The Ottawa Hospital | L'Hôpital d'Ottawa

Canadian Malaria Network
Réseau canadien sur le paludisme

Canadian Malaria Network
Standard Operating Procedures

Date of Issue: May 2015

Agency Name: Canadian Malaria Network

Umbrella Organization: The Ottawa Hospital

Lead Contact: Dr. Anne McCarthy

This is the SOP for the Health PEI (satellite of CHU Dr-Georges-L-Dumont) CMN Site

(E.g. National Coordinating Site)

Affiliated Satellite Sites: Not Applicable

To find distributing CMN sites or to **OBTAIN PARENTERAL THERAPY** please visit our website http://thinkottawamedicine.ca/clinical-care/canadian-malaria-network/ and click the 'CMN Pharmacy & Physician Contact List' OR email any inquires to candianmalarianetwork@toh.on.ca

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PURPOSE

Malaria continues to be a major cause of death worldwide and is the principal life-threatening infection facing Canadian travellers in malaria-endemic areas. Severe *P. falciparum* malaria infections may have a mortality rate of 20% or higher. Patients require immediate hospitalization and urgent, intensive medical management, including parenteral malaria therapy. Severe malaria is not a common disease in Canada, with an average of 25 cases per year (range 7 - 61 cases annually from 2001-2014). However, these cases are dispersed throughout Canada, and attest to the need for distribution of scarce antimalarial drugs for treatment of severe malaria across the country.

Artesunate, the preferred medication for the treatment of severe malaria due to *P. falciparum,* and quinine, a possible alternative when artesunate is contraindicated, are only available in Canada through Health Canada's Special Access Program, a program that allows practitioners to request access to drugs that are unavailable for sale in Canada. Although quinidine is equally efficacious in treating malaria, it is not recommended due to a risk of life-threatening cardiotoxicity and the requirement for cardiac monitoring.

The Canadian Malaria Network was created in collaboration with Health Canada's Special Access Program and the Public Health Agency of Canada due to the potential for adverse outcomes associated with delays in acquiring parenteral malaria therapy. The Canadian Malaria Network (CMN) is established in 13 medical centres across Canada and maintains rapid access to strategically-located supplies of intravenous artesunate and quinine for the treatment of severe *P. falciparum*. In addition, each of the participating centers has a designated physician with experience in treating malaria who is willing to assist and provide guidance in the management of malaria infections. These life-saving drugs are available 24 hours per day by contacting participating pharmacies. After-hours medical assistance can be obtained by contacting the infectious disease consultant on call at the respective center. Each Centre provides surveillance data to Health Canada on all malaria cases treated with these drugs.

HISTORY

Quinine

From the inception of the Canadian Malaria Network in 2001, IV quinine was made available through the Canadian Malaria Network in collaboration with Health Canada's Special Access Program. Artesunate (see below) is now the treatment of choice for severe malaria, however, Quinine should be used if artesunate cannot be tolerated OR when the only indication for parenteral therapy is VOMITING or failure to tolerate oral therapy.

Artesunate

"*On June 21, 2007, the Food and Drug Administration (FDA) approved investigational new drug (IND) protocol #76,725, entitled Intravenous Artesunate for Treatment of Severe Malaria in the United States. This IND makes a new class of antimalarial medication, artemisinins, available in the United States for the first time. The Walter Reed Army Institute of Research (WRAIR) has been conducting studies in several countries using artesunate, and has agreed to provide a supply of this medication to CDC*".[1]

In 2009, through Health Canada's Special Access Program, the WRAIR began to supply the Canadian Malaria Network with IV-Artesunate. It is the same product supplied by the U.S. Centers for Disease Control.

The drug is supplied on the condition that it is used in accordance with the latest information available. Data surrounding its usage and effects (contained on Form A and Form B) are sent to WRAIR and Health Canada, as per the requirements of Health Canada's Special Access Program[2].

[1]CDC. Artesunate is available to treat severe malaria in the United States. http://www.cdc.gov/malaria/diagnosis_treatment/artesunate.html , Accessed March 13, 2014.

[2] Health Canada. Special Access Program. http://www.hc-sc.gc.ca/dhp-mps/acces/drugs-drogues/index-eng.php. Accessed March 13, 2014.

EPIDEMIOLOGY

Global

Malaria is widespread in tropical and subtropical regions around the equator, including much of Sub-Saharan Africa, Asia, and the Americas. According to the latest estimates, there were about 219 million cases of malaria in 2010 and an estimated 660,000 deaths. Malaria mortality rates have fallen by more than 25% globally since 2000. Most deaths occur among children living in Africa where a child dies every minute from malaria.

Canadian

The chart below summarizes the information available for Malaria in Canada.

Year	# Malaria Cases Reported to Public Health Agency of Canada	# Severe Malaria Cases Accessing IV Drugs through the CMN
2001	430	15
2002	347	7
2003	365	13
2004	375	20
205	365	12
2006	333	16
2007	384	16
2008	372	20
2009	356	23
2010	514	34
2011	517	30
2012	477	33
2013	-	54
2014	-	61
Total (2001-2014)	4835	354

Note: The number of malaria cases reported to the Public Health Agency of Canada in 2013 and 2014 has not been published.

Figure I: Country of Origin of severe malaria cases 2001-2013

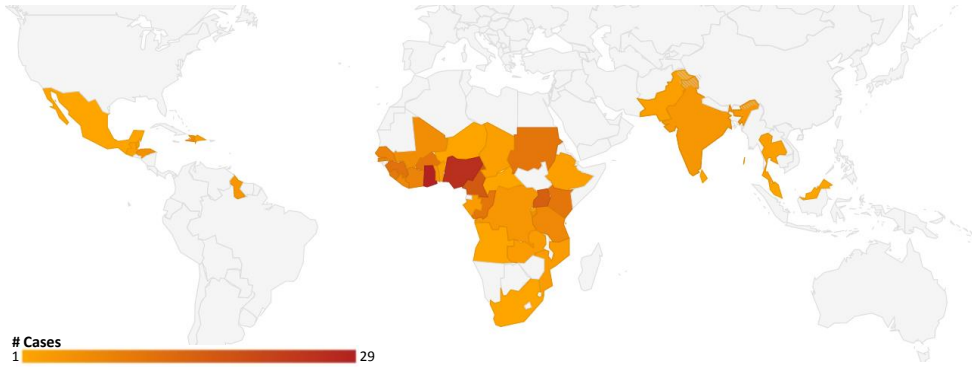
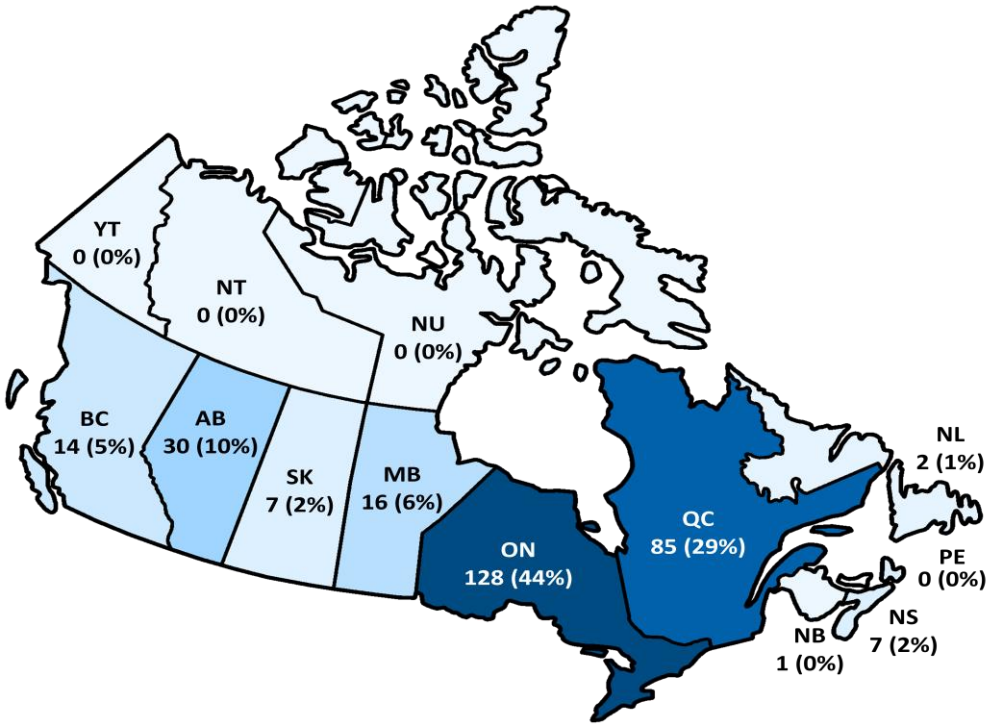


Figure II: WHO Defined Severe Malaria Cases Reported to CMN in Canada 2001-2014



MALARIA QUICK REFERENCE

Prevention

Summary of recommendations for the prevention of malaria by the Committee to Advise on Tropical Medicine and Travel (CATMAT). *(2014).* Canada Communicable Disease Report CCDR. Volume 40-7.

Diagnosis & Treatment

Summary of recommendations for the diagnosis and treatment of malaria by the Committee to Advise on Tropical Medicine and Travel (CATMAT). *(2014).* Canada Communicable Disease Report CCDR. Volume 40-7.

DEFINITIONS

Site – A hospital pharmacy that is designated with the duty of ordering IV antimalarial drugs from the CMN National Coordinating Pharmacy. Sites are typically located in large urban centres where the majority of severe malaria cases present. Sites are given enough drug to cover the population they operate within as well as supply satellite's with drug.

Satellite – A hospital pharmacy that carries one treatment regimen of IV antimalarial medication, and orders its drugs from the designated Site.

Special Access Program[3] - The Health Canada Special Access Programme (SAP) allows practitioners to request access to drugs that are unavailable for sale in Canada. This access is limited to patients with serious or life-threatening conditions on a compassionate or emergency basis when conventional therapies have failed, are unsuitable, or are unavailable.

Adverse Drug Reaction (ADR)[4] – All noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions.

The phrase "responses to a medicinal product" means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out.

Serious Adverse Event (SAE) or Serious Adverse Drug Reaction (Serious ADR)[5] **-** Any untoward medical occurrence that at any dose:

- results in death,
- is life-threatening,
- requires inpatient hospitalization or prolongation of existing hospitalization,
- results in persistent or significant disability/incapacity, or
- is a congenital anomaly/birth defect

[3] http://www.hc-sc.gc.ca/dhp-mps/acces/drugs-drogues/sapfs_pasfd_2002-eng.php
[4] http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/ich/efficac/e6-eng.php
[5] http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/ich/efficac/e6-eng.php

RESPONSIBILITIES

CMN Coordinating Centre

- Ensure adequate stocks of parenteral antimalarial drugs
- Produce monthly reports on usage of antimalarial drugs
- Perform yearly audits of the Canadian Malaria Network
- Ensure the CMN website and Site/Satellite contact information is up to date
- Ensure Malaria Treatment Guidelines are up to date
- Ensure Malaria Package information is up to date
- Obtain and process data from pharmacists on drug usage
- Obtain and process Forms A & B from physicians requesting / using IV artesunate or IV quinine
- Obtain, process and report to Health Canada adverse effects related to IV Artesunate or IV Quinine

Site Pharmacists and/or Designee

- Order IV antimalarial drug from the CMN National Coordinating Centre, using the Drug Request Form
- Distribute drug with Forms A, B & Adverse Event Reporting Form to requesting physicians within a timely manner
- Report to CMN each case of artesunate/quinine dispensed to physicians using the Dispensing Record
- Notify the CMN Coordinating office of changes to pharmacy contact information or pharmacists/technicians in charge of IV Artesunate or IV Quinine drugs
- Maintain communications and drug supply with satellite site(s) (if applicable)
- Distribute drug to satellite sites (if applicable)
- Send all forms to the CMN by email (CanadianMalariaNetwork@toh.on.ca) or fax (613-767-8164)

Satellite Pharmacists

- Order IV antimalarial drug from the designated nearby Site
- Distribute drug with Forms A, B & Adverse Event Reporting Form to requesting physicians within a timely manner
- Report to CMN each case of artesunate/quinine dispensed to physicians using the Dispensing Record
- Notify the CMN Coordinating office and your nearest Site of changes to contact information
- Send all forms to the CMN by email (CanadianMalariaNetwork@toh.on.ca) or fax (613-767-8164)

Physicians

- Order drug from the nearest participating pharmacy
- Complete Form A on Day 1 of treatment
- Complete Form B on Day 7 of treatment
- Complete the Adverse Event Reporting Form as soon as any adverse event is detected (if applicable)
- Send all forms to the CMN by email (CanadianMalariaNetwork@toh.on.ca) or fax (613-767-8164)

PROCEDURES

A. Physicians:

Physician Drug Request

1. **Find a Participating Pharmacy**

   Consult the CMN website to determine the nearest participating pharmacy.

   CMN Website: http://thinkottawamedicine.ca/clinical-care/canadian-malaria-network/

2. **Request Drug by Phone**

   Contact the pharmacy to request drug. For after-hours assistance, dial the switchboard number and ask for the main pharmacy or ID-pharmacist on call.

3. **Arrange for Delivery**

   The pharmacy will arrange for the drug to be delivered to physicians. The package will include:

   a) One complete treatment regimen of drug (for artesunate, typically 8 vials for an average-size person; for quinine, typically 15 amps for an average-size person with loading dose)
   b) Instructions for drug administration
   c) Forms A, B & Adverse Event Reporting Form.

4. **Treat the Patient**

   If any questions about treatment or complications arise, contact the nearest ID-Physician on call. A list of ID-Physicians affiliated with the CMN is located on the CMN website, on the Contacts page, next to each major regional participating pharmacy.

5. **Report Data**

   Fill out Form A one day after treatment begins, and Form B seven days after treatment began. The forms should be sent by email to CanadianMalariaNetwork@toh.on.ca or by fax to 613-737-8164.

6. **Report Adverse Drug Reactions (if applicable)**

   If a suspected adverse drug reaction related to Artesunate or Quinine occurs, fill out the Suspected Adverse Reaction Report Form, and submit it by email to CanadianMalariaNetwork@toh.on.ca or by fax to 613-737-8164.

B. Pharmacies

Becoming a Site or Satellite

1. **Meet with the CMN National Program Coordinator.**

   The Coordinator will discuss the demand for the site/satellite and outline the roles and responsibilities of individuals involved.

   - Coordinator Phone: 613-737-8184
   - Coordinator Fax: 613-737-8164
   - Email: CanadianMalariaNetwork@toh.on.ca

2. **Collect Contact Information**

   Identify the primary and secondary contacts for the Pharmacy and Physician Infectious Disease Consultant. Send the contact information to the Canadian Malaria Network email address to upload onto the CMN Website.

   - Email: CanadianMalariaNetwork@toh.on.ca
   - CMN Website: http://thinkottawamedicine.ca/clinical-care/canadian-malaria-network/

3. **Request Initial Drug Shipment**

   SITES: Contact the CMN Pharmacy to request drug to be sent to the Site's location. The new Site must fill out and send the CMN Pharmacy the Drug Requisition Form. Sites will receive a minimum of 16 vials of artesunate and 12 amps of quinine.

   SATELITES: Contact the parent site's pharmacy to request drug to be sent to your satellite's location. Procedures vary by hospital. Most sites arrange shipping and absorb the cost. For questions or concerns, contact the CMN Pharmacy. Satellites will receive 8 vials of artesunate and 3 or 6 amps of quinine.

   For any shipments originating from the Canadian Malaria Network Coordinating Centre, The CMN arranges the shipping, and the Ottawa Hospital site covers the cost.

   - Coordinating Pharmacy Phone: 613-737-8970
   - Coordinating Pharmacy Fax: 613-739-6834
   - Email: CanadianMalariaNetwork@toh.on.ca

Site-to-Satellite Drug Distribution

1. **Order drug**

   SITES: Ensure that your drug supply is sufficient enough to supply all satellites depending on you. If more drug is needed, fill out and send in the CMN Pharmacy Drug Requisition Form.

   SATELLITES: To make a request for more drug from a site, complete the CMN Pharmacy Drug Requisition Form and send it to your local site coordinator. The most up-to-date coordinator contact information can be found on the CMN website: http://thinkottawamedicine.ca/clinical-care/canadian-malaria-network/

2. **Ship drug**

   Sites arrange shipping to the satellite site.

   Cost: Sites and satellites should discuss shipping arrangements. Most sites arrange shipping and absorb the cost, but alternate arrangements can be made between facilities to cover shipment cost.

Site/Satellite- to- non-Site/Satellite Hospital Drug Distribution

1. **Order drug**

   A hospital pharmacy will contact the site or satellite to obtain one treatment regimen of drug.

2. **Ship drug**

   The drug should be shipped with Drug Information, Form A, Form B, and the Adverse Event Reporting Form. The Site or Satellite arranges the shipping, and the receiving hospital covers the cost.

3. **Complete Dispensing Record**

   SITES & SATELLITES: Complete the Dispensing Record Form, which details the contact information of the requesting MD and the patient's initials and birth date. Send the form immediately to the CMN Coordinating Centre following dispensing.

4. **Order additional drug**

   SITES: If necessary, order additional drug from the CMN Coordinating Centre using the CMN Pharmacy Drug Requisition Form

   SATELLITES: Order additional drug from the nearest Site using the CMN Pharmacy Drug Requisition Form

Coordinating Centre

Data Collection

All data is collected using four forms. Forms A, B, and the Suspect Adverse Reaction Reporting Form are available on the CMN website.

Pharmacies:

1. Pharmacy Dispensing Record, which is submitted by the pharmacy dispensing one complete treatment regimen of drug. The form contains the contact information of the attending physician and the name and initials of the patient. The information included on this form is used to locate the responsible physician if Forms A and B are not received.

Physicians:

2. **Form A** is to be completed by the physician within 24 hours of administration of IV therapy. It contains information regarding physician contact information, patient demographics, birth country and travel history, prevention measures, date and details of illness, the patient's presenting symptoms, and time delays to receive and administer IV therapy.

3. **Form B** is to be completed by the physician within 7 days of patient follow-up. It contains information about treatment, complications of malaria, stepdown therapy, supportive treatments, outcomes, and evaluation of the Canadian Malaria Network.

4. **The Suspected Adverse Reaction Report** is to be completed by physicians if they suspect an adverse reaction from IV therapy. The information in this form is sent to Health Canada and is used to fill out a CIOMS report. The adverse events data on artesunate is also sent to the US Army supplier.

Drug Information

Drug Shipping Costs

The Canadian Malaria Network covers the cost of the drug.

Coverage of shipping costs from:

1. **CMN Coordinating Centre to Site or Satellite**

   The CMN Coordinating Centre covers the cost of shipping from the Ottawa Hospital to the designated site or satellite location.

2. **Site to Satellite**

   The site arranges the shipping, and usually sites absorb the cost of shipment. However, alternative arrangements have been made between some institutions where satellites cover the cost. Please ensure there is a meeting between the site and satellite coordinators to discuss this issue.

3. **Site or Satellite to non-Site or Satellite Hospital**

   The site or satellite arranges the shipping, and the receiving hospital covers the cost.

Drug Storage

Artesunate

Artesunate: 110mg/ml vials store at 2-10°C.

Stability Data: The investigational product, Artesunate Acid, Lot AA241-1-10-01 is stable, within specifications, when stored at the temperature conditions defined below. Any temperature excursion within these parameters should not have a negative impact on the Artesunate Acid and its integrity should not be affected.

Artesunate Acid dry powder remains stable and within specification under the temperature conditions as follows:

a. A period of up to 12 months at the storage condition of 30°C ± 2°C /65%RH ± 5% RH
b. A period of up to 9 months at the storage condition of 40°C ± 2°C/ 75%RH ± 5% RH
c. A period of up to 24 months at the storage conditions not exceeding 25°C ± 2°C/ 60%RH ± 5%RH.

Diluent: Phosphate buffer maybe stored at 2-30°C (note: phosphate crystals may form in the buffer at lower temperatures; these will dissolve if gently warmed) . The CMN coordinating Pharmacy located at the Ottawa Hospital, stores their diluent at room temperature (between 15-25°C).

Quinine

Store below 25°C. Protect from light.

Drug Expiry

Artesunate

The vials of parenteral Artesunate do not have an expiry date, only a manufacturing date.

The supplier (The United States Army Medical material Development Activity – USAMMDA, Fort Detrick Maryland) will inform the keeper of the medication (The Ottawa Hospital- Pharmacy Department) when the product can no longer be used.

Determination of the product expiry date is based on purity and potency tests performed on the malaria medication at regular intervals (q 12 months). This is in accordance with the FDA's recommendations on stability testing of New Drug Substance Products.

Once The Ottawa Hospital has been informed of the upcoming expiry date, all centres and sites across Canada will be contacted and new supplies will be shipped to the corresponding destinations.

For any questions or concerns, please contact CanadianMalariaNetwork@toh.on.ca

Quinine

The expiry date is clearly marked on the ampoules and outer packages. The CMN Coordinating Centre regularly monitors the expiry of Quinine.

Emergency Room Notice Template

Emergency Department Notice

Severe Malaria Medication is <u>IN STOCK</u>!

IV Artesunate and IV Quinine are in stock. These drugs are used to treat severe and complicated malaria infections, and are made available by Health Canada's Special Access program and are provided by the Canadian Malaria Network.

Criteria for Severe Falciparum Malaria

EITHER

History of recent possible exposure and no other related pathology
OR
Asexual forms of *Plasmodium falciparum* on blood smear

AND
Any one or more of the following 15 features:

1. Hyperparasitemia (>2% in non-immune, >5% in semi-immune)
2. Impaired consciousness or coma
3. Prostration (unable to walk or sit up without assistance)
4. Multiple convulsions (>2 in 24hrs)
5. Respiratory distress (acidotic breathing)
6. Respiratory failure / Pulmonary edema / ARDS
7. Circulatory collapse / shock (SBP<80mmHg adults and <50mmHg children)
8. Acute kidney injury / renal failure (Cr >265µmol/L or >upper limit for age for children)
9. Jaundice (Total bilirubin >45µmol/L)
10. Abnormal spontaneous bleeding/DIC
11. Hypoglycemia (<2.2mmol/L)
12. Metabolic Acidosis / Acidemia (pH<7.25, HCO3<15mmol/L)
13. Severe anemia (< 50g/L, in children; <70g/dL, in adults)
14. Hemoglobinuria (macroscopic)
15. Hyperlactataemia (lactate >5mmol/L)

***Note**: Fever occurring in a traveller within three months of returning from a malaria-endemic area is a medical emergency and should be investigated urgently with thick and thin blood films for malaria.*

How to access IV Artesunate or IV Quinine:

Daytime (Please insert local procedure information here.)

Contact a QEH Pharmacist at 902-894-2482 or 902-894-2024

QEH Pharmacy hours of Operation are:

- Monday - Friday: 0800h - 1930h
- Saturday & Sunday & holidays: 0800h - 1600h

Night time (Please insert local procedure information here.)

Outside of QEH Pharmacy normal hours of operation (see above), contact QEH Telecommunications (902- 894-2111) and have them page the QEH Pharmacist on-call.

Responsibilities Following Drug Administration:

1. Notify the hospital pharmacy of your request / use of drug.
2. Complete Form A on Day 1 of treatment.
3. Complete Form B on Day 7 of treatment.
4. Complete the Adverse Event Reporting Form as soon as any adverse event is detected (if applicable).
5. Send all forms to the Canadian Malaria Network by email (CanadianMalariaNetwork@toh.on.ca) or fax (613-737-8164).

Malaria Treatment Guidelines:

World Health Organization. Management of severe malaria – A practical handbook. Third edition. April 2013
http://www.who.int/malaria/publications/atoz/9789241548526/en/

Please consult your local infectious diseases physician for medical advice, or refer to the directory of malaria specialist physicians on the Canadian Malaria Network website.

CANADIAN MALARIA NETWORK

The Canadian Malaria Network (CMN) is established in 32 medical centres across Canada and maintains and facilitates rapid access to strategically-located supplies of intravenous artesunate and quinine for the treatment of severe malaria.

To get more information about treatment of severe malaria or to request drug from a Canadian Malaria Network institution, please visit the website: http://thinkottawamedicine.ca/clinical-care/canadian-malaria-network/

National Coordinating Office

The Ottawa Hospital
Division of Infectious Diseases
Telephone (Pharmacy): 613-737-8970
Telephone (Physician): 613-737-8184
Fax: 613-737-8164
Email: CanadianMalariaNetwork@toh.on.ca
Website: http://thinkottawamedicine.ca/clinical-care/canadian-malaria-network/

Contact (Please insert local contact information here.)

1) Drug Distribution: Contact a QEH Pharmacist at 902-894-2482 or 902-894-2024

QEH CMN Contact: Jennifer Boswell (Antimicrobial Stewardship Pharmacist) 902-894-2587

2) Dr. Greg German - 902-894-2515 or call QEH Switchboard (902-894-2111) to page

3) QEH is a CMN satellite site of CHU Dr-Georges-L.-Dumont. Designated physician (for Clinical Information) - Dr. Gabriel Girouard

(ID Consultant and Medical Microbiologist) or the Microbiologist on-call : page through 506-862-4000

CMN CONTACT INFORMATION

General

- Fax: 613-737-8164
- Email: CanadianMalariaNetwork@toh.on.ca
- Website 1: http://thinkottawamedicine.ca/clinical-care/canadian-malaria-network/
- Website 2: http://www.phac-aspc.gc.ca/tmp-pmv/quinine/

CMN Coordinating Centre

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To find distributing CMN sites or to **OBTAIN PARENTERAL THERAPY** please visit our website http://thinkottawamedicine.ca/clinical-care/canadian-malaria-network/ and click the 'CMN Pharmacy & Physician Contact List' OR email any inquires to candianmalarianetwork@toh.on.ca

REFRENCES

Canadian Malaria Network. http://thinkottawamedicine.ca/clinical-care/canadian-malaria-network/

Summary of recommendations for the prevention of malaria by the Committee to Advise on Tropical Medicine and Travel (CATMAT). 2014. Canada Communicable Disease Report: Volume 40-7. http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/14vol40/dr-rm40-07/dr-rm40-07-prev-eng.php

Summary of recommendations for the diagnosis and treatment of malaria by the Committee to Advise on Tropical Medicine and Travel (CATMAT). 2014. Canada Communicable Disease Report: Volume 40-7. http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/14vol40/dr-rm40-07/dr-rm40-07-diag-eng.php

Health Canada. Special Access Program. http://www.hc-sc.gc.ca/dhp-mps/acces/drugs-drogues/sapfs_pasfd_2002-eng.php

World Health Organization. Guidelines for the Treatment of Malaria. 2010. Second Edition. http://www.who.int/malaria/publications/atoz/9789241547925/en/index.html

World Health Organization. Management of Severe Malaria – A Practical Handbook. 2013. Third Edition. http://www.who.int/malaria/publications/atoz/9789241548526/en/index.html

StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP. http://www.stata.com/

APPENDIX

The appendix includes the following forms:

Appendix I: Drug Requisition Form | Formulaire De Réquisition Des Médicaments

The Drug Requisition Form is completed by a network site and sent to the coordinating centre **OR** this form is completed by a satellite site and sent to their parent site to obtain more IV therapy for malaria.

Appendix II: Form A (English) | Formulaire A (français)

Form A is to be completed by the physician within 24 hours of administration of IV therapy. It contains information regarding physician contact information, patient demographics, birth country and travel history, prevention measures, date and details of illness, the patient's presenting symptoms, and time delays to receive and administer IV therapy.

Appendix III: Form B (English) | Formulaire B (français)

Form B is to be completed by the physician within 7 days of patient follow-up. It contains information about treatment, complications of malaria, stepdown therapy, supportive treatments, outcomes, and evaluation of the Canadian Malaria Network.

Appendix IV: Suspected Adverse Reaction Report (English) | Déclaration d'effets indésirables présumés (français)

The Suspected Adverse Reaction Report is to be completed by physicians if they suspect an adverse reaction from IV therapy. The information in this form is sent to Health Canada and is used to fill out a CIOMS report. The adverse events data on artesunate is also sent to the US Army supplier.

Appendix V: Pharmacy Dispensing Record | Dossier Distribution

The Pharmacy Dispensing Record is to be completed by both sites and satellites. The form should include the contact information of the requesting MD and the patient's initials, sex, birth date and weight. The form is sent immediately to the CMN Coordinating Centre following dispensing in order for the CMN to follow-up.

NOTE: Click on the title of the form for a fillable PDF version of the form OR visit the Canadian Malaria Network website: http://thinkottawamedicine.ca/clinical-care/canadian-malaria-network/

Appendix I:

Drug Requisition Form | Formulaire De Réquisition Des Médicaments

The Drug Requisition Form is completed by a network site and sent to the coordinating centre **OR** this form is completed by a satellite site and sent to their parent site to obtain more IV therapy for malaria.

The Ottawa Hospital | L'Hôpital d'Ottawa

CANADIAN MALARIA NETWORK
DRUG REQUISITION FORM

To: _____

Attention: _____

Site Name: _____

Requested by: _____

Address: _____

Telephone Number: _____

Date of Request: _____

Date Supplies Required at Site: _____

Drug Name	Quantity on Hand	Quantity Requested
Artesunate 110mg vials		
Phosphate Buffer 12mL vials		
Quinine Dihydrochloride 600mg/2mL ampoules		

PLEASE complete the following table:

DISPENSING(S) SINCE YOUR LAST SHIPMENT			
Drug Name	**Date Dispensed (dd/mm/yy)**	**Quantity of Vials/Ampoules Issued to Subject OR Site**	**Lot# Used**

Please fax to 613-739-6834 or email to CanadianMalariaNetwork@toh.on.ca

Form Version: October 2013

Appendix II:

Form A (English) | Formulaire A (français)

Form A is to be completed by the physician within 24 hours of administration of IV therapy. It contains information regarding physician contact information, patient demographics, birth country and travel history, prevention measures, date and details of illness, the patient's presenting symptoms, and time delays to receive and administer IV therapy.

PARENTERAL THERAPY FOR SEVERE MALARIA - FORM A
To be completed by the Attending Physician *CMN ID:_____*

1. Date of request (D/M/Y) : ____/____/____
2. Drug requested (check all that apply):
   ❑ Artesunate* ❑ Quinine
   **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: _____
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. malariae
   ❑P. ovale ❑P. knowlesi ❑Unknown
   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): _____
   Who prescribed the drug?
   ❑MD in Canada ❑MD in country of acquisition
   ❑Self prescribed ❑Other (specify): _____
10. Indication for use of IV antimalarial therapy (check all that apply):
    ❑ Continued vomiting or unable to tolerate oral therapy (Note: if this is the only indication for IV therapy, then QUININE preferred)
    ❑ Hyperparasitemia (>2% in non-immune, >5% in 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<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 occur....
    a) Hours to contact individual responsible for dispensing IV malaria 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) at day 7 and send it in.

Form Version: September 2013

PLEASE COMPLETE AND RETURN TO THE CMN COORDINATING CENTRE WITHIN 7 DAYS OF IV DRUG REQUEST BY E-MAIL: CanadianMalariaNetwork@toh.on.ca OR BY FAX: 613-737-8164
Parenteral artesunate and quinine are provided by Health Canada's Special Access Program through the Canada Malaria Network (CMN).

Appendix III:

Form B (English) | Formulaire B (français)

Form B is to be completed by the physician within 7 days of patient follow-up. It contains information about treatment, complications of malaria, stepdown therapy, supportive treatments, outcomes, and evaluation of the Canadian Malaria Network.

PARENTERAL THERAPY FOR SEVERE MALARIA - FORM B

To be completed by the Attending Physician *CMN ID:*

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

2. REQUESTING/ATTENDING PHYSICIAN
   - Name: _____
   - Hospital/site: _____
   - City: _____ Province: _____
   - Tel#: _____ Fax#: _____
   - Email: _____

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:
     - Artesunate: _____
     - Quinine: _____
   - 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 (>2% non-immune,>5% 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<15mmol/L)
     - ❑ Severe anemia (Hb<70g/L in adults and <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 specify: _____

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: _____

Completed by: _____
Date: ____/____/____ Tel #: _____
Email: _____

Thank you very much for completing this form.
Your cooperation is greatly appreciated.

Form Version: September 2013

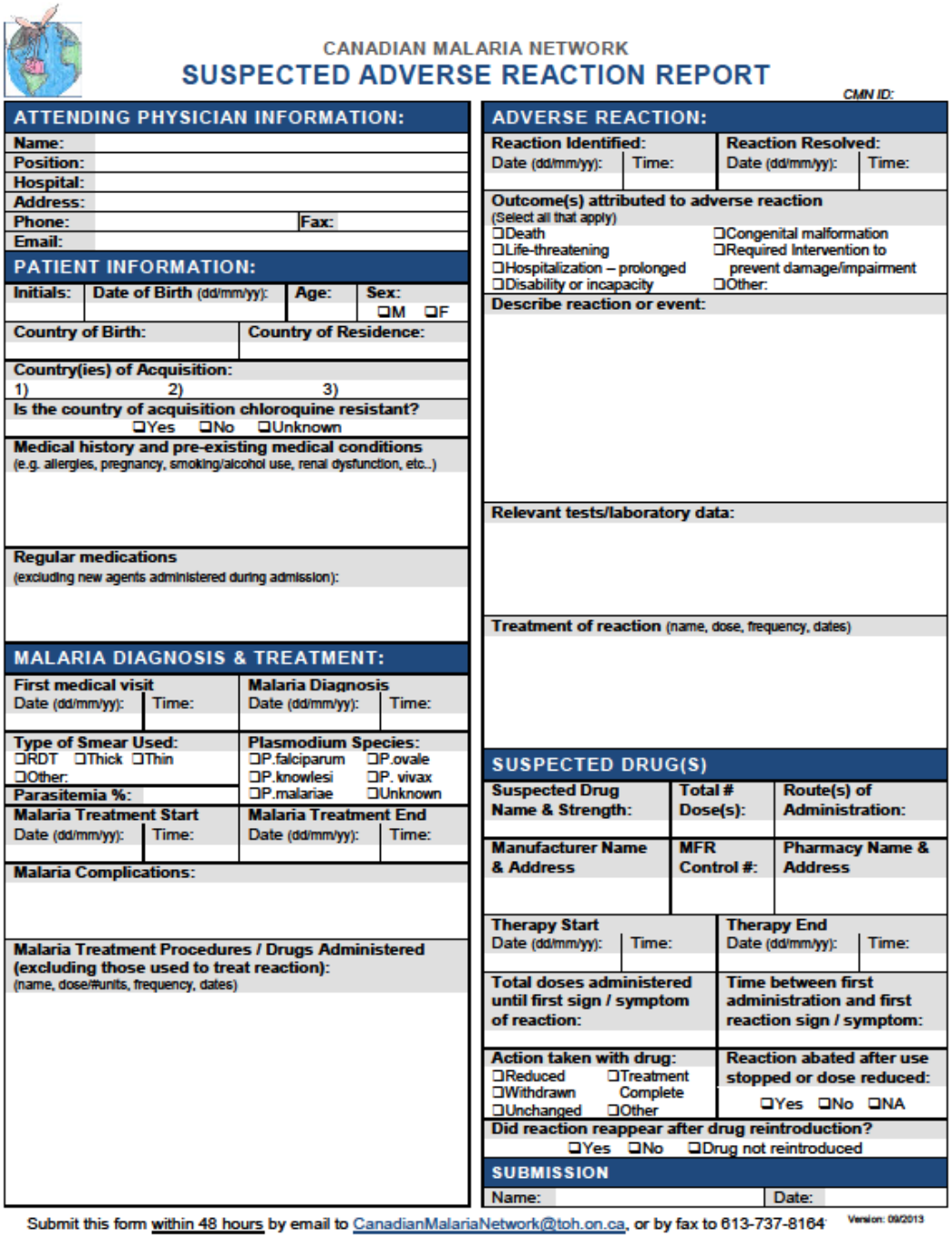
PLEASE COMPLETE AND RETURN TO THE CMN COORDINATING CENTRE WITHIN 7 DAYS OF IV DRUG REQUEST BY E-MAIL: CanadianMalariaNetwork@toh.on.ca OR BY FAX: 613-737-8164

Parenteral artesunate and quinine are provided by Health Canada's Special Access Program through the Canada Malaria Network (CMN).

Appendix IV:

Suspected Adverse Reaction Report (English) | Déclaration d'effets indésirables présumés (français)

The Suspected Adverse Reaction Report is to be completed by physicians if they suspect an adverse reaction from IV therapy. The information in this form is sent to Health Canada and is used to fill out a CIOMS report. The adverse events data on artesunate is also sent to the US Army supplier.



CANADIAN MALARIA NETWORK

SUSPECTED ADVERSE REACTION REPORT

CMN ID:

ATTENDING PHYSICIAN INFORMATION:

Name:
Position:
Hospital:
Address:
Phone: Fax:
Email:

PATIENT INFORMATION:

Initials: | Date of Birth (dd/mm/yy): | Age: | Sex: ❑M ❑F

Country of Birth: | Country of Residence:

Country(ies) of Acquisition:
1) 2) 3)

Is the country of acquisition chloroquine resistant?
❑Yes ❑No ❑Unknown

Medical history and pre-existing medical conditions
(e.g. allergies, pregnancy, smoking/alcohol use, renal dysfunction, etc..)

Regular medications
(excluding new agents administered during admission):

MALARIA DIAGNOSIS & TREATMENT:

First medical visit
Date (dd/mm/yy): | Time:

Malaria Diagnosis
Date (dd/mm/yy): | Time:

Type of Smear Used:
❑RDT ❑Thick ❑Thin
❑Other:

Plasmodium Species:
❑P.falciparum ❑P.ovale
❑P.knowlesi ❑P. vivax
❑P.malariae ❑Unknown

Parasitemia %:

Malaria Treatment Start
Date (dd/mm/yy): | Time:

Malaria Treatment End
Date (dd/mm/yy): | Time:

Malaria Complications:

Malaria Treatment Procedures / Drugs Administered (excluding those used to treat reaction):
(name, dose/#units, frequency, dates)

ADVERSE REACTION:

Reaction Identified:
Date (dd/mm/yy): | Time:

Reaction Resolved:
Date (dd/mm/yy): | Time:

Outcome(s) attributed to adverse reaction
(Select all that apply)
❑Death
❑Life-threatening
❑Hospitalization – prolonged
❑Disability or incapacity
❑Congenital malformation
❑Required Intervention to prevent damage/impairment
❑Other:

Describe reaction or event:

Relevant tests/laboratory data:

Treatment of reaction (name, dose, frequency, dates)

SUSPECTED DRUG(S)

Suspected Drug Name & Strength: | Total # Dose(s): | Route(s) of Administration:

Manufacturer Name & Address | MFR Control #: | Pharmacy Name & Address

Therapy Start
Date (dd/mm/yy): | Time:

Therapy End
Date (dd/mm/yy): | Time:

Total doses administered until first sign / symptom of reaction:

Time between first administration and first reaction sign / symptom:

Action taken with drug:
❑Reduced ❑Treatment Complete
❑Withdrawn
❑Unchanged ❑Other

Reaction abated after use stopped or dose reduced:
❑Yes ❑No ❑NA

Did reaction reappear after drug reintroduction?
❑Yes ❑No ❑Drug not reintroduced

SUBMISSION

Name: | Date:

Submit this form within 48 hours by email to CanadianMalariaNetwork@toh.on.ca, or by fax to 613-737-8164

Version: 09/2013

Appendix V:

Pharmacy Dispensing Record | Dossier Distribution

The Pharmacy Dispensing Record is to be completed by both sites and satellites. The form should include the contact information of the requesting MD and the patient's initials, sex, birth date and weight. The form is sent immediately to the CMN Coordinating Centre following dispensing in order for the CMN to follow-up.

Canadian Malaria Network
Réseau canadien sur le paludisme

PHARMACY DISPENSING RECORD FOR IV ARTESUNATE AND IV QUININE

REQUESTING PHYSICIAN (OR OTHER CONTACT)

Name:_____ Title:_____
Hospital:_____ Department:_____
City:_____ Province:_____
Telephone:_____ Email:_____

PATIENT INFORMATION:

Initials (first/middle/last):_____
Date of Birth (dd/mm/yy):_____
Sex: ❑Male ❑Female
Weight:_____kg

PHARMACY DISPENSING SITE

City:_____
Hospital:_____

Prescribing Physician and/or Contact have consulted with an Infectious Disease Physician:
❑Yes ❑No ❑Don't know
If no/don't know, please remind the physician / requestor of the availability of the Canadian Malaria Network 24-hour Infectious Disease Contacts and information resources available on the CMN website (http://www.phac-aspc.gc.ca/tmp-pmv/quinine/)

Medication dispensed (including Information Package with Forms A and B)
❑Artesunate + Phosphate buffer diluent
Vials Artesunate:_____ # Vials Diluent:_____
❑Quinine (one kit of 7 ampoules)

Method of Shipping/Arrangements for Pick-Up and Delivery *(Note: Artesunate must be shipped as a refrigerated item)*:_____
_____
_____
_____

Date Dispensing Completed (dd/mm/yy):_____ Time:_____
Dispensed by (Name of Pharmacy Personnel):_____

Complete and Return to the CMN Coordinating Centre within 24 Hours of Dispensing by E-Mail: CanadianMalariaNetwork@toh.on.ca or by Fax: 613-737-8164

Version: November 2013