WHO Guidance for Prevention and Treatment of Malaria in Pregnancy

WHO recommends a three-pronged approach to malaria in pregnancy (MIP) which includes: intermittent preventive treatment (IPTp); insecticide-treated nets (ITNs) and prompt and effective case management. WHO's guidance for each prong is summarized below.

Intermittent Preventive Treatment in pregnancy (IPTp)

In areas of moderate-to-high malaria transmission, IPTp with sulfadoxine-pyrimethamine (SP) is recommended for all pregnant women at each scheduled antenatal care visit. WHO recommends a schedule of four antenatal care visits.

- The first IPTp-SP dose should be administered as early as possible during the 2nd trimester of gestation
- Each SP dose should be given at least 1 month apart
- The last dose of IPTp with SP can be administered up to the time of delivery, without safety concerns
- IPTp should ideally be administered as directly observed therapy (DOT)
- SP can be given either on an empty stomach or with food
- Folic acid at a daily dose equal or above 5 mg should not be given together with SP as this counteracts its efficacy as an antimalarial. WHO recommends daily iron and folic acid supplementation in pregnant women at the dose of 30-60 mg of elemental iron and 0.4 mg of folic acid, to reduce the risk of low birth weight infants, maternal anemia and iron deficiency at term.
- SP should not be administered to women receiving cotrimoxazole prophylaxis

Sources:
1. Updated WHO Policy Recommendation on Use of IPTp, October 2012
2. WHO Policy Brief for the Implementation of Intermittent Preventive Treatment of Malaria in Pregnancy using Sulfadoxine-Pyrimethamine (IPTp-SP) 11 April 2013

Insecticide-treated nets (ITNs)

- ITNs should be provided to women as early in the pregnancy as possible, at the ANC clinic or through other sources in the public or private sectors.
- The WHO Global Malaria Programme recommends distribution of ITNs, more specifically LLINs, to achieve full coverage of populations at risk of malaria. The best opportunity for rapidly scaling up malaria prevention is free or highly subsidized distribution of LLINs through existing public health services (both routine and campaigns).

Sources:
1. A Strategic Framework for Malaria Prevention and Control during Pregnancy in the African Region, WHO 2004.
2. WHO Global Malaria Programme: Position Statement on ITNs, 2007

Diagnosis

- "Prompt parasitological confirmation by microscopy or alternatively by RDTs is recommended in all patients suspected of malaria before treatment is started.
- Treatment solely on the basis of clinical suspicion should only be considered when a parasitological diagnosis is not accessible."

Source: Guidelines for the Treatment of Malaria, Second Edition, WHO 2010

Treatment:

Effective case management of malaria illness for all pregnant women in malarious areas must be assured (*Source: A Strategic Framework for Malaria Prevention and Control during Pregnancy in the African Region, WHO 2004.)*

Uncomplicated malaria: "Pregnant women in the first trimester with uncomplicated falciparum malaria should be treated with quinine plus clindamycin for seven days (and quinine monotherapy if clindamycin is not available). Artesunate plus clindamycin for seven days is indicated if this treatment fails." Specifically:

First trimester:

- Quinine plus clindamycin to be given for 7 days (artesunate plus clindamycin for 7 days is indicated if this treatment fails). If clindamycin is unavailable or unaffordable, then quinine monotherapy should be given.
- An ACT is indicated only if this is the only treatment immediately available, or if treatment with 7-day quinine plus clindamycin fails, or if there is uncertainty about patient compliance with a 7-day treatment.

Second and third trimesters:

- ACT known to be effective in the country/region or artesunate plus clindamycin to be given for 7 days or quinine plus clindamycin to be given for 7 days (with the exception of DHA+PPQ for which there is insufficient information in second and third trimesters of pregnancy to use as first line therapy). Note: If clindamycin is unavailable or unaffordable, then the monotherapy should be given.

Patients with HIV infection who develop malaria should receive prompt, effective antimalarial treatment regimens as recommended in the relevant sections of these guidelines. Treatment or intermittent preventive treatment with sulfadoxine-pyrimethamine should not be given to HIV-infected patients receiving cotrimoxazole (trimethoprim plus sulfamethoxazole) prophylaxis.

Complicated malaria: Parenteral antimalarials should be given to pregnant women with severe malaria in full doses without delay. Parenteral artesunate is preferred over quinine in the second and third trimesters, because quinine is associated with recurrent hypoglycaemia. In the first trimester, the risk of hypoglycaemia is lower and the uncertainties over the safety of the

artemisinin derivatives are greater. However, weighing these risks against the evidence that artesunate reduces the risk of death from severe malaria, both artesunate and quinine may be considered as options until more evidence becomes available. Treatment must not be delayed; so if only one of the drugs artesunate, artemether or quinine is available, then it should be started immediately.

Dosages: Artemether plus lumefantrine (ALu): This is currently available as a fixed-dose formulation with dispersible or standard tablets containing 20 mg of artemether and 120 mg of lumefantrine. The recommended treatment is a 6-dose regimen over a 3-day period. The dosing is based on the 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. This extrapolates to 1.7/12 mg/kg body weight of artemether and lumefantrine, respectively, per dose, given twice a day for 3 days, with a therapeutic dose range of 1.4–4 mg/kg of artemether and 10–16 mg/kg of lumefantrine. **Artemsisinins:** The only recent change is the higher maintenance dose of parenteral artesunate recommended (2.4 mg/kg body weight), which is based on pharmacokinetic and pharmacodynamic studies, and by extrapolation from studies with oral artesunate. **Quinine treatment** for severe malaria was established before modern clinical trial methods were developed. Several salts of quinine have been formulated for parenteral use, but the dihydrochloride is the most widely used. Peak concentrations following intramuscular quinine in severe malaria are similar to those following intravenous infusion. Pharmacokinetic modeling studies suggest that a loading dose of quinine (i.e. 20 mg salt/kg body weight – twice the maintenance dose) reduces the time needed to reach therapeutic plasma concentrations. The maintenance dose of quinine (10 mg salt/kg body weight) is administered at 8-hour intervals, starting 8 hour after the first dose. Following initial parenteral treatment, once the patient can tolerate oral therapy, it is essential to continue and complete treatment with an effective oral antimalarial using a full course of an effective ACT (artesunate plus amodiaquine or artemether plus lumefantrine or dihydroartemisinin plus piperaquine) or artesunate (plus clindamycin or doxycycline) or quinine (plus clindamycin or doxycycline).

Source: Guidelines for the Treatment of Malaria, Second Edition, WHO 2010