Global **Malaria** Programme

Testing for G6PD deficiency for safe use of primaquine in radical cure of *P. vivax* and *P. ovale* malaria

Policy brief

World Health Organization

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BACKGROUND

Primaquine is currently the only medicine for treating relapses of *Plasmodium vivax* and *P. ovale* malaria, due to its specific activity against malaria hypnozoites. Despite a reduced sensitivity of these parasites in some countries, requiring increased doses, primaquine has remained highly effective for anti-relapse therapy since its introduction in 1952. The full potential of this medicine to prevent relapses and reduce the transmission of vivax malaria has however not been fully used, owing to concerns about its safety. The medicine induces dose-dependent acute haemolytic anaemia in individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency, a genetically X-linked disorder. This condition is widely prevalent affecting over 350 million people globally, with a prevalence of 3–35% in tropical areas.

The recommended dosage for safe use of primaquine must therefore be adapted to the G6PD status of the patient. This status is, however, rarely known, except in the few countries (e.g. Malaysia and the Philippines) in which G6PD testing is part of newborn screening programmes. Often, G6PD testing is not available at points of care after a diagnosis of *P. vivax* or *P. ovale* malaria. As a result, primaquine is usually given without prior G6PD testing – thus exposing some patients to the risk for haemolytic anaemia – or is not administered – exposing patients to the risk for repeated relapses of *P. vivax* malaria, with consequent morbidity and transmission.

When new point-of-care G6PD tests became available, WHO convened in October 2014 a group to review the evidence from recent evaluations of the performance of testing devices appropriate for use in tropical and resource-limited settings *(1)*. The conclusions were reviewed by the Malaria Policy Advisory Committee and by the Technical Expert Group on Malaria Chemotherapy for inclusion in the third edition of the WHO Guidelines for the treatment of malaria *(2)*.

The aim of this policy brief is to disseminate the new WHO recommendations on G6PD testing to ensure safe administration of primaquine for preventing relapse of *P. vivax* and *P. ovale* malaria. It offers national malaria control programmes guiding principles and practical advice on:

- classification and testing of G6PD deficiency, highlighting the differences between males and females;
- a diagnostic and treatment algorithm for qualitative point-of-care G6PD testing and anti-relapse treatment with primaquine;
- tables for dosing primaquine and information on the sourcing of quality-assured primaquine;
- checklists for counselling patients, recognizing the symptoms of acute haemolytic anaemia and managing side-effects;
- risk–benefit assessments before administering primaquine without G6PD testing, including considerations for G6PD testing in specific countries and geographical areas;
- quantitative and qualitative G6PD tests and the preferred product characteristics of qualitative G6PD tests for use at points of care and
- planning and conducting G6PD testing at country level.

WHO RECOMMENDATION

The G6PD status of patients should be used to guide administration of primaquine for preventing relapse.

- To prevent relapse, treat *P. vivax* or *P. ovale* malaria children and adults (except pregnant women, infants aged < 6 months, women breastfeeding infants aged < 6 months, women breastfeeding older infants unless they are known not to be G6PD deficient and people with G6PD deficiency) with a 14-day course of primaquine at 0.25–0.5 mg base/kg body weight daily in all transmission settings.
- In people with G6PD deficiency, consider preventing relapse by giving primaquine at 0.75 mg base/kg body weight once a week for 8 weeks, with close medical supervision for potential primaquine-induced haemolysis.
- When a patient's G6PD status is unknown and G6PD testing is not available, a decision to prescribe primaquine must be based on an assessment of the risks and benefits of adding primaquine.
- For women who are pregnant or breastfeeding, consider weekly chemoprophylaxis with chloroquine until delivery and breastfeeding are completed; then, on the basis of the woman's G6PD status, treat with primaquine to prevent future relapse *(2)*.

EXPECTED BENEFITS

Complete treatment of *P. vivax* and *P. ovale* malaria requires treatment of both blood-stage infections (to achieve immediate clinical cure and thus avoid progression to severe disease) and liver-stage infections (to prevent future relapses and avoid onward transmission). Wide-scale implementation of the new WHO recommendations on safe administration of primaquine for preventing relapses is expected to have a positive impact for both individuals and public health.

- Safe administration of primaquine on the basis of the results of G6PD testing will reduce morbidity due to relapse in patients with *P. vivax* or *P. ovale* malaria. At the same time, wider G6PD testing will reduce the risk of G6PD-