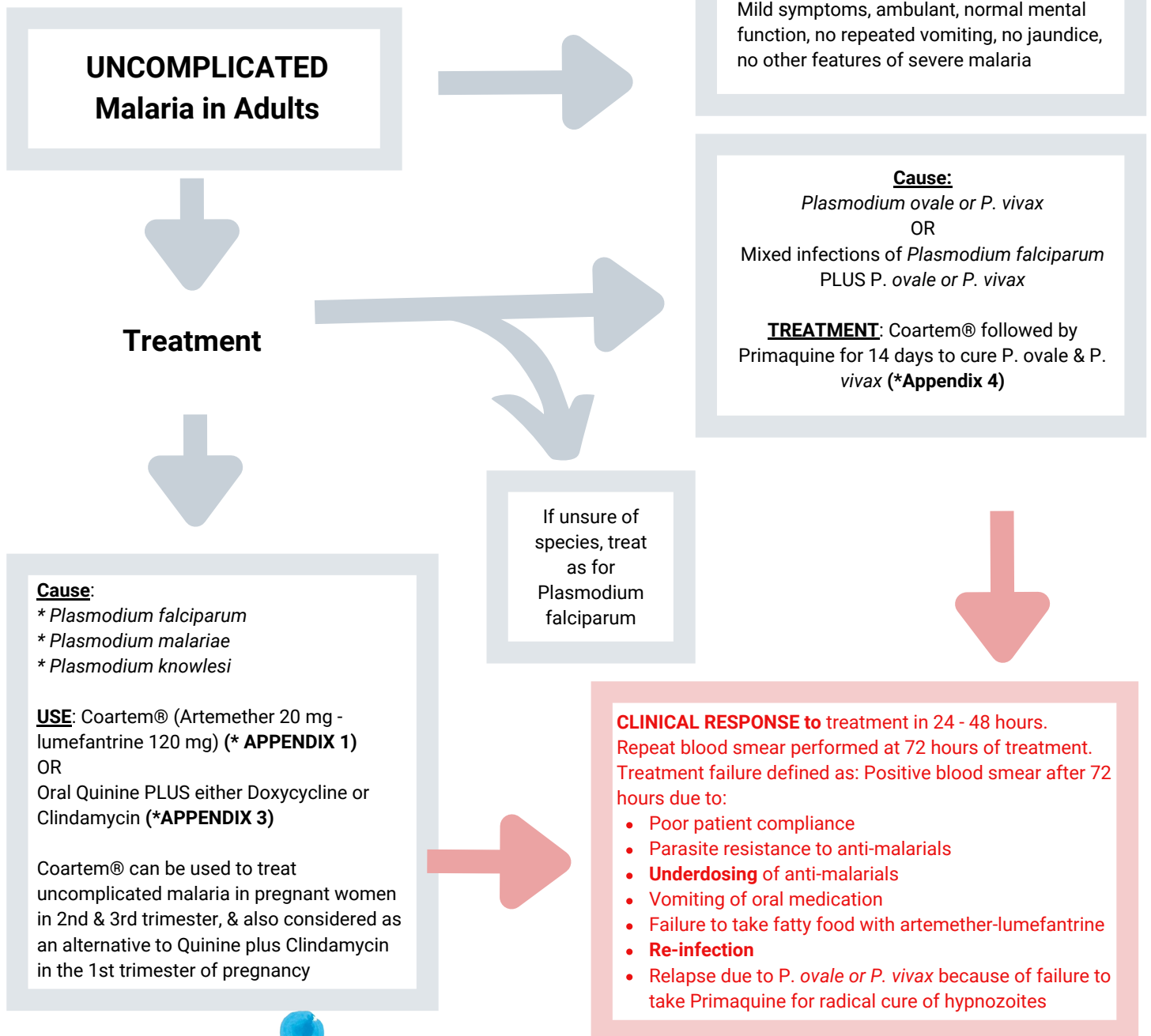


# Newsletter

## Update on Malaria Part 3 Treatment Guidelines

Compiled by Dr Trisha Moodley



## SEVERE/COMPLICATED Malaria in Adults

### Treatment

Cause: Usually *P.falciparum*:

**TREATMENT:** Artesunate IVI OR if not available Quinine IVI (\*APPENDIX 5)

**Once able to tolerate ORAL treatment**, follow with:  
Coartem® (Artemether 20 mg - lumefantrine 120 mg) (\* APPENDIX 1) OR Oral Quinine PLUS either Doxycycline or Clindamycin (\*APPENDIX 3)

#### PRE-TRANSFER MANAGEMENT:

Drug treatment

- IM artesunate 2.4 mg/kg stat
- IM quinine 20 mg salt/kg stat divided into 10 mg/kg diluted to a concentration of 60 - 100 mg/mL given into each anterior thigh).

#### GENERAL MANAGEMENT:

- Check blood glucose - correct the hypoglycaemia
- Hypotensive/shock - IV fluid resuscitation with normal saline
- Respiratory distress - oxygen per mask
- Fever > 39 C - administer paracetamol
- Convulsions - IV or rectal diazepam

**DEFINED AS:** Hyperparasitaemia > 4%

#### CLINICAL FEATURES:

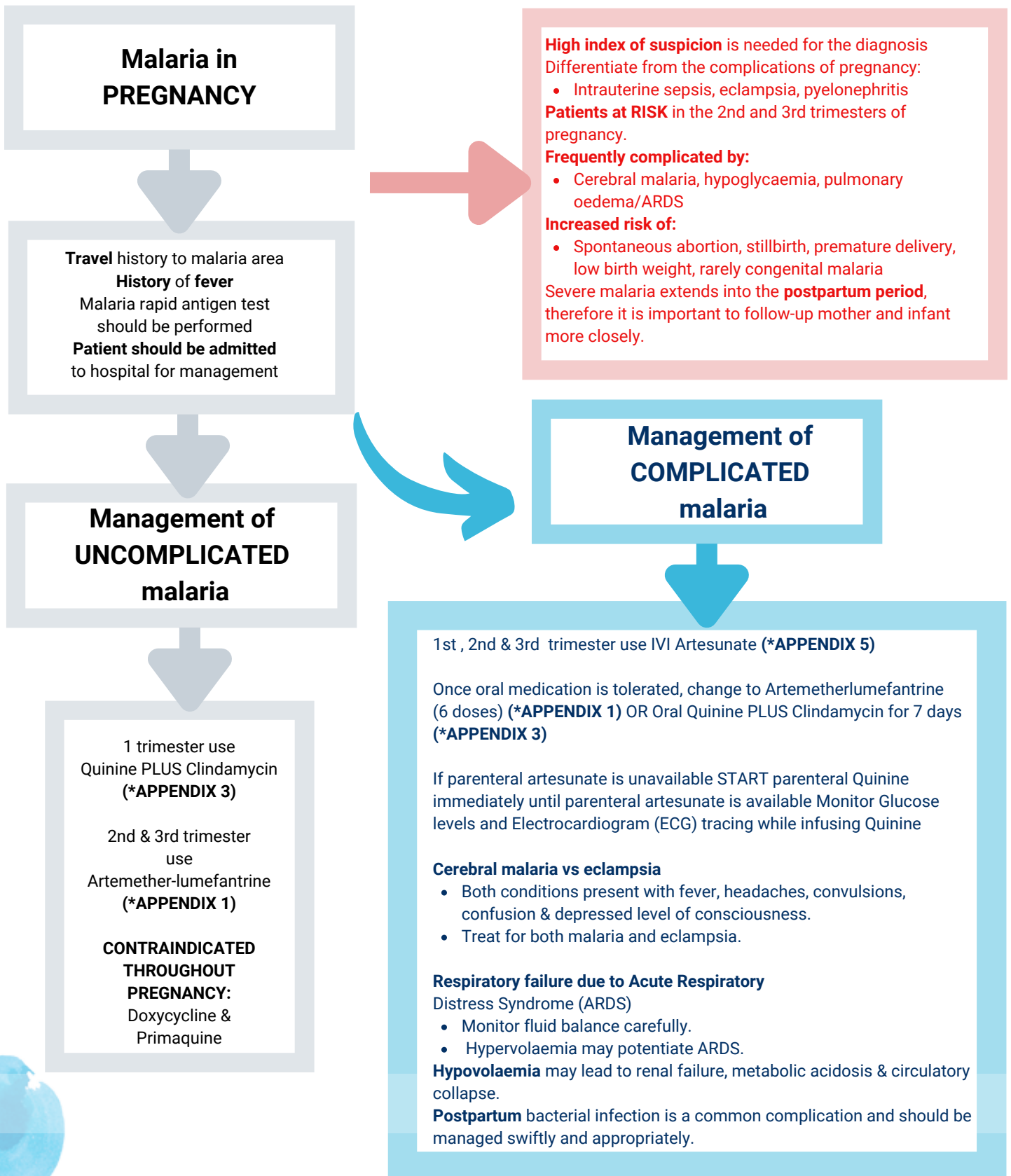
- Impaired consciousness
- Prostration
- Multiple convulsions: > 2 episodes in 24 hours
- Acidotic breathing & respiratory distress
- Acute pulmonary oedema & acute respiratory distress syndrome
- Circulatory collapse or shock
- Anuria
- Jaundice
- Abnormal bleeding

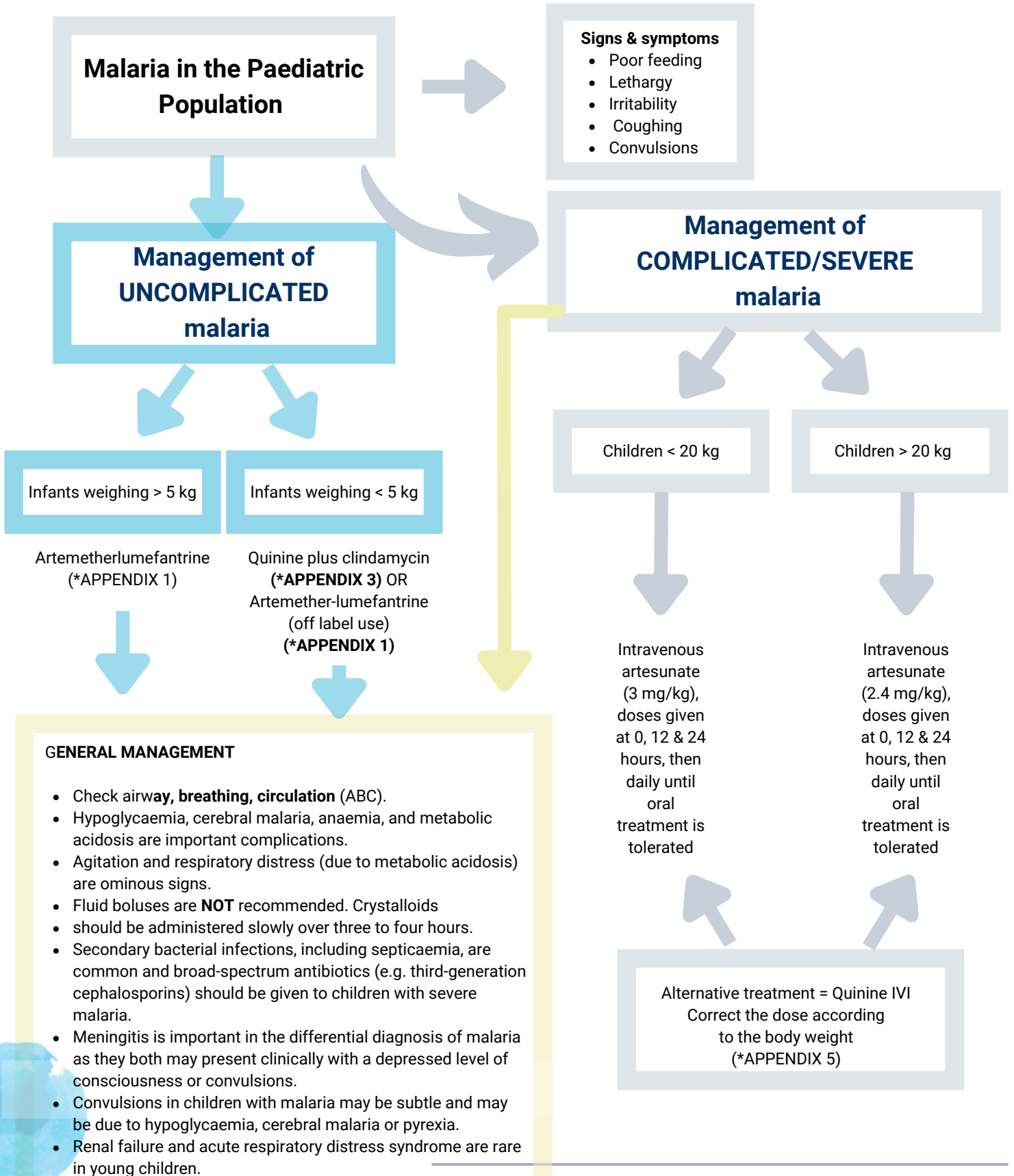
#### LABORATORY FEATURES:

- Hypoglycaemia (< 2.2 mmol/L or < 40 mg/dL)
- Metabolic acidosis (plasma bicarbonate < 15 mmol/L)
- Severe normocytic anaemia (< 7 g/dL)
- Haemoglobinuria
- Hyper-lactataemia (lactate > 5 mmol/L)
- Renal impairment (serum creatinine > 265 µmol/L)
- Pulmonary oedema (radiological)

#### SUPPORTIVE MANAGEMENT

- Admission to ICU
- Intravenous fluid management + urine output monitoring
- Regular glucose monitoring
- Temperature regulation + management
- Monitor BP, Pulse rate, Respiratory rate and Level of consciousness
- Administer IVI antibiotics
- Stress ulcer prophylaxis





**Signs & symptoms**

- Poor feeding
- Lethargy
- Irritability
- Coughing
- Convulsions

**Management of COMPLICATED/SEVERE malaria**

Children < 20 kg

Children > 20 kg

Intravenous artesunate (3 mg/kg), doses given at 0, 12 & 24 hours, then daily until oral treatment is tolerated

Intravenous artesunate (2.4 mg/kg), doses given at 0, 12 & 24 hours, then daily until oral treatment is tolerated

Alternative treatment = Quinine IV  
Correct the dose according to the body weight (\*APPENDIX 5)

**GENERAL MANAGEMENT**

- Check airway, **breathing, circulation** (ABC).
- Hypoglycaemia, cerebral malaria, anaemia, and metabolic acidosis are important complications.
- Agitation and respiratory distress (due to metabolic acidosis) are ominous signs.
- Fluid boluses are **NOT** recommended. Crystalloids should be administered slowly over three to four hours.
- Secondary bacterial infections, including septicaemia, are common and broad-spectrum antibiotics (e.g. third-generation cephalosporins) should be given to children with severe malaria.
- Meningitis is important in the differential diagnosis of malaria as they both may present clinically with a depressed level of consciousness or convulsions.
- Convulsions in children with malaria may be subtle and may be due to hypoglycaemia, cerebral malaria or pyrexia.
- Renal failure and acute respiratory distress syndrome are rare in young children.

## Malaria in HIV & AIDS

### Treatment

#### Co-infected patients with HIV/AIDS & malaria

- **Admit** to hospital for close monitoring.
- Treatment as for **uncomplicated** OR **complicated** malaria algorithms as on pages 1 & 2.
- **Assess HIV status**
  - As immune suppression worsens, the risk of severe malaria increases.
- Assess renal function
  - Renal failure is a complication in HIV/AIDS patients.
- Monitor **electrolyte disturbances** and correct as needed.
- **Empiric antibiotic therapy** (3rd generation cephalosporin) is recommended to prevent secondary bacterial infections.

#### KEY FACTS TO NOTE WITH TREATMENT OF MALARIA IN PATIENTS WITH HIV/AIDS: (\*APPENDIX 2)

- Co-treatment with artemether-lumefantrine & efavirenz-based ARV's reduces lumefantrine concentrations - **HIGH RISK** of treatment failure.
- Recommendation: extend artemether-lumefantrine treatment duration to 5 days.
- **HIV-infected children** on zidovudine, receiving artesunate + amodiaquine = are at an increased risk of neutropaenia.
- **Hepatotoxicity** develops in patients taking artesunate + amodiaquine + efavirenz (Amodiaquine is not available in South Africa).
- **Sulfadoxine pyrimethamine** is not recommended for the treatment of malaria in South Africa, AND should not be given to patients taking cotrimoxazole.

\* Appendices adapted from: South African Guidelines for the Prevention of Malaria - updated January 2019.

## \*APPENDIX 1

<p><b>Artemether-lumefantrine (Oral)</b> <b>Coartem®</b> (fixed dose artemisinin-based combination therapy, ACT; Novartis South Africa (Pty) Ltd) One tablet contains artemether 20 mg PLUS, lumefantrine 120 mg</p>	<p>5 to &lt; 15 kg</p>	<p>One tablet stat, followed by one tablet after 8 hours. Then one tablet twice daily for the following 2 days (total course = 6 tablets).</p>
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### ADVANTAGES FOR USE:

- Rapid clinical & parasitological response
- Improved cure rates
- Decreased malaria transmission
- Delayed antimalarial drug resistance
- Short treatment course (6 doses over 3 days)
- Good tolerability
- ONLY indicated for treatment of uncomplicated malaria

<p>15 to &lt; 25 kg</p>	<p>Two tablets stat, followed by two tablets after 8 hours. Then two tablets twice daily for the following 2 days (total course = 12 tablets).</p>
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<p>25 to &lt; 35 kg</p>	<p>Three tablets stat, followed by three tablets after eight hours. Then three tablets twice a day for the following 2 days (total course = 18 tablets).</p>
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<p>35 to &lt; 65 kg</p>	<p>Four tablets stat, followed by four tablets after eight hours. Then four tablets twice daily for the following 2 days (total course = 24 tablets).</p>
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### SIDE EFFECTS:

sleep disturbances, headaches, dizziness, palpitation, abdominal pain, anorexia, cough, arthralgia, asthma, fatigue.

<p>&gt; 65 kg</p>	<p>Dosage as for &gt; 35 kg. Close monitoring required.</p>
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### SPECIAL PRECAUTIONS:

- Do not administer in patients with prolonged QT interval OR in patients with a family history of congenital prolonged QT syndrome.
- Don't administer in patients with risk factors for cardiotoxicity. i.e. hypokalaemia or hypomagnesaemia.

<p>&gt; 85 kg</p>	<p>Extend the treatment course to FIVE days, administering FOUR tablets per dose, twice daily for a total of 10 doses. (off-label recommendation)</p>
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NOTE: administer with food/milk containing at least 1.2 g fat to ensure adequate absorption



## \*APPENDIX 2

	Increased concentrations	Decreased concentrations
<b>Artemether</b>	Ketoconazole	Lopinavir/ritonavir Nevirapine Efavirenz Etravirine Rifampicin
<b>Lumefantrine</b>	Lopinavir/ritonavir Darunavir/ritonavir Ketoconazole Nevirapine	Rifampicin Efavirenz Mefloquine Etravirine

## \*APPENDIX 3

### Quinine (Oral)

(Aspen quinine® oral)

One tablet contains 300 mg quinine sulphate

10 mg salt/kg body weight every 8 hours Duration: 7 days

### Doxycycline (Oral)

One capsule/tablet contains 50 mg or 100 mg doxycycline

Use in combination with quinine: 100 mg (OR 2.2 mg/kg in children) twice daily for at least 7 days. NOTE: avoid in pregnancy and children under eight years of age.

### Clindamycin (Oral)

One tablet contains 150 mg clindamycin

Use in combination with quinine in pregnancy and children under eight years of age: 10 mg/kg twice daily for seven days.

## \*APPENDIX 4

### Chloroquine (Oral)

Use for CONFIRMED non-falciparum malaria only. One tablet contains 150 mg chloroquine base.

#### ADULTS

1.5 g over 3 days. Initially 600 mg, Followed by 300 mg 6 - 8 hours later, and, 300 mg once daily on 2nd & 3rd days.

#### CHILDREN

Initial dose: 10 mg base/kg then 5 mg base/kg 6 – 8 hours later, AND 5 mg base/kg once daily on nd 3rd 2 and days.

### Primaquine (Oral)\*

One tablet contains 26.3 mg primaquine phosphate = 15 mg primaquine base.

\*Not registered in South Africa; provision for Section 21 use.

#### ADULTS

15 mg base daily for 14 days following standard treatment, OR 0.25 - 0.5 mg base/kg daily for 14 days. (a 14-day course is needed for radical cure of *P. ovale* & *P. vivax*) In mild G6PD deficiency - 45 mg base once a week for eight weeks. CONTRAINDICATED in pregnancy & women who are breastfeeding a child under 6 months of age.

#### CHILDREN

0.25 - 0.3 mg base/kg daily for 14 days. In mild G6PD deficiency: 0.5 - 0.8 mg base/kg weekly for 8 weeks. CONTRAINDICATED in children under 6 months of age, G6PD deficiency.

## \*APPENDIX 5

**Artesunate  
(intravenous)**

**Garsun®**

**injectable**

**Equity**

**Pharmaceuticals**

**(Pty) Ltd**

Patients weighing > 20 kg: 2.4 mg/kg at 0, 12 and 24 hours then daily until patient can tolerate oral treatment.

Children weighing < 20 kg: 3 mg/kg at 0, 12 and 24 hours then daily until patient can tolerate oral treatment.

**Quinine**

**Adco-quinine®**

**injectable**

**(Adcock Ingram)**

### **ADULTS**

Loading dose: 20 mg/kg body weight of quinine dihydrochloride salt, diluted in 5 - 10 mL/kg body weight of 5% Dextrose water, given by intravenous infusion over 4 hours.

Maintenance dose: eight hours after loading dose, 10 mg/kg body weight of quinine dihydrochloride salt, diluted in 5 - 10 mL/kg of a Dextrose containing solution, given intravenously over 4 hours.

Administered every 8 hours until the patient can tolerate oral medication (usually by 48 hours).

### **CHILDREN**

Loading dose: 20 mg/kg body weight of quinine dihydrochloride salt, diluted in 5 - 10 mL/kg body weight of 5% Dextrose water, given by intravenous infusion over 4 hours.

Maintenance dose: 10 mg/kg body weight of quinine dihydrochloride salt, diluted in 5 - 10 mL/kg of a Dextrose containing solution, given intravenously over 4 hours.

## **References**

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