



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

Policy brief



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

Policy brief



# Table of contents

<b>Background</b>	<b>1</b>
<b>WHO recommendation</b>	<b>2</b>
<b>Expected benefits</b>	<b>2</b>
<b>Primaquine and G6PD deficiency</b>	<b>3</b>
<b>Point-of-care testing for G6PD deficiency in males and females</b>	<b>6</b>
<b>Algorithm for qualitative testing for G6PD deficiency at points of care and safe administration of primaquine to prevent relapse of <i>P. vivax</i> and <i>P. ovale</i> malaria in male and female patients</b>	<b>7</b>
Treatment options for male and female patients according to their G6PD status	8
Dosage, administration and sourcing of quality-assured primaquine	10
Patient counselling and detection of primaquine-induced haemolysis	11
Management of side-effects	12
Risk–benefit assessment for safe administration of primaquine when G6PD deficiency testing is not available	12
<b>Considerations in implementing the new recommendations</b>	<b>14</b>
Quantitative and qualitative G6PD testing methods and preferred product characteristics of point-of-care G6PD tests	14
Introducing or extending a G6PD testing system at country level	16
<b>Further research</b>	<b>18</b>
<b>References</b>	<b>18</b>
<b>Annex. Characteristics of qualitative G6PD tests</b>	<b>20</b>

## TABLES

<b>Table 1.</b> Relations between G6PD deficiency genotypes, enzyme activity and sensitivity to primaquine	5
<b>Table 2.</b> Calculation of dose of primaquine per body weight	10
<b>Table 3.</b> Checklist for establishing a G6PD testing system at country level	16
<b>Table A1.</b> Diagnostic performance of qualitative tests for G6PD deficiency	20
<b>Table A2.</b> Assessment of different commercially available G6PD diagnostic screening tests in male subjects from different countries	21
<b>Table A3.</b> Assessment of different commercially available G6PD diagnostic screening tests in female subjects from different countries	22
<b>Table A4.</b> Characteristics of commercially available qualitative, point-of-care G6PD tests	23

## FIGURES

<b>Figure 1.</b> Prevalence of G6PD deficiency	3
<b>Figure 2.</b> Endemicity of <i>P. vivax</i> malaria in 2010	3
<b>Figure 3.</b> Red cell survival and degree of anaemia following daily primaquine in different G6PD deficiency variants	4
<b>Figure 4.</b> Qualitative G6PD deficiency testing with currently available point-of-care tests in males and females	6
<b>Figure 5.</b> Change in haemoglobin levels after exposure to daily primaquine for 14 days at 0.25 mg/kg/day in four women heterozygous for G6PD deficiency	7
<b>Figure 6.</b> Haemolytic response of the same person after daily and after weekly administration of primaquine	8
<b>Figure 7.</b> Algorithm for qualitative point-of-care testing and safe administration of primaquine to prevent relapse of <i>P. vivax</i> or <i>P. ovale</i> malaria in male and female patients	9

## BOXES

<b>Box 1.</b> Checklist for patient counselling	11
<b>Box 2.</b> Checklist of symptoms of acute haemolytic anaemia	11
<b>Box 3.</b> Checklist for management of side-effects	12
<b>Box 4.</b> Preferred product characteristics of qualitative point-of-care G6PD tests	15

## 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-

预览已结束，完整报告链接和二维码如下：

[https://www.yunbaogao.cn/report/index/report?reportId=5\\_26806](https://www.yunbaogao.cn/report/index/report?reportId=5_26806)

