Supplementary material

Supplementary Table 1 Treatment of uncomplicated malaria [1]

Uncomplicated *P. falciparum* malaria (all treatments are oral)
Artemisinin Combination Therapy (ACT)
3-day regimens • **Artemether-lumefantrine** (fixed dose combination (FDC)) 20 mg artemether /120 mg lumefantrine per tablet Dosing: Number of tablets per dose according to pre-defined weight bands (5–14 kg: 1 tablet; 15–24 kg: 2 tablets; 25–34 kg: 3 tablets; and > 34 kg: 4 tablets) given twice a day for 3 days ** Therapeutic dose range: 1·4–4 mg/kg of artemether and 10–16 mg/kg of lumefantrine. • ***Dihydroartemisinin-piperaquine*** (FDC) 40 mg of dihydroartemisinin and 320 mg piperaquine per adult tablet 20 mg of dihydroartemisinin and 160 mg piperaquine per paediatric tablet Dosing: 4 mg/kg dihydroartemisinin and 18 mg/kg piperaquine once a day for 3 days. Children under 25 kg body weight should receive at least 24 mg/kg/day of piperaquine *** Therapeutic dose range: 2–10 mg/kg/day dihydroartemisinin and 16–26 mg/kg/day piperaquine • **Artesunate-mefloquine** (both FDC and loose tablets available) Dosing: 4 mg/kg/day artesunate given once a day for 3 days and 25 mg/kg of mefloquine either split over 2 days as 15 and 10 mg/kg or over 3 days as 8·3 mg/kg/day once a day for 3 days. Therapeutic dose range: 2-10 mg/kg/dose/day of artesunate and 7-11 mg/kg/dose/day of mefloquine. N.B. Reuse of mefloquine within 60 days of first treatment is associated with an increased risk of neuropsychiatric reactions • **Artesunate-amodiaquine** (both FDC and loose tablets available) Dosing: 4 mg/kg/day artesunate and 10 mg/kg/day amodiaquine once a day for 3 days. Therapeutic dose range: 2-10 mg/kg/day artesunate and 7·5-15 mg/kg/dose amodiaquine. • **Artesunate+sulfadoxine-pyrimethamine** (loose tablets) Dosing: 4 mg/kg/day artesunate given once a day for 3 days and 25/1·25 mg/kg sulfadoxine/pyrimethamine on day 1 as a single dose. Therapeutic dose range: 2-10 mg/kg/day artesunate, sulfadoxine 25-70 mg/kg and 1·25-3·5 mg/kg pyrimethamine. **7-day ACT regimens**

- **Artesunate + EITHER tetracycline OR doxycycline OR clindamycin**

Dosing: Artesunate 2 mg/kg once daily plus tetracycline (4 mg/kg four times daily or doxycycline (3·5 mg/kg once daily) or clindamycin (10 mg/kg twice daily) for 7 days.

Non-ACT regimens

- **Atovaquone-proguanil** (FDC)
  250 mg of atovaquone and 100 mg proguanil per tablet

Dosing: 15 mg/kg of atovaquone and 6 mg/kg proguanil (4 tablets for adult) once a day for 3 days.

- **Quinine + tetracycline/doxycycline/clindamycin** for 7 days

Dosing: Quinine10 mg/kg/dose three times daily plus tetracycline (4 mg/kg four times daily or doxycycline (3·5 mg/kg once daily) or clindamycin (10 mg/kg twice daily) for 7 days.

Recurrent uncomplicated *P. falciparum* malaria

WHO suggests a cut-off of 4 weeks interval between initial and recurrent parasitaemia to crudely distinguish between reinfection and recrudescence. Advice is to use an alternative 7-day ACT or non-ACT if the recurrence occurs within 28 days and any ACT if the recurrence is after 28 days.

Uncomplicated *P. vivax* malaria

- **Chloroquine**
  10 mg/kg base once daily for 2 days followed by 5 mg/kg for 1 day

If chloroquine resistance suspected

- **ACT** (except artesunate-sulfadoxine-pyrimethamine) for 3 days

Anti-relapse treatment for hypnozoites in liver

- primaquine 0·5 mg/kg 14 days (if G6PD is normal) or
- primaquine 0·75 mg/kg weekly for 8 weeks (if G6PD deficient) dependent on risk assessment (severity of local G6PD variants, availability of blood transfusion, probability and predicted health impact of relapses)

Treatment of *P. ovale* and *P. malariae*,

- as for *P. vivax, P. ovale* needs anti-relapse treatment as well.

Treatment of *P. knowlesi*

- as for *P. falciparum*

Contraindications:

- Doxycycline and tetracycline are contraindicated in pregnancy/lactation (Class-D drugs) and children aged less than 8 years.
- Primaquine is contraindicated in severe G6PD deficiency, infants less than 6 months, pregnancy/lactation unless infant is G6PD normal.

**Artemether-lumefantrine should be taken with food containing fat to optimise lumefantrine absorption since exposure is the principal determinant of cure.

***Young children receive a higher mg/kg piperaquine dose than adults because of a higher risk of failing treatment.

Supplementary Table 2 Treatment of suspected ACT resistant malaria

Patients with uncomplicated *P. falciparum* malaria and travel history to countries with artemisinin resistance
ACT
If an ACT is available which is still effective against the likely drug resistant strain this is recommended (doses as Supplementary Table 1)
Non-ACT
• **Atovaquone-proguanil** • **Quinine + either tetracycline or doxycycline or clindamycin** for 7 days
N.B. • Admit the patient • Monitor the clinical and parasitological response until recovery or asexual parasite clearance. • Follow up at 4-weeks to ensure cure
Patients with severe *P. falciparum* malaria and travel history to countries with artemisinin resistance
• Intravenous artesunate PLUS intravenous quinine (expert opinion, no evidence)

References

1. World Health Organization. Guidelines for the treatment of malaria-3rd edition. Geneva, 2015.