The fatality rate of severe malaria can be up to 20% even when managed in modern intensive care units. The most important factors that determine patient survival are early diagnosis and appropriate therapy. It should be emphasized that the majority of infections and deaths due to malaria are preventable.
Common Pitfalls in Diagnosis and Management of Malaria

 Errors in diagnosis
1. Failure to obtain history of travel and exposure.
2. Failure to suspect malaria in patients at risk.
4. Failure to order both thick and thin blood films.
5. Failure to repeat blood films if initial films are negative.
6. Failure to identify *P. falciparum* in a patient co-infected with *P. vivax*.
7. Failure to suspect/diagnosis concomitant infections (eg., TB, bacterial, viral).
8. Failure to monitor patient for hypoglycemia.
9. Failure to recognize respiratory distress/metabolic acidosis.
10. Failure to perform an ophthalmoscopic examination for the presence of papilloedema and malarial retinopathy.
11. Misidentification of *P. knowlesi* species as *P. malariae* or *P. falciparum*.

 Errors in management
1. Delays in starting antimalarial medication.
2. Inadequate nursing care.
3. Selection of inappropriate antimalarial agent(s).
4. Incorrectly calculated dosage of antimalarial.
5. Inappropriate route of administration of antimalarial agent(s).
6. Failure to determine history of recent antimalarial use.
7. Failure to change to oral therapy as soon as patient can tolerate (after minimum of 24 hours in severe malaria).
8. Failure to monitor for adverse effects of antimalarial drugs.
9. Failure to check blood glucose in a patient with seizures and coma.
10. Failure to treat possible meningitis in patients with compatible signs and symptoms, particularly if lumbar puncture is delayed.
11. Unnecessarily prolonged duration of therapy.
13. Failure to recognize pulmonary edema.
14. Failure in identification or treatment of metabolic acidosis.
15. Failure to recognize and control seizures, particularly those that may be ‘subtle’.
16. Failure to identify and treat severe anemia.
17. Unnecessary delay in initiation of dialysis.
18. Use of unproven and potentially dangerous ancillary treatment
19. Failure to review antimalarial treatment for a patient whose condition is deteriorating
20. Failure to consult Infectious Diseases or Tropical Medicine Service.

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Map is intended as a visual aid only.

For country specific information, refer to Appendix 1 in the 2014 CATMAT Malaria guidelines at
SECTION 3: General Guidelines for Malaria Management in Adults

Principles of Care for Adult Patients with Malaria

1. This is a medical emergency as death can result rapidly from untreated falciparum malaria.

2. All patients with malaria due to *P. falciparum* must be admitted to hospital or an observation unit for a minimum of 8 hours to ensure tolerance of treatment and to confirm decreasing parasitemia with treatment.

3. If the species is not unequivocally identified, treat as *P. falciparum* until further identification.

4. Treat all *P. falciparum* as chloroquine resistant (treatment may only be modified by Infectious Disease Service).

5. Patients from Southeast Asia (esp. Malaysia) with parasites resembling *P. malariae* likely have a new species of malaria, *P. knowlesi*. These patients should be treated in the same manner as for *P. falciparum* malaria. (Clin Infect Dis 2008;46:165)

6. Severe or complicated disease (see Table 1, page 7) requires management in an intensive care unit setting.

7. Infectious diseases (ID) consult is required for all positive malaria smears. The Haematology Laboratory should also notify ID of all positive malaria smears. Pharmacy is to call ID upon any initial prescription for antimalarials. Potential duplication or triplication in calls to ID is preferable to lack of consultation.

The following questions need to be considered in managing patients with malaria:

1. Is the species *falciparum* or non-*falciparum*?
   - *Falciparum* malaria is a medical emergency
   - Treatment will vary according to the species of malaria

2. Does the patient meet any of the criteria for severe malaria (see Table 1 p.7)?
   - All patients with severe or complicated malaria require therapy with parenteral antimalarials

3. If non-severe malaria, can the patient tolerate oral therapy?
   - If the answer is no, the patient’s treatment should not be delayed, but should begin with parenteral therapy (IV quinine preferably). Therapy can be changed to the oral route as soon as the patient can tolerate it.
Table I: Criteria for Severe *Falciparum* Malaria in Adults

<table>
<thead>
<tr>
<th>Asexual forms of <em>Plasmodium falciparum</em> on blood smear</th>
<th>AND</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Any</em> one or more of the following features:</td>
<td></td>
</tr>
<tr>
<td>1) Parasitemia of:</td>
<td></td>
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<tr>
<td>• ≥5% for non-immune* adults or</td>
<td></td>
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<tr>
<td>• ≥10% for semi-immune** adults</td>
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<td>2) Prostration (severe weakness—unable to sit or stand without assistance)</td>
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<td>3) Impaired consciousness or coma</td>
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<td>4) Multiple convulsions (&gt; 2 within 24 hours)</td>
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<tr>
<td>5) Respiratory distress (acidotic breathing)</td>
<td></td>
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<tr>
<td>6) Respiratory failure/pulmonary edema/ARDS</td>
<td></td>
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<tr>
<td>7) Circulatory collapse/shock (SBP&lt;80mm Hg in adults)</td>
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<tr>
<td>8) Acute kidney injury/renal impairment (creatinine &gt; 265 umol/L)</td>
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<tr>
<td>9) Jaundice (Total bilirubin &gt;45 μmol/L)</td>
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<tr>
<td>10) Abnormal bleeding/DIC</td>
<td></td>
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<tr>
<td>11) Hypoglycemia (blood glucose &lt; 2.2 mmol/L)</td>
<td></td>
</tr>
<tr>
<td>12) Severe anemia (haematocrit &lt; 20%; Hb &lt; 70 g/L in adults)</td>
<td></td>
</tr>
<tr>
<td>13) Hemoglobinuria (macroscopic)</td>
<td></td>
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<tr>
<td>14) Acidosis (arterial pH &lt; 7.25 or bicarbonate &lt; 15 mmol/L)</td>
<td></td>
</tr>
<tr>
<td>15) Hyperlactataemia (lactate &gt; 5 mmol/L)</td>
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</tbody>
</table>

*Non-immune = those born in non-endemic countries or low-transmission settings, such as travellers.*

**Semi-immune = individuals with recent long-term residence in an endemic country and prior episodes of malaria. *Note:* Immunity is considered lost after a period of 6-12 months living out of the malaria endemic country.

*Note:* If patient meets above criteria, begin therapy with intravenous antimalarials STAT and ADMIT TO ICU for monitoring. *(Do not delay* initiation of IV antimalarial while awaiting transfer to ICU)*

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Algorithm for the Management of Malaria

**MALARIA SUSPECTED:**
Blood smear thick and thin, Rapid Diagnostic Test for malaria antigens, blood cultures, CBC, Scr, BUN, liver enzymes, glucose

- **Malaria Smear NEGATIVE**
  - If symptoms (fever, flu-like illness) persist, repeat malaria smears and RDT Q12-24 for total of 3

- **Malaria Smear POSITIVE**
  - Determine Species and Percent Parasitism
    - **Falciparum** species, or species not known
      - Indication for **parenteral** therapy? (severe malaria [Table 1], >5% (non-immune) or 10% (semi-immune) parasitism, or unable to tolerate oral
        - **YES***
          - Follow **Treatment Guideline A – Parenteral Therapy**
            - Admit (ICU admission if severe malaria)
          - *Note: Consulting physician must complete Parenteral Therapy Forms A and B provided with drug and available at http://thinkottawamedicine.ca/clinical-care/canadian-malaria-network/
        - **NO**
          - Follow **Treatment Guideline A – Oral Therapy**
            - Admit for minimum of 8 hrs observation after initial antimalarial dose. Repeat blood smears before discharge to ensure no increase in parasitemia

- **Non Falciparum** Malaria
  - Follow treatment Guideline B

- **Malaria Smear NEGATIVE**
  - Change to oral therapy as per guidelines
SECTION 4: Treatment Guidelines

Treatment Guideline A: Management of P. falciparum Malaria

P. falciparum malaria OR malaria parasites on blood smear but species not confirmed

1) Admission Orders:
   Complete Malaria order set for patients with malaria (in EPIC)

2) Drug Therapy:
   Must be started on a STAT basis as the doubling time for P. falciparum is 6 hours. Indicate antimalarial selection in Malaria order set for patients with malaria--Falciparum Malaria or Species Unknown (in EPIC). (Refer to Section 6)

   a) ORAL THERAPY
      Initial oral therapy is indicated if these 3 criteria are met:
      (1) less than 5% parasitemia (non-immune adults) or less than 10% parasitemia (semi-immune adults)
      (2) no evidence of severe or complicated disease (see Table 1, p. 7)
      (3) able to tolerate oral medications

      Select one of the following options:
      (1) ATOVAQUONE/ PROGUANIL (MALARONE®) X 3 days (preferred regimen unless patient previously on Malarone® prophylaxis or CrCl ≤ 30 mL/min or pregnancy)
      OR
      (2) QUININE X 7 days with DOXYCYCLINE* (preferred over clindamycin; contraindicated in pregnancy/breastfeeding) X 7 days (2nd choice regimen; if doxycycline contraindicated, see below)
      OR
      (3) QUININE X 7 days with CLINDAMYCIN* (use in pregnancy or breastfeeding) X 7 days

      *The second agent (i.e., doxycycline or clindamycin) can be delayed for 24 to 48 hours following initiation of QUININE therapy.

   b) PARENTERAL THERAPY
      Parenteral therapy is indicated if:
      (1) the patient meets criteria for severe malaria (See Table 1; p. 7) – artesunate IV preferred
      OR
      (2) the patient does not have severe malaria but is unable to tolerate oral drugs (e.g., refused or vomiting) – quinine IV preferred

      Note: Patients with severe malaria should be admitted to ICU for monitoring. Do not delay initiation of IV artesunate or quinine while awaiting transfer to ICU.
**Note:** When parenteral therapy is used for the treatment of severe malaria (vs non-severe but unable to take oral therapy), a minimum of 24 hours of parenteral therapy is recommended (irrespective of the patient’s ability to tolerate oral medication earlier).

i) **ARTESUNATE IV**

   - **Drug of Choice** for severe malaria
     - Give first dose **STAT**; total course is 4 doses (**Note:** may switch to oral therapy after 3rd dose if patient can tolerate oral therapy—all 4 doses recommended in pregnancy)
     - Follow-on therapy with oral antimalarial agents is essential, and should be started 4 hours after the last artesunate IV dose. (Malarone® is preferred; however, oral quinine* with either doxycycline or clindamycin are alternatives).
     - If, in the rare case, the patient cannot tolerate oral medication following 4 doses of artesunate, options include continuing artesunate IV daily for up to 7 days total, or switching to a 7 day course of IV clindamycin or IV doxycycline (Special Access drug). Choice should be made in consultation with an Infectious Diseases specialist.
     - For more information on use of artesunate IV, refer to the [IV artesunate monograph](#) in Section 5.

*Note:* if 4 doses of artesunate IV are administered (as opposed to switching to oral after 3 doses if the patient can tolerate oral at that time), then doxycycline or clindamycin alone (without quinine) may be used as follow-on therapy in cases where Malarone® is not an appropriate follow-on option.

**OR**

ii) **QUININE DIHYDROCHLORIDE IV**

   - Indicated in:
     1) non-severe malaria but patient cannot take oral therapy
     2) severe malaria if artesunate IV not available or not tolerated

   - IV pump is required for quinine IV administration.
   - Switch to oral medication (see below) once oral therapy is tolerated.
   - Unless stepped down to oral Malarone® (see below), quinine should be combined with seven days of either doxycycline (preferred; contraindicated in pregnancy or breastfeeding) or clindamycin (if pregnancy/breastfeeding)
   - The second agent can be delayed for 24-48 hours following initiation of quinine therapy
   - Total treatment course of quinine (parenteral plus oral) is 7 days.

If **IV quinine is prescribed for severe malaria**:

   - Give loading dose **STAT**. (Omit loading dose if patient has received quinine or quinidine in the previous 24 hours or a dose of mefloquine in previous 2 weeks or if treating non-severe malaria). If history of recent treatment with quinine, quinidine or mefloquine is unclear, and/or if benefits of a loading dose are felt to outweigh the risk, cardiac monitoring is recommended.
   - **START** maintenance dose immediately following the loading dose. Continue with intermittent infusion q8h for a minimum of 24 hours, then switch to oral medication if appropriate, once tolerated.

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4 See Table 2 for dosing guidelines
5 All patients requiring artesunate IV or quinine IV must have Malaria Forms A and B completed
• If IV quinine is required > 48hrs and patient remains severely ill or continues to have acute renal injury, change dosing interval to Q12H after 48hrs. Full dose can be continued if patient is receiving dialysis.

For more information on use of quinine IV, refer to the IV quinine monograph in Section 5.

**Stepdown** to oral therapy as soon as possible *(after minimum of 24 hours of IV therapy if severe malaria)* with either a 3 day course of Malarone® tablets (preferred) OR oral quinine with either doxycycline (preferred over clindamycin; contraindicated in pregnancy/breastfeeding) or clindamycin to complete 7 day course.

Please make follow-up appointment with TROPICAL MEDICINE (tel: 613-798-5555 ext 19388 or fax 613-761-5260) at one week post discharge.
Treatment Guideline B: Management of Non-falciparum malaria

Malaria parasites on blood smear are confirmed as *P. vivax* or *P. ovale* or *P. malariae*

1) Admission Orders:
   Complete Malaria order set for patients with malaria (in EPIC)-- (Refer to Section 6)

2) Drug Therapy:
   Indicate antimalarial selection in Malaria order set for patients with malaria--Non-Falciparum Malaria (in EPIC). (Refer to Section 6)
   Please note that except for New Guinea, chloroquine remains the drug of choice for non-falciparum malaria (consult Tropical Medicine physician for therapy if patient from New Guinea)

   Management of *P. vivax* or *P. ovale* involves an initial treatment phase with chloroquine followed by a cure phase (with primaquine) to eradicate parasites from the liver and prevent relapse. (This is termed “radical cure”). Cure phase is not required if species is *P. malariae*.

   a) Initial Drug therapy:
      i) Chloroquine X 3 days
      OR
      ii) If patient unable to take oral therapy, treat with quinine IV as per guideline for *P. falciparum* malaria.

   b) Followed by *(if G6PD levels are normal and patient is not pregnant/breastfeeding—see below)*
      i) Primaquine X 14 days (to be started when able to tolerate oral therapy and normal G6PD level documented)

   c) Please make follow-up appointment with TROPICAL MEDICINE (tel: 613-798-5555 ext 19388 or fax 613-761-5260) at one week post discharge.

   Primaquine use is contraindicated in those who have severe deficiency of G6PD because it may cause life threatening hemolytic anemia. Please do G6PD test** for all confirmed *P. vivax* or *P. ovale* malaria infections. Do not prescribe primaquine until results available.

   **Send blood specimen in an EDTA (purple stopper) tube to biochemistry with the routine biochemistry/hematology requisition.

   Primaquine use is contraindicated in pregnancy (even if normal levels of G6PD due to unknown status of G6PD in fetus). Pregnant patients should be maintained on chloroquine prophylaxis after the treatment course: 500 mg salt (310mg base) orally once weekly during the pregnancy and primaquine therapy prescribed after delivery if no contraindication.

   In breastfeeding, test infant for G6PD deficiency and provide to mother if both mother and infant enzyme levels normal.

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6 See Table 2 for dosing guidelines
Treatment of Malaria in Pregnancy

Pregnant women with malaria are more likely to develop severe disease compared to non-pregnant women. Malaria can result in significant morbidity and mortality in both pregnant woman and the fetus, including miscarriage, premature labour, low birth weight, and potentially death. Thus, it is essential that malaria in the pregnant patient be treated immediately, and the benefits of drug therapy outweigh any risks for both the mother and baby. Because pregnant women are more prone to hypoglycemia, both from the infection and use of IV quinine, close monitoring of blood glucose is essential.

The following is a summary of the preferred drug regimens for treatment of malaria in pregnancy.

1) Uncomplicated, confirmed P. vivax or P. ovale or P. malariae malaria:
   ➢ Chloroquine (same treatment schedule as with non-pregnant adults)

   **Note:** Primaquine phosphate should not be prescribed during pregnancy for radical cure of P. vivax or P. ovale infections. After treatment with chloroquine, pregnant women should be maintained on chloroquine prophylaxis (500 mg salt or 310mg base orally once weekly) during their pregnancy and primaquine therapy prescribed after delivery if no contraindication.

2) Uncomplicated malaria caused by P. falciparum infection:
   ➢ Oral quinine with clindamycin X 7 days

3) Severe or complicated malaria caused by P. falciparum:
   Artesunate IV **(total of four doses recommended)**, followed by a 7-day course of clindamycin

**Notes:** Full doses of all antimalarials should be used in pregnant patients.

Artesunate is now recommended as first line treatment for severe malaria in all trimesters of pregnancy. Quinine IV may be used if artesunate is not tolerated or not available. Quinine IV should be used in preference to artesunate IV for the management of non-severe malaria when oral therapy is not tolerated, as recommended for the general population. Oral therapy with quinine plus clindamycin should be substituted as soon as the patient can tolerate medication.

Atovaquone/proguanil (Malarone®) is generally not indicated for use in pregnancy due to a lack of adequate, well-controlled studies in pregnant women. However, use of Malarone® may be considered if the recommended treatment options are not tolerated, following assessment of the potential risks and benefits.

References


## Table II: Antimalarial Drug Dosing Guidelines for Adults

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult Dose</th>
<th>Special Notes</th>
<th>Adverse Effects / Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARTESUNATE</td>
<td>2.4 mg/kg STAT, then repeat dose in 12, 24 and 48 hours from initial dose</td>
<td>Drug of choice for severe or complicated malaria</td>
<td>Usually well tolerated; anorexia, dizziness, taste alteration, nausea, diarrhea, reversible decrease in reticulocyte count, delayed hemolytic anemia, increased liver enzymes, bradycardia, heart block, and rare allergic reactions (e.g. urticaria, pruritis, dyspnea). CBC weekly x 4 weeks following therapy is required to monitor for delayed haemolytic anemia.</td>
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<td></td>
<td>Dose based on actual (total) body weight</td>
<td>A minimum of 24 hours of IV therapy is required for severe malaria</td>
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<td></td>
<td></td>
<td>Total dose is 7.2 - 9.6 mg/kg. No dose adjustment required for renal or liver dysfunction</td>
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<td></td>
<td></td>
<td>Recommended in all trimesters of pregnancy</td>
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<td></td>
<td></td>
<td>Has been administered intramuscularly if no venous access</td>
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<td></td>
<td></td>
<td>Special Access; stocked at TOH General &amp; Civic Campuses. Made available by the Canadian Malaria Network</td>
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<tr>
<td>INTRAVENOUS</td>
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<tr>
<td>ATOVAQUONE / PROGUANIL</td>
<td>4 tabs PO daily (1000 mg atovaquone plus 400 mg proguanil)</td>
<td>Treatment length is 3 days All tablets given as a single daily dose at same time each day</td>
<td>Nausea, vomiting, abdominal pain, diarrhea, headache, transient increase in liver enzymes; rarely: rash, seizures, hepatitis, mouth ulceration, allergic reactions including anaphylaxis Concomitant use of rifampin, metoclopramide, tetracycline, efavirenz or boosted protease-inhibitors can decrease atovaquone concentrations May potentiate effects of warfarin Use not recommended in patients with CrCl &lt; 30 ml/min</td>
</tr>
<tr>
<td>MALARONE® ORAL</td>
<td></td>
<td>Must be given with fatty food or high-fat milk for adequate absorption</td>
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<tr>
<td></td>
<td></td>
<td>If vomiting occurs within 1 hour, repeat full dose</td>
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<td></td>
<td></td>
<td>Do not use if patient had received Malarone® as malaria prophylaxis</td>
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<tr>
<td>CHLOROQUINE PHOSPHATE</td>
<td>1.55 g base over 3 days as follows: 4 tabs (620mg base) STAT, then 2 tabs (310 mg base) 6 hours later; then 2 tabs (310 mg base) daily X 2 days</td>
<td>Treatment length is 3 days May be given with food</td>
<td>Nausea, vomiting, diarrhea, headache, visual disturbances, generalised pruritus (esp. in African-Canadians—not indicative of drug allergy) Should not be used in individuals with a history of epilepsy or generalised psoriasis</td>
</tr>
<tr>
<td>ORAL</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| CLINDAMYCIN ORAL OR IV | LOADING DOSE: 10mg/kg IV  
MAINTENANCE DOSE: 5 mg/kg Q8H IV or 300 mg q6h PO | Start within 24-48 hours of initiation of QUININE therapy  
Treatment length is 7 days  
Change to oral therapy ASAP  
Use as second agent only if doxycycline contraindicated | Nausea, vomiting, diarrhea, pseudomembranous colitis, rash |
|----------------------------|---------------------------------|-------------------------------------------------|--------------------------------------------------|
| DOXYCYCLINE ORAL | 100 mg PO BID | Start within 24-48 hours of initiation of QUININE therapy  
Treatment length is 7 days  
Give with food to minimize GI upset  
IV formulation available through Health Canada’s Special Access Program | GI upset, photosensitivity, vaginal candidiasis  
Take in an upright position with plenty of water to avoid esophageal ulceration  
Contraindicated in pregnancy and breastfeeding; however, may be used during breastfeeding if no other treatment options  
Do not give with antacids, calcium, iron |
| MALARONE® (See Atovoquone / proguanil) | | | |
| PRIMAQUINE PHOSPHATE ORAL | 30 mg base/day | Used for radical cure in *P. vivax* and *P. ovale* infections  
Always obtain G6PD level prior to prescribing  
Treatment length is 14 days  
Give with food to minimize GI side effects | Headache, nausea, abdominal pain, rash, leukopenia, QT prolongation, methemoglobinemia, hemolysis in G6PD deficiency  
Contraindicated in pregnancy  
Risk of embryo-fetal toxicity; avoid pregnancy during treatment and up to next menses in women of childbearing potential. For men, the product monograph suggests avoiding pregnancy in partner for 3 months  
For outpatient prescriptions, please order as both base & salt [i.e., primaquine 30 mg base (= 56.2 mg primaquine phosphate)] |
| QUININE DIHYDROCHLORIDE INTRAVENOUS | LOADING DOSE: quinine dihydrochloride 7 mg/kg* (5.8 mg/kg base) in 100 ml D5W, infused over 30 minutes via infusion pump, immediately followed by: MAINTENANCE DOSE: quinine dihydrochloride 10 mg/kg* (8.3 mg/kg base) in 500 ml D5W Q8H; each dose infused over 2 to 4 hours via infusion pump | Omit loading dose if patient has received QUININE or QUINIDINE in the previous 24 hours, or a dose of MEFLOQUINE in the previous 2 weeks, or if treating non-severe malaria. If patient remains severely ill or has AKI and requires IV quinine for more than 48 hours, reduce frequency to Q12H (note, full doses may be used in hemodialysis). Switch to oral therapy ASAP (NB: a minimum of 24 hours of IV therapy is required for severe malaria). Treatment length is 7 days. Special Access; stocked at TOH General & Civic Campuses. Made available by the Canadian Malaria Network. | Tinnitus, nausea, vertigo, headache, blurred vision, hypoglycemia, occasional cardiac conduction disturbances. Caution or avoid concomitant use with drugs that may prolong the QT interval (e.g., amiodarone). Contraindicated in myasthenia gravis. May increase digoxin levels by 25-40%. In pregnancy, risks to mother and baby from malaria outweigh risk of drug. |
| QUININE SULFATE | 600 mg salt (500 mg base) Q8H | Treatment length is 7 days. Give with food or milk. If recurrent vomiting, switch to parenteral therapy. | Same as for intravenous QUININE DIHYDROCHLORIDE. |

ORAL

| 300 mg capsules (250 mg base/capsule) | 600 mg salt (500 mg base) Q8H | Treatment length is 7 days. Give with food or milk. If recurrent vomiting, switch to parenteral therapy. | Same as for intravenous QUININE DIHYDROCHLORIDE. |

* Base dose on ideal body weight in obesity.
Table III: Base/Salt Equivalents of Selected Antimalarial Drugs

<table>
<thead>
<tr>
<th>DRUG</th>
<th>BASE (mg)</th>
<th>SALT (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroquine phosphate (oral)</td>
<td>155 mg</td>
<td>250 mg</td>
</tr>
<tr>
<td>Primaquine phosphate (oral)</td>
<td>15 mg</td>
<td>26.3 mg</td>
</tr>
<tr>
<td>Quinine dihydrochloride (IV)</td>
<td>5 mg</td>
<td>6 mg</td>
</tr>
<tr>
<td></td>
<td>5.8 mg</td>
<td>7 mg</td>
</tr>
<tr>
<td></td>
<td>8.3 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td></td>
<td>16.7 mg</td>
<td>20 mg</td>
</tr>
<tr>
<td>Quinine sulfate (oral)</td>
<td>500 mg</td>
<td>600 mg</td>
</tr>
</tbody>
</table>
## SECTION 5: IV Antimalarial Information

### TOH Parenteral Manual Monograph: IV Artesunate

<table>
<thead>
<tr>
<th>PARENTERAL DRUG THERAPY MANUAL</th>
<th>NAME OF MEDICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>OTHER NAMES</td>
<td>ARTESUNATE *</td>
</tr>
<tr>
<td>Artesun®</td>
<td>CLASSIFICATION</td>
</tr>
</tbody>
</table>

### INDICATIONS
- Treatment of severe and complicated malaria due to *Plasmodium falciparum*.

### ADMINISTRATION

**Product from the United States (Walter Reed Supply)**
- Reconstitute each vial of 110 mg of artesunate base by slowly injecting (against vial wall) 11 mL of the provided phosphate buffer diluent to get a concentration of 10 mg/mL. Gently swirl for 5 to 6 minutes.
- IV direct: administer over 1-2 minutes into the tubing of a freely running IV solution of D5W or NS.
- IM (if IV access cannot be obtained).
- Administer dose within 60 minutes of reconstitution.
- Observe patient for 30 minutes following administration for signs of a hypersensitivity reaction.

**Product from China (Artesun®)**
- Reconstitute each vial of 120 mg of artesunate base with the contents (2 mL) of the provided ampoule of sodium bicarbonate solvent. Shake the vial (not too vigorously) for several minutes to mix well until the powder is completely dissolved and the solution is clear. The solution should clear in a few minutes. Discard if the solution does not clear or a precipitate is present.
- IV direct (preferred): add the contents (10 mL) of the supplied ampoule of NS diluent to the vial containing the reconstituted artesunate solution. Shake to mix well. Solution should be clear. Discard if the solution appears cloudy or a precipitate is present. This will yield a concentration of artesunate of 10 mg/mL. Administer over 1-2 minutes into the tubing of a freely running IV solution of D5W or NS.
- IM (if IV access cannot be obtained): add 4 mL of the supplied NS diluent to the vial containing the reconstituted artesunate solution. Shake to mix well. Solution should be clear. Discard if the solution appears cloudy or a precipitate is present. This will yield a concentration of artesunate of 20 mg/mL. Preferred site of injection: anterior thighs; depending on volume to administer, may need to divide dose and inject in several sites.
- Administer dose within 60 minutes of reconstitution.
- Observe patient for 30 minutes following administration for signs of a hypersensitivity reaction.

### POTENTIAL ADMINISTRATION HAZARDS
- Hypersensitivity (rare): rash, urticaria, itching, swelling, watery eyes, dyspnea, hypotension, anaphylaxis.
- Cardiovascular: bradycardia.
- GI: anorexia, nausea, vomiting, cramps, diarrhea, taste alteration.
- CNS: dizziness, lightheadedness, headache, insomnia, tinnitus.
- Reversible decrease in reticulocyte count.
- Increased liver enzymes
- Arthralgias, muscle disorders, fatigue, fever, malaise, cough, nasal symptoms.
- Local reactions: pain at injection site.

### DOSAGE
- For adults and children weighing 20 kg and over: 2.4 mg/kg IV/IM at time 0, 12, 24 and 48 hours (total of 4 doses or 9.6 mg/kg).
- For children weighing less than 20 kg: 3 mg/kg IV/IM at time 0, 12, 24 and 48 hours (total of 4 doses or 12 mg/kg).
- First dose should be administered STAT. May change to oral therapy (see Miscellaneous section) after the 3rd parenteral dose if patient can tolerate oral therapy.

.../Cont.
DOSAGE (Cont.)
- Dosage in renal impairment: no dosage adjustment is necessary.
- Dosage in hepatic impairment: no dosage adjustment is necessary.
- Obese patients should be dosed based on actual body weight (i.e., no maximum dose).

COMPATIBILITY, STABILITY

Product from the United States (Walter Reed Supply)
- Store unreconstituted vial between 2-10°C.
- Phosphate buffer diluent may be stored between 2-30°C; in colder temperatures, phosphate crystals or precipitate may form; these will dissolve if gently warmed. Diluent should only be used if solution is clear and colourless after warming.
- Stable 60 minutes after reconstitution. Discard any unused solution.

Product from China (Artesun®)
- Store manufacturer’s package containing artesunate, sodium bicarbonate and NS at room temp below 30°C. Protect from light.
- Reconstituted solution should be stored below 30°C and used within 60 minutes. Discard any unused solution.

MISCELLANEOUS
- Follow-on oral therapy with either Malarone® (atovaquone and proguanil), or quinine with either doxycycline or clindamycin is essential, and should be started at least 4 hours after the last dose of artesunate.

REFERENCES
86, 97, 98, 115, 168, 553, 554, 555, 556.

* Available via Health Canada’s Special Access Programme through the Canadian Malaria Network

Limited revision 2013, 2014, 2016, 2017
# TOH Parenteral Manual Monograph: IV Quinine

## PARENTERAL DRUG THERAPY MANUAL

<table>
<thead>
<tr>
<th>OTHER NAMES</th>
<th>NAME OF MEDICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quininject ®</td>
<td>QUININE dihydrochloride *</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CLASSIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimalarial</td>
</tr>
</tbody>
</table>

## INDICATIONS
- Treatment of severe and complicated malaria due to *Plasmodium falciparum*.
- Treatment of non-complicated malaria in patients unable to take oral therapy.

## ADMINISTRATION
- Intermittent IV infusion (preferred): for loading dose: dilute dose in 100 mL of D5W or NS (at TOH, dilute in D5W) and infuse over 30 minutes. For maintenance dose: dilute dose in 10 mL/kg of D5W or NS (at TOH, dilute in 500 mL of D5W) and administer over 2-4 hours. Must be administered by an infusion pump.
- IM: only if IV administration is not possible.

## POTENTIAL ADMINISTRATION HAZARDS
- Hypersensitivity: rash.
- Cardiovascular: cardiac conduction disturbances, hypotension.
- GI: nausea, vomiting, abdominal pain, diarrhea.
- Cinchonism: tinnitus, nausea, vertigo, headache, disturbed vision.
- Hemolysis (rare), hypoprothrombinemia, hypoglycemia.
- Local reactions: with IM use: pain, local irritation at injection site.

## DOSAGE

**Note:** Loading dose not recommended if patient received quinine or quinidine within the preceding 24 hours, mefloquine within the preceding 2 weeks, or IV quinine for non-severe malaria in a patient who cannot tolerate oral therapy.

- **Loading dose:** quinine dihydrochloride 7 mg/kg (quinine base 5.8 mg/kg) IV, immediately followed by maintenance dose.
- **Maintenance dose:** quinine dihydrochloride 10 mg/kg (quinine base 8.3 mg/kg) IV, repeated q8h until the patient can swallow and no longer meets criteria for severe malaria. Reduce quinine maintenance dose by one-third to one-half in patients requiring more than 48 hours of IV therapy.
- **IM:** (only if IV route is not possible) quinine dihydrochloride 10 mg/kg (quinine base 8.3 mg/kg) IM q8h.

## COMPATIBILITY, STABILITY
 *(Consult NAPRA compounding standards; information provided below refers to physical/chemical stability and not to sterility)*

- Store ampoules at room temp. Protect from light.
- Compatible with D5W and NS.

## MISCELLANEOUS
- Switch to oral therapy as soon as possible; minimum of 24 hours of IV quinine if treating severe malaria.
- Quinine dihydrochloride 20 mg = quinine base 16.7 mg.

## REFERENCES

5, 97, 134, 208

* Available via Health Canada’s Special Access Programme through the Canadian Malaria Network

Full revision 2018
Therapy for Severe *Falciparum* Malaria: Intravenous Artesunate

**INTRAVENTOUS ARTESUNATE**

**Generic Name:** Artesunate

**Classification:** Antimalarial; Anti-Protozoal agent; Artemisinin derivative

**Indications:** Treatment of choice for severe and complicated malaria and infections due to chloroquine-resistant or multi-drug resistant strains of malaria.

**Presentation:**

**US product (Walter Reed supply):** Artesunate 110 mg/vial; sterile powder with diluent (phosphate buffer) for reconstitution.

**Chinese product (Artesun®):** Artesunate 120 mg/vial; 1 x 2 mL amp sodium bicarbonate 50 mg/mL for reconstitution and 1 x 10 mL amp of 0.9% sodium chloride injection (normal saline or NS) per package.

**Storage:**

**US product (Walter Reed supply):** Store at 2-10 °C. Buffer may be stored at 2-30 °C (note: phosphate crystals may form in the buffer at lower temperatures; these will dissolve if gently warmed). Discard if buffer is not clear and colourless upon rewarming.

**Chinese product (Artesun®):** Store below 30°C. Protect from light.

**Reconstitution:**

**US product (Walter Reed supply):** Reconstitute each 110 mg vial of artesunate with 11 mL of phosphate buffer diluent. Gently swirl for 5 to 6 minutes for a resultant concentration of 10 mg/mL. May be mixed with 5 mL of 5% dextrose or NS prior to injection if desired.

**Chinese product (Artesun®):** Reconstitute each 120 mg vial of artesunate with the contents (2 mL) of the provided ampoule of sodium bicarbonate solvent. Shake the vial (not too vigorously) for several minutes until the powder is completely dissolved and the solution is clear. (The solution should clear in a few minutes after reconstitution.) Discard if the solution does not clear or a precipitate is present. For IV administration: Add the contents (10 mL) of the supplied ampoule of NS diluent to the vial containing the reconstituted artesunate solution. Shake to mix well. Solution should be clear. Discard if the solution appears cloudy or a precipitate is present. This will yield a concentration of artesunate of 10 mg/mL. For IM administration (only if IV access cannot be obtained): add 4 mL of the supplied NS diluent to the vial containing the reconstituted artesunate solution. Shake to mix well. Solution should be clear. Discard if the solution appears cloudy or a precipitate is present. This will yield a concentration of artesunate of 20 mg/mL.

**Stability:** Stable 1 hour after reconstitution. Discard any unused solution. Drug should be administered as soon as possible following reconstitution or further dilution.

**Compatible Fluids:** Dextrose 5% in Water, Normal Saline

**Incompatible Fluids:** Water for injection (no data).

**Product Expiration Date:**

**US product (Walter Reed supply):** Artesunate vials currently do not have a specified expiry date, as testing of the product is ongoing.
**Chinese product (Artesun®):** As per package.

**DOSAGE/ADMINISTRATION FOR SEVERE *FALCIPARUM MALARIA*:**

Currently, a 4-dose regimen of intravenous artesunate is recommended:
For adults and children weighing 20 kg and over: 2.4 mg/kg IV at 0, 12, 24 and 48 hours. (Total dose is 9.6 mg/kg). Obese patients should be dosed based on actual body weight (i.e. no maximum dose).
For children weighing less than 20 kg: 3 mg/kg IV at 0, 12, 24 and 48 hours. (Total dose is 12 mg/kg).
First dose should be administered STAT.
Each dose should be administered IV push over 1 to 2 minutes into an established IV line immediately following reconstitution of drug.
The patient may be switched to oral therapy after a minimum of 24 hours (3 doses) of artesunate IV if they are able to tolerate oral medication at that time.

For IM administration (Chinese product): Preferred site of injection is anterior thigh; depending on the volume to administer, may need to divide dose and inject in several sites.

**ADDITIONAL INFORMATION:**

- Patient should be observed for 30 minutes following administration for signs of an allergic reaction (e.g. itching, swelling, shortness of breath, chest pain, watery eyes).
- **Due to reports of delayed hemolytic anemia, patients require weekly CBCs for four weeks following treatment with artesunate.**
- Dose adjustment of artesunate is not required in renal or liver dysfunction.
- **Pregnancy:** Artesunate IV is preferred over quinine IV for the treatment of severe malaria in all trimesters of pregnancy.
- Patients who meet criteria for severe malaria should receive a minimum of 24 hours (i.e., 3 doses) of parenteral artesunate before switching to oral follow-on therapy (irrespective of the patient’s ability to tolerate oral medication earlier)
- Due to its short half-life (< 2 hours), malaria can recrudesce following treatment with artesunate IV within days to weeks unless treatment is followed with a longer acting agent. Thus, follow-on therapy with oral antimalarial agents is essential, and should be started 4 hours after the last artesunate IV dose.
- Although not routinely recommended, in emergency situations artesunate may be administered intramuscularly into the anterior thigh (e.g., in the rare event that venous access is not immediately possible.) Reconstitution instructions for the Chinese product for IM administration are provided above. For the US product (Walter Reed supply), the same preparation, dilution and dosage as for IV administration should be used.
- Unused stock must be returned to the pharmacy/distribution site.

**SECOND AGENT:**

Although rapid acting, artesunate does not completely eliminate all parasites. As a result, oral antimalarial therapy is required as follow-on therapy (see below). The oral agent(s) should be started 4 hours after the last dose of artesunate IV. Malarone® is the preferred agent (unless patient had received prophylaxis with Malarone®, is pregnant, or CrCl <30 ml/min); quinine# with either doxycycline or clindamycin are alternatives.

If, in the rare case, patients cannot tolerate oral medication following the 4 doses of artesunate, options include continuing artesunate IV daily for up to 7 days total, or switching to a 7 day course of doxycycline IV (100 mg Q12H or 2 mg/kg Q12H (max 100 mg) for pediatric (≥ 8 years old) patients; Special Access drug) or clindamycin IV (10 mg/kg loading dose, followed by approximately 5 mg/kg IV Q8H).
Choice should be made in consultation with an Infectious Diseases specialist.

**ORAL FOLLOW-ON THERAPY:**
Start either a 3-day course of Malarone® tablets* (preferred) or a 7-day course of quinine# with either doxycycline or clindamycin.

*Note: if 4 doses of IV artesunate are administered (as opposed to switching to oral after 3 doses if the patient can tolerate oral at that time), then doxycycline or clindamycin alone (without quinine) may be used as follow-on therapy in cases where Malarone® is not an appropriate follow-on option.

The recommended doses of oral agents are listed in the following table:

<table>
<thead>
<tr>
<th>Oral Antimalarial Agents: Recommended Drug Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DRUG</strong></td>
</tr>
<tr>
<td>Malarone® <em>(Atovaquone/Proguanil)</em></td>
</tr>
<tr>
<td>Adult tablet: Atovaquone 250 mg/Proguanil 100 mg per tablet</td>
</tr>
<tr>
<td>Pediatric tablet: Atovaquone 62.5 mg/Proguanil 25 mg per tab</td>
</tr>
<tr>
<td>Quinine sulphate <em>(Note: quinine sulphate 600 mg = 500 mg quinine base)</em></td>
</tr>
<tr>
<td>Doxycycline <em>(Note: Contraindicated in pregnancy, breastfeeding, and age &lt; 8 years)</em></td>
</tr>
<tr>
<td>Clindamycin <em>(Note: use only if unable to take Malarone® or doxycycline)</em></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

* While doxycycline is contraindicated during pregnancy, it may be used during breastfeeding and in children < 8 years of age for the treatment of malaria if other options (i.e., Malarone® and clindamycin) are not possible.

**ARTESUNATE ADVERSE EFFECTS:**

Artesunate is very well tolerated in adults and children. Occasional side effects include anorexia, dizziness, light headedness, taste alteration, nausea, diarrhea, reversible decrease in reticulocyte count, increased liver enzymes, bradycardia, heart block, and rare allergic reactions (e.g., urticaria, pruritis, dyspnea).

**Hemolytic anemia:** Cases of delayed hemolytic anemia (either recurrent or persistent) following use of artesunate (8 to 32 days after therapy) for severe malaria have been reported worldwide. Patients with high pre-treatment parasitemia may be at a higher risk. Although possibly attributable to the disease itself, there have been cases reported with the drug distributed through the CMN. Due to this risk, Health Canada and the CMN recommend a CBC be performed weekly for 4 weeks following treatment with parenteral artesunate to monitor patients for anemia. In addition, patients treated with artesunate IV should be counselled to report signs of hemolysis, such as dark urine, yellowing of skin or whites of eyes, fever, abdominal pain, pallor, fatigue, shortness of breath and/or chest pain.
QUININE DIHYDROCHLORIDE

Trade Name / Generic Name: Quininject / Quinine dihydrochloride

Classification: Antimalarial; Anti-Protozoal agent; Antipyretic

Indications: Treatment of severe and complicated malaria and infections due to chloroquine-resistant or multi-drug resistant strains of malaria.

Presentation: Quinine dihydrochloride 600 mg/2 mL amp.

Storage: Store below 25°C. Protect from light.

Reconstitution: Not required.

Stability: Discard any unused solution.

Compatible Fluids: Normal Saline; Dextrose 5% in Water

Incompatible Fluids: None known.

DOSAGE/ADMINISTRATION FOR SEVERE FALCIPARUM MALARIA:

Note: mg/kg dosage is the same for children and adults
Base dose on ideal body weight (IBW) in obesity

LOADING DOSE:
Requires administration via IV pump:
- Quinine dihydrochloride 7 mg/kg IBW (equivalent to quinine base 5.8 mg/kg)
- Diluted in 100 mL of isotonic fluid (D5W preferred) by intravenous infusion over 30 minutes, then start maintenance dose.
- Commence maintenance dose immediately after loading dose.

EXCEPTIONS FOR LOADING DOSE:
- Loading dose should NOT routinely be administered if patient has received quinine or quinIDine within the proceeding 24 hours, or a dose of mefloquine within the preceding 2 weeks due to the risk of cumulative toxicity
  - Maintenance dosing should be used for these patients.
  - If history is unclear, and/or if benefits of a loading dose are felt to outweigh the risk, cardiac monitoring is recommended.
- A loading dose is NOT required if quinine IV is used in patients without severe malaria whose only indication for parenteral anti-malarial is vomiting or inability to tolerate oral therapy.
MAINTENANCE DOSE:
- Quinine dihydrochloride 10 mg/kg IBW (equivalent to quinine base 8.3 mg/kg)
  - Diluted in 10 mL/kg of isotonic fluid (D5W preferred) by intravenous infusion over 4 hours.
  - Repeat every 8 hours until indication (e.g., % parasitemia, minimum of 24 hours of therapy if severe malaria) for IV quinine therapy no longer exists and/or patient can swallow, then switch to oral therapy to complete treatment course (see below).
  - If patient requires more than 48 hours of parenteral therapy and patient remains severely ill or continues to have acute renal injury, change dosing interval to Q12H after 48hrs. Full dose can be continued if patient is receiving dialysis.

ADDITIONAL INFORMATION:
- Intravenously, the drug should be given slowly (maximum rate 5 mg/kg salt per hour; exception: 7 mg/kg loading dose above) to avoid the risk of cardiovascular toxicity; pulse and blood pressure should be closely monitored and the rate of infusion attenuated if dysrhythmias occur.
- Due to the limited supply of artesunate IV, quinine IV is recommended for use (providing no contra-indications) in patients without severe malaria whose only indication for parenteral anti-malarial is vomiting or inability to tolerate oral therapy.
- Replace with oral therapy as soon as possible (see exception below).
- If quinine IV is prescribed for a patient who meets criteria for severe malaria, a minimum of 24 hours of parenteral therapy (i.e., 3 maintenance doses) should be administered before switching to oral therapy (irrespective of their ability to tolerate oral medication earlier)
- Therapy should be withdrawn immediately if signs of haemolysis appear.
- There are a number of side effects linked to quinine administration, known as cinchonism. Hypersensitive patients may react in this way even to small doses.
- Intramuscular administration should be used only as a last resort, since it is highly irritating and may cause focal necrosis and abscess formation.
- Parenteral quinidine should be used only if parenteral quinine is unavailable; cardiac monitoring is required.

QUININE ADVERSE EFFECTS:
Cinchonism (tinnitus, impaired hearing, headache, nausea, disturbed vision, vomiting, abdominal pain, diarrhea, vertigo), hypersensitivity (urticaria, pruritus, skin flushing, thrombocytopenia), fever, rashes, dyspnea, angioedema, precipitation of asthma, haemoglobinuria, hypoglycaemia (quinine-induced hyperinsulinaemia), hypoprothrombinaemia, renal failure, cardiotoxicity (dysrhythmias, asystole, hypotension, anginal symptoms), CNS disturbances, oculotoxicity (sudden blindness), injection site (abscess, focal necrosis and pain after IM administration).

PRECAUTIONS:
- Check for hypersensitivity to quinine or quinidine before administration.
- Use with caution in patients with a history of cardiovascular disease, renal dysfunction, glucose-6-phosphate dehydrogenase deficiency, asthma or atopy, or myasthenia gravis.
- Monitor vital signs, blood glucose, and ECG if history of underlying cardiac disease.
- Avoid rapid injection.
- In seriously ill patients with renal failure, maintain the full dosage regimen for at least 48 hours.
SECOND AGENT:

A second agent (doxycycline or clindamycin) should be started either concurrently with quinine IV or as soon as possible when patient can take oral therapy. If this is not possible, IV doxycycline (100 mg Q12H or 2 mg/kg Q12H (max 100 mg) for pediatric (≥ 8 years old) patients; Special Access drug) or IV clindamycin (10 mg/kg loading dose, followed by approximately 5 mg/kg IV Q8H) may be prescribed.

STEPDOWN THERAPY:

Stepdown to oral therapy as soon as possible with either a 3 day course of Malarone® tablets (preferred, unless patient had received prophylaxis with Malarone®, is pregnant, or CrCl <30 ml/min) or oral quinine with either doxycycline or clindamycin to complete 7 day course.

The recommended doses of oral agents are listed in the following table:

### Oral Antimalarial Agents: Recommended Drug Doses

<table>
<thead>
<tr>
<th>DRUG</th>
<th>ADULT DOSE</th>
<th>PEDIATRIC DOSE</th>
</tr>
</thead>
</table>
| Malarone® (Atovaquone/Proguanil) | 4 adult tablets (taken all at once with food) daily for 3 days             | According to weight:  
| Adult tablet: Atovaquone 250 mg/Proguanil 100 mg per tablet |                                            | 5-8 kg: 2 pediatric tablets daily x 3 days  
| Pediatric tablet: Atovaquone 62.5 mg/Proguanil 25 mg per tab |                                            | 9-10 kg: 3 pediatric tablets daily x 3 days  
| Quinine sulphate (Note: quinine sulphate 600 mg = 500 mg quinine base) | 600 mg orally Q8H for 7 days                                                   | 11 – 20 kg: 1 adult tablet daily x 3 days  
| Doxycycline (Note: Contraindicated in pregnancy, breastfeeding, and age < 8 years)* | 100 mg BID for 7 days                                                         | 21 – 30 kg: 2 adult tablets daily x 3 days  
| Clindamycin (Note: use only if unable to take Malarone® or doxycycline) | 300 mg q6h for 7 days                                                        | 31 – 40 kg: 3 adult tablets daily x 3 days  
|                                                                                       |                                                            | > 40 kg: 4 adult tablets daily x 3 days                                               |

* While doxycycline is contraindicated during pregnancy, it may be used during breastfeeding and in children < 8 years of age for the treatment of malaria if other options (i.e., Malarone® and clindamycin) are not possible.
SECTION 6: Sample Orders / Forms

Admission Orders for Patients with Malaria

1) Diagnosis: ______________________(species) malaria; _____% parasitemia
2) Admit to:__________________ (Admit to ICU if criteria for severe malaria met—(See Table)
3) Consult Infectious Disease Service
4) Begin Drug Therapy STAT (According to disease category)
5) Vital signs and neurovitals Q4H x 24 hours, then reassess.
6) Activity:
7) Diet:
8) Notify physician and do STAT glucose if patient’s level of consciousness deteriorates.
9) Blood glucose by point of care testing q4h for 24 hours, then reassess. Hypoglycemia may be treated as per the ‘Subcutaneous Insulin Administration’ standard orders.
10) O₂ saturation q4h X 24 hours, then reassess. If O₂ saturation is less than 92%, notify physician
11) IV fluids: _______________________; run at _____________ ml/hr.
12) Intake/output x 24 hrs, then reassess.
13) Limit IV fluid intake (excluding volume used to administer IV quinine, if applicable) to 1.5 to 2 litres per 24 hrs during the first 48-72 hrs due to risk of ARDS.
14) Baseline laboratory investigation upon admission: (already have thick and thin films, RDT) 
   STAT:  blood cultures X 2 if not already performed 
   CBC with differential 
   Na, K, Cl, Serum Creatinine (Scr), urea, AST, ALT, LDH, Tbili, LDH, glucose 
   Urine R&M
15) Repeat CBC, Na, K, Cl, Scr, urea, AST, ALT, LDH, Tbili, glucose QAM x 3 days, or longer while on IV antimalarial.
16) Send blood for G6PD test (EDTA purple stopper tube). Note result may take up to 3 days.
17) Repeat malaria smears (thick and thin) Q12H X 24 hours, then daily X 2
18) Repeat malaria smears (thick and thin) on day 7 of admission, and if symptoms (e.g., fever) recur. If patient is discharged from hospital, please provide requisitions for blood smears upon discharge, with results to Tropical Medicine Clinic.
19) Forms A and B must be filled if IV artesunate or IV quinine is used (sent with drug supply)

20) Provide outpatient requisitions for CBC weekly x 4 weeks if patient received IV artesunate.

21) Book outpatient follow-up appointment for 1 week after discharge with Tropical Medicine Clinic, (tel: 613-798-5555 ext 19388 or fax 613-761-5260).
Antimalarial Drug Therapy Orders for Patients with Malaria

Patient Weight: _________ kg

Falciparum Malaria or Species Unknown:

Severe malaria: *Criteria for severe malaria met (see Table 1, p.7):*

Begin IV drug therapy STAT—Do not delay initiation of IV antimalarial if awaiting transfer to ICU/ward

- Artesunate IV (drug of choice, including during pregnancy):
  - 2.4 mg/kg = _________ mg IV direct STAT, then Q12H x 2 doses. Assess patient for oral therapy after 3rd dose. If patient cannot take oral therapy, administer a 4th dose of IV Artesunate (2.4 mg/kg) 24 hours after the previous dose. Then reassess patient for a switch to oral therapy. *Attending team to contact ID if patient cannot tolerate oral therapy after 4th artesunate dose.*
  
  In pregnancy, administer all 4 doses of artesunate IV before changing to oral therapy. Dose based on total body weight.

- If / when oral therapy is possible after 3rd or 4th dose, change to:
  - Malarone® (Atovaquone/Proguanil) 4 tablets PO daily x 3 days; (must be administered with fatty food or high fat milk)
    
    If Malarone® contraindicated (e.g., CrCl less than 30 mL/min or patient received Malarone® prophylaxis or pregnant), then
    
    - Doxycycline 100 mg PO q12h X 7 days*, administer with food and full glass of water (preferred regimen, unless pregnant/breastfeeding)
    - OR Clindamycin 450 mg PO q6h x 7 days* (use only if cannot take doxycycline, or if pregnant/breastfeeding)

*If patient received less than 4 doses of artesunate, add quinine to doxycycline or clindamycin:

- Quinine sulphate 600 mg PO q8h x 7 days

- Start oral therapy four hours after last dose of Artesunate IV

Severe malaria and artesunate contraindicated:

- Quinine dihydrochloride IV :
  - Loading dose: 7 mg/kg = ________ mg IV in 100 mL D5W over 30 minutes STAT
  - Maintenance dose: 10 mg/kg = ________ mg IV q8h in 500 mL D5W; **start immediately** after loading dose; **infuse each dose over 4 hours**
  
  Dose based on ideal body weight in obese patients.

  **Omit loading dose if patient received Quinine or Quinidine in the previous 24 hours or a dose of Mefloquine in previous 2 weeks**

- After 24 hours of IV quinine therapy, assess patient for oral therapy. When oral therapy is possible, change to:
  - Malarone® (Atovaquone/Proguanil) 4 tablets PO daily x 3 days (must administer with fatty food or high-fat milk)
If Malarone® contraindicated (e.g., CrCl less than 30 mL/min or patient received Malarone® prophylaxis or pregnant), then

- Quinine sulphate 600 mg PO q8h to complete 7 days of therapy, with Doxycycline 100 mg PO q12h x 7 days; administer with food and full glass of water (preferred regimen, unless pregnant/breastfeeding)

OR

- Quinine sulphate 600 mg PO q8h to complete 7 days of therapy, with Clindamycin 300 mg PO q6h x 7 days (use only if cannot take doxycycline, or if pregnant/breastfeeding)

*If patient remains severely ill and cannot receive oral therapy at 48 hours, order new maintenance dose of Quinine dihydrochloride 10 mg/kg IV q12h and start Clindamycin 600 mg IV q8h.*

**Non-severe malaria, but patient cannot tolerate oral therapy:**

- Quinine dihydrochloride IV:
  
  10 mg/kg = ______ mg IV q8h in 500 mL D5W; **first dose STAT**;

  infuse each dose over 4 hours

  **Dose based on ideal body weight in obese patients.**

  - Change to oral therapy as soon as patient can tolerate PO:

    - Malarone® (Atovaquone/Proguanil) 4 tablets PO daily x 3 days (must administer with fatty food or high-fat milk)

If Malarone® contraindicated (e.g., CrCl less than 30 mL/min or patient received Malarone® prophylaxis or pregnant), then

- Quinine sulphate 600 mg PO q8h to complete 7 days of therapy, with Doxycycline 100 mg PO q12h x 7 days; administer with food and full glass of water (preferred regimen, unless pregnant/breastfeeding)

OR

- Quinine sulphate 600 mg PO q8h to complete 7 days of therapy, with Clindamycin 300 mg PO q6h x 7 days (use only if cannot take doxycycline, or if pregnant/breastfeeding)

**Non-severe malaria and patient can tolerate oral therapy:**

**First dose STAT**

- Malarone® (Atovaquone/Proguanil) 4 tablets PO daily x 3 days; (must administer with fatty food or high fat milk)

If Malarone® contraindicated (e.g., CrCl less than 30 mL/min or patient received Malarone® prophylaxis or pregnant), then

- Quinine sulphate 600 mg PO q8h x 7 days, with Doxycycline 100 mg PO q12h X 7 days; administer with food and full glass of water (preferred regimen, unless pregnant/breastfeeding)
Quinine sulphate 600 mg PO q8h x 7 days, with Clindamycin 300 mg PO q6h X 7 days (use only if cannot take doxycycline, or if pregnant/breastfeeding)

**Non-Falciparum Malaria**

- Chloroquine phosphate 1000 mg (4 x 250 mg tablets) PO STAT, then 500 mg (2 tablets) 6 hours later, then 500 mg (2 tablets) daily X 2 days (Note: chloroquine phosphate 250 mg tablet is equivalent to 155 mg chloroquine base)

  *If G6PD level is documented as normal & patient is not pregnant/breastfeeding, start*

- Primaquine base 30 mg (2 x 15 mg tablets) PO daily x 14 days (administer with food)

If patient cannot tolerate chloroquine, or chloroquine not available, then:

- Malarone® (Atovaquone/Proguanil) 4 tablets PO daily x 3 days; (must administer with fatty food or high fat milk)

  *If G6PD level is documented as normal & patient is not pregnant/breastfeeding, start*

- Primaquine base 30 mg (2 x 15 mg tablets) PO daily x 14 days (administer with food)

*If at any time, any oral antimalarial medication is vomited within 60 minutes of administration, repeat the full dose. If vomiting recurs, call physician to change to parenteral therapy.*
Canadian Malaria Network (CMN) Form A & B (English & French)

(See below)
CANADIAN MALARIA NETWORK
FORM A - MANDATORY INITIAL ASSESSMENT FORM
To be completed by the Attending Physician with use of parenteral therapy for severe malaria

1. Date of request (D/M/Y): ____/____/____

2. Drug requested (check all that apply):
   - [ ] US Artesunate* (USA Product) LOT# AA-241-1-10-01
   - [ ] Chinese Artesunate* (Chinese Product) LOT#__________
   - [ ] Quinine LOT#__________
   - [ ] Mefloquine
   *For artesunate request, monitor CBC weekly for four weeks. Low risk for delayed hemolysis; if this occurs, the CMN must be notified

3. REQUESTING/ATTENDING PHYSICIAN
   Name: ____________________________
   Hospital/site: ____________________________
   City: ____________________________ Province: ____________________________
   Tel#: ____________________________ Fax#: ____________________________
   Email: ____________________________ (required)

4. PATIENT DEMOGRAPHICS
   Initials (first/middle/last): __________/________/________
   Date of birth (D/M/Y): ______/____/____
   Sex: [ ] Male [ ] Female, Pregnant: [ ] Yes [ ] No
   Birth Country: ____________________________
   If <18 years, country of parental origin: ____________________________
   Canadian Resident?: [ ] Yes [ ] No
   Visitor?: [ ] Yes [ ] No

5. PATIENT TRAVEL INFORMATION
   Presumed country(ies) of acquisition:
   1) ______ 2) ______ 3) ______
   Date departed Canada (D/M/Y): ______/____/____
   Date returned in Canada (D/M/Y): ______/____/____
   Reasons for travel (check all that apply):
   - [ ] Visiting friends/relatives
   - [ ] Volunteer/missionary
   - [ ] Business
   - [ ] Education
   - [ ] Vacation
   - [ ] Medical tourism
   - [ ] Immigration
   - [ ] Military
   Other, specify ____________________________

6. PREVENTION MEASURES
   Pre-travel advice sought: [ ] Yes [ ] No
   If yes, with whom?:
   - [ ] GP/family physician
   - [ ] Travel medicine clinic
   Other: ____________________________
   Insect precautions?: [ ] Yes [ ] No [ ] Unknown
   Was chemoprophylaxis...
   Suggested?: [ ] Yes [ ] No [ ] Unknown
   Prescribed?: [ ] Yes [ ] No [ ] Unknown
   Used?: [ ] Yes [ ] No [ ] Unknown
   If used, chemoprophylaxis type:
   - [ ] Chloroquine
   - [ ] Doxycycline
   - [ ] Malarone
   - [ ] Mefloquine
   Other (specify): __________
   Adherence: Did they take the drug as prescribed (before, during, after travel, missed <2 doses)?
   - [ ] Yes [ ] No [ ] Unknown

7. PATIENT ILLNESS
   Date became ill (D/M/Y): ______/____/____
   Date of 1st physician visit (D/M/Y): ______/____/____
   Was the patient admitted to hospital?: [ ] Yes [ ] No
   If yes, date admitted (D/M/Y): ______/____/____

8. DIAGNOSIS
   Diagnosis lab-confirmed: [ ] Yes [ ] No
   Date (D/M/Y): ______/____/____
   Test used (check all that apply): [ ] RDT [ ] Thick smear
   [ ] Thin smear [ ] Other (specify): ____________________________
   Malaria species (check all that apply):
   - [ ] P. falciparum
   - [ ] P. vivax
   - [ ] P. ovale
   - [ ] P. knowlesi
   - [ ] P. malariae
   - [ ] P. malariae
   - [ ] P. ovale
   - [ ] P. knowlesi
   - [ ] P. malariae
   Percent parasitemia (initial): ______ %
   Percent parasitemia (at start of IV therapy): ______ %

9. Has the patient had other medical treatment for this episode of malaria?
   - [ ] Yes [ ] No [ ] Unknown
   If yes, specify what drug(s):
   [ ] MD in Canada [ ] MD in country of acquisition
   [ ] Self prescribed [ ] Other (specify): ____________________________

10. Indication for use of IV antimalarial therapy (check all that apply):
    - [ ] Continuous vomiting or unable to tolerate oral therapy (Note: this is the only indication for IV therapy, then QUININE preferred)
    - [ ] Hyperparasitemia (i.e., ≥2% in children <5 yrs; older children & adults: ≥5% if non-immune; ≥10% if semi-immune)
    - [ ] Impaired consciousness or coma
    - [ ] Prostration (unable to walk or sit up without assistance)
    - [ ] Multiple convulsions (>2 in 24hrs)
    - [ ] Respiratory distress (acidoic breathing)
    - [ ] Respiratory failure / Pulmonary edema / ARDS
    - [ ] Circulatory collapse / shock (SBP<80mmHg in adults and <50mmHg in children)
    - [ ] Acute kidney injury / renal failure (Cr >265µmol/L or >upper limit for age for children)
    - [ ] Jaundice (Total bilirubin >45µmol/L)
    - [ ] Abnormal spontaneous bleeding/DIC
    - [ ] Hypoglycemia (<2.2mmol/L)
    - [ ] Metabolic Acidosis / Acidemia (pH<7.25, HCO3<15mmol/L)
    - [ ] Severe anemia (Hb <70g/L in adults and <50g/L in children)
    - [ ] Hemoglobinuria (macroscopic)
    - [ ] Hyperlactataemia (lactate >5mmol/l)
    - [ ] Other (specify): ____________________________

11. The following refer to time taken to begin IV therapy and is used to establish where/why delays occurred:
    a) Hours to contact individual responsible for dispensing IV therapy through the Canadian Malaria Network (#hours): ______
    b) Hours from request until drug received by pharmacy (#hours): ______
    c) Hours from time received in pharmacy until drug administered (#hours): ______
    d) Comments/perceived reasons for delay(s), if any: ____________________________

12. Other Comments:

Completed by: ____________________________
Date: ______/____/____ Tel #: ____________________________
Email: ____________________________

Thank you very much for completing this form.
Please complete Form B (follow-up) and send it in.

Version: December 2017

Please complete and return to the CMN Coordinating Centre within 24 hours of starting IV drug treatment by e-mail: canadianmalarianetwork@toh.on.ca or by fax: 613-761-5260.
Parenteral artesunate and quinine are provided by Health Canada’s Special Access Program through the Canada Malaria Network (CMN)
Veuillez remplir ce formulaire et le retourner au centre de coordination du RCP par courriel, à canadianmalarianetwork@toh.on.ca, ou par télécopieur, au 613-761-5260

L’artésunate et la quinine pour administration parentérale sont fournis par le Programme d’accès spécial de Santé Canada, par l’entremise RCP.

Version: décembre 2017
CANADIAN MALARIA NETWORK
FORM B- MANDATORY FOLLOW UP FORM
To be completed by the Attending Physician following the use of parenteral therapy for severe malaria

1. Follow-up Visit Date (D/M/Y): __________/________/________

2. REQUESTING/ATTENDING PHYSICIAN
   Name: ________________________________________________
   Hospital/site: __________________________________________
   City: ___________________________ Province: _____________
   Tel#: __________________________ Fax#: _____________________
   Email: ________________________________________________ (required)

3. PATIENT DEMOGRAPHICS
   Initials (first/middle/last): __________/________/________
   Date of birth (D/M/Y): __________/________/________
   Sex: ☐ Male ☐ Female

4. TREATMENT
   Date diagnosed (D/M/Y): __________/________/________
   Date IV drug requested (D/M/Y): __________/________/________
   Drug requested (check all that apply):
   ☐ Artesunate  ☐ Quinine
   Date of 1st IV drug dose (D/M/Y): __________/________/________
   Number of doses of IV drug administered: __________
   Number of vials of IV drug used:
   _______ Vials of US Artesunate* (US Product)
   Lot AA-241-1-10-01
   _______ Vials of Chinese Artesunate* (Chinese Product)
   Lot# ________________________________
   _______ Ampoules of Quinine
   Lot # ________________________________

   Step-down therapy or second antimalarial
   (please specify and give number of days of therapy):
   ☐ Clindamycin (#days): __________________________
   ☐ Doxycycline (#days): __________________________
   ☐ Malarone (#days): __________________________
   ☐ Quinine oral (#days): __________________________
   ☐ Other (specify): ____________________ (#days): ________

5. MALARIA OUTCOMES
   Malaria complications developed during admission
   (check all that apply):
   ☐ Hyperparasitemia (i.e., ≥2% in children <5 yrs; older children & adults: ≥5% if non-immune; ≥10% if semi-immune)
   ☐ Impaired consciousness or coma
   ☐ Prostration (unable to walk or sit up without assistance)
   ☐ Multiple convulsions (>2 in 24hrs)
   ☐ Respiratory distress (acidotic breathing)
   ☐ Respiratory failure/Pulmonary edema/ARDS
   ☐ Circulatory collapse/shock (SBP<80mmHg in adults and <50mmHg in children)
   ☐ Acute kidney injury/renal failure (Cr >265µmol/L or >upper limit for age for children)
   ☐ Jaundice (Total bilirubin >45µmol/L)
   ☐ Abnormal spontaneous bleeding/DIC
   ☐ Hypoglycemia (<2.2mmol/L)
   ☐ Metabolic Acidosis/Acidemia (pH<7.25, HCO3<15m
   ☐ Severe anemia (Hb<70g/L in adults/ <50g/L in children)
   ☐ Hemoglobinuria (macroscopic)
   ☐ Hyperlactataemia (lactate >5mmol/l)
   ☐ Hemolysis
   ☐ Sepsis (specify organism):
   ☐ Multiorgan Failure
   ☐ Other (specify):

   Maximum parasitemia level recorded: __________ %
   Days until negative smear achieved: __________
   Total number of days hospitalized: __________
   Total number of days in ICU: __________

   Supportive treatments:
   ☐ Dialysis, (#days): __________________
   ☐ Mechanical ventilation, (#days): __________
   ☐ Blood transfusion, (#units): __________
   ☐ Antibiotics (specify): __________________________
   ☐ Other (specify): __________________________

   Patient outcome as of today (check all that apply):
   ☐ Alive
   ☐ Still hospitalized
   ☐ Discharged on date (D/M/Y): __________/________/________
   ☐ Deceased on date (D/M/Y): __________/________/________

   Were there any complications or adverse events related to the IV antimalarial drug?: ☐ Yes ☐ No
   If yes, please complete the CMN Suspected Adverse Reaction Form and briefly specify event below:
   __________________________________________________________
   __________________________________________________________
   __________________________________________________________

6. CANADIAN MALARIA NETWORK EVALUATION
   Is this program to provide IV malaria therapy helpful to you? ☐ Yes ☐ No
   Did you consult with a physician through the Canadian Malaria Network? ☐ Yes ☐ No
   If yes, was this a beneficial interaction? ☐ Yes ☐ No
   Comments: __________________________________________________________
   __________________________________________________________
   __________________________________________________________
   Suggestions to improve the program:
   __________________________________________________________
   __________________________________________________________
   __________________________________________________________
   Other Comments: __________________________________________________________
   __________________________________________________________
   __________________________________________________________
   Completed by: ________________________________
   Date: __________/________/________ Tel #: ________________________________
   Email: ________________________________________________

Version: December 2017

Please complete and return to the CMN Coordinating Centre on day 7 following start of IV drug treatment by e-mail: canadianmalarianetwork@toh.on.ca or by fax: 613-761-5260
Parenteral artesunate and quinine are provided by Health Canada’s Special Access Program through the Canada Malaria Network (CMN).
RÉSEAU CANADIEN SUR LE PALUDISME
FORMULAIRE B - FORMULAIRE APRÈS LE TRAITEMENT

A remplir par le médecin traitant après l’administration d’un traitement parentéral contre le paludisme grav

13. Date de suivi (J/M/A): ____/____/____

14. MéDECIN DEMANDEUR/TRAITANT
Nom: _____________________________
Hôpital/Établissement: ___________________________
Ville: ____________________________ Province: _____________________________
Tél#: ____________________________ Fax#: _____________________________
Courriel: __________________________

15. DONNÉES DÉMOGRAPHIQUES DU PATIENT
Initiales (1er prénom/2e prénom/nom de famille): ___________ ___________ ___________
Date de naissance (J/M/A): ____/____/____
Sexe: ❑ Masculin ❑ Féminin

16. TRAITEMENT
Date du diagnostic (J/M/A): ____/____/____
Date de la demande du médicament IV (J/M/A): ____/____/____
Médicament requis (cocher aux endroits appropriés):
❑ Artésunate ❑ Quinine
Date de la 1re dose du médicament IV (J/M/A): ____/____/____
Nombre de doses IV administrées: ________________________
Nombre de flacons IV utilisés:
Artésunate: ________________________
Quinine: ________________________

Traitements régressif ou deuxième traitement antipaludéen (veuillez préciser le traitement et indiquer le nombre de JOURS du traitement):
❑ Clindamycine (#jours): ________________________
❑ Doxycycline (#jours): ________________________
❑ Malarone (#jours): ________________________
❑ Quinine orale (#jours): ________________________
❑ Autre (préciser): ________________________ (#jours): ________________________

17. EFFETS DU PALUDISME
Complications du paludisme développés lors de l'admission (cocher aux endroits appropriés):
❑ Hyperparasitémie (i.e., enfants<5 ans: ≥2%; enfants plus vieux et adultes: ≥5% si non-immun et ≥10% si semi-immun)
❑ Trouble de conscience ou coma
❑ Prostration (incapable de marcher ou s’asseoir sans aide)
❑ Multiples convulsions (≥2 crises en 24 heures)
❑ Détresse respiratoire (acidose respiratoire)
❑ Arrêt respiratoire / œdème pulmonaire/SDRA
❑ collapsus circulatoire / état de choc (PAS<80mmHg chez les adultes et <50mmHg chez les enfants)
❑ Lésions rénales aigües / insuffisance rénale (Créat.>265 µmol/L ou limite supérieure selon l’âge chez les enfants)
❑ Ictère (bilirubine totale>45 µmol/L)
❑ Saignements spontanés anormaux / CIVD
❑ Hypoglycémie (<2,2mmol/L)
❑ Acidose métabolique / acidémie (pH<7,25, HCO3<15 mmol/L)
❑ Anémie grave (Hb<70g/L chez les adultes et <50g/L chez les enfants)
❑ Hémoglobinurie (macroscopique)
❑ Hyperlactatémie (lactate>5mmol/L)
❑ Hémolyse
❑ Sepsis (préciser l’organisme): ________________________
❑ Défaillance multisystémique
❑ Autre (préciser): ________________________
Parasitémie maximal enregistré: ___________%
Nombre de jours avant un résultat négatif au frottis: _________
Nombre de jours d’hospitalisation: ________________________
Nombre de jours aux soins intensifs: ________________________

18. ÉVALUATION DU RCP
Ce programme visant à fournir un traitement antipaludéen IV vous est-il utile? ❑ Oui ❑ Non
Avez-vous consulté un médecin par l’entremise du Réseau canadien sur le paludisme? ❑ Oui ❑ Non
Si oui, vos échanges ont-ils été fructueux?
❑ Oui ❑ Non
Commentaires: ________________________
Suggestions pour améliorer le programme: ________________________
Complété par: ________________________
Date: ____/____/____ Tél #: ________________________
Courriel: ________________________

MERCI D’AVOIR REMPLI CE FORMULAIRE. NOUS VOUS REMERCIIONS GRANDEMENT DE VOTRE COLLABORATION.

Version: décembre 2017
SECTION 8: References


SECTION 9: Internet Resources

1. **Canadian Malaria Guidelines:**
   Committee to Advise on Tropical Medicine and Travel (CATMAT). Canadian recommendations for the prevention and treatment of malaria. 2014
   

2. **Malaria Diagnosis & Treatment in the United States.**
   Centers for Disease Control and Prevention.
   
   Available at: [http://www.cdc.gov/malaria/diagnosis_treatment/index.html](http://www.cdc.gov/malaria/diagnosis_treatment/index.html)

3. **World Health Organization Guidelines:**
   

4. **World Health Organization Severe Malaria Guidelines**
   

5. **Canadian Malaria Network (CMN) via Department of Medicine Website**
   CMN contact list and forms A&B, Available at: [http://thinkottawamedicine.ca/clinical-care/canadian-malaria-network/](http://thinkottawamedicine.ca/clinical-care/canadian-malaria-network/)