By the end of this session you should be able to:

- Understand how to use primaquine and tafenoquine in the management of liver-stage uncomplicated *P. vivax* malaria
Vivax has a dormant liver stage which causes relapses.

NB: Some infections may not lead to hypnozoites; some hypnozoites may not relapse.

Primaquine (14-days)

No test for liver stage of vivax

Chloroquine (3-days)
Overview of *P. vivax* malaria treatment

- **To treat the acute malaria infection**
  - Chloroquine (x 3 days)

- **To prevent the relapse of malaria**
  - Primaquine (14 days)
  - OR
  - Tafenoquine (1 day)

*Disclaimer: ACTs are also used prior to PQ in many countries*
Primaquine (PQ) & tafenoquine (TQ) are liver-stage treatments

- PQ and TQ clear parasites that lie dormant in the liver and prevent relapses

- In patients with low levels of G6PD enzyme activity, PQ and TQ can cause haemolysis (destroy red blood cells) leading to AHA that may be life-threatening

- Using a G6PD point-of-care test allows health care workers to select the appropriate radical cure treatment (PQ or TQ or no liver stage treatment) and thereby minimize the risk of haemolysis in patients with low levels of G6PD activity.

G6PD: glucose-6-phosphate dehydrogenase
When tafenoquine **SHOULD NOT** be prescribed

- Pregnant women
- Women breastfeeding infants under 6 months
- Children under 16 years of age
- Women breastfeeding older children with low G6PD activity

*G6PD activity less than 6.1 U/g Hb*
Who SHOULD NOT be prescribed primaquine

Pregnant women*

Women breastfeeding* infants under 6 months

Babies under 6 months

Women breastfeeding* older children with low G6PD enzyme activity

[*Consider weekly chemoprophylaxis with chloroquine until delivery and breastfeeding are completed, then, on the basis of G6PD status, treat with primaquine to prevent future relapse.]*
Dosage and administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Primaquine (PQ)</th>
<th>Tafenoquine (TQ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>For the radical cure (prevention of relapse) of <em>P. vivax</em> malaria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>6 months and older</td>
<td>16 years and older</td>
</tr>
<tr>
<td>G6PD testing</td>
<td>Qualitative or quantitative test</td>
<td>Quantitative G6PD test mandatory</td>
</tr>
<tr>
<td>G6PD enzyme activity</td>
<td>$\geq 4.1 , \text{U/g Hb}^*$</td>
<td>$\geq 6.1 , \text{U/g Hb}^*$</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Breastfeeding women</td>
<td>No</td>
<td>Only if infant is G6PD normal (G6PD = 6.1 U/g Hb or higher).</td>
</tr>
</tbody>
</table>

*Not for use in pregnant women or women breastfeeding infants younger than 6 months; *u/g Hb: Units of G6PD activity per gram of haemoglobin
Treatment algorithm

- [Insert in country treatment algorithm – see example job aids]
A reminder of G6PD activity by gender

G6PD enzyme activity

Normal (equal to or more than 6.1 U/g Hb)

Deficient (equal to or less than 4.0 U/g Hb)

U/g Hb: Units of G6PD activity per gram of haemoglobin
G6PD testing will guide the choice of primaquine and tafenoquine dosing

<table>
<thead>
<tr>
<th>G6PD activity</th>
<th>Primaquine</th>
<th>Tafenoquine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normal</strong>: Greater than or equal to 6.1 U/g Hb</td>
<td>0.25mg /kg daily for 14 days</td>
<td>300mg Single dose if aged 16 years or older</td>
</tr>
<tr>
<td><strong>Intermediate</strong>: 4.1 to 6.0 U/g Hb Risk of haemolysis</td>
<td>0.25 mg/kg daily for 14 days</td>
<td>No</td>
</tr>
<tr>
<td><strong>Deficient</strong>: Less than or equal to 4.0 U/g Hb High risk of haemolysis</td>
<td>0.75 mg/kg weekly for 8 weeks</td>
<td>No</td>
</tr>
</tbody>
</table>

- G6PD testing minimizes the risk of haemolysis due to the drug
- Patients with deficient / intermediate G6PD activity should be closely followed-up for signs of haemolysis
- U/g Hb: Units of G6PD activity per gram of haemoglobin
Do you have any questions or concerns about treating patients based on their G6PD activity?
Why is it important to know the G6PD activity of your patient?

- Primaquine or tafenoquine can protect patients from repeated attacks of vivax malaria which can cause anaemia, severe disease and death.
- In patients with less than normal G6PD activity, primaquine or tafenoquine is more likely to cause red blood cells to rupture / burst (haemolysis or even AHA*)
- Knowing the G6PD activity will allow you to choose the right dosing for your patient.

*acute haemolytic anaemia
What information do you provide to patients about liver-stage treatment (e.g. primaquine) normally?
Good patient counselling is important to ensure patients complete their course of treatment (1/3)

- Provide information about *P. vivax* and G6PD deficiency

- Ask if they understand what you have explained, and what they think about the guidance you have given

- Advise patients about the signs and symptoms of AHA

- Advise patients that if they notice **ANY** of the signs and symptoms of AHA they should immediately **stop primaquine and report to their health facility**

- Advise patients that if they notice **ANY** signs and symptoms of AHA **after tafenoquine treatment they should report to their health facility immediately**
What are the signs and symptoms you should discuss with patients? (2/3)

- The most common sign or symptom of Acute Haemolytic Anaemia is dark urine – with a red or black colour.

Other signs and symptoms of Acute Haemolytic Anemia are:
- Fatigue
- Breathlessness, or shortness of breath
- Back pain
- Yellowing of the skin or whites of eyes
- Pallor – an unhealthy pale appearance
- Rapid heart rate
- Fever
- Nausea and/or vomiting
Good patient counselling is important to ensure patients complete their course of treatment (3/3)

• Ask the patient if they have any concerns or worries about taking their treatment

• For patients taking primaquine - request patients to tell you about their plan to take primaquine over the coming two weeks at home

• Ensure that patients know to take the medicines with food to reduce gastro-intestinal adverse events (or adverse events).
Frequently Asked Questions activity
Treatment practical: Mini-scenarios

• You will receive three short scenarios to read and answer by yourself.

• For each scenario write how you will treat the patient described

• Make sure you include a rationale for your answer

• Be prepared to discuss your answers and rationale
The goal of *P. vivax* malaria treatment is to clear blood and liver stage parasites (radical cure)

- Tafenoquine (TQ) & primaquine (PQ) can cause severe haemolysis in patients with low levels of G6PD activity – this can be prevented by correctly identifying patients who should receive TQ or daily PQ
- PQ can be administered to children 6 months or older who are G6PD normal or intermediate (with careful follow-up)
- TQ can only be administered to vivax patients who are age 16 years and above with G6PD normal activity
- All patients should be informed about signs of AHA – even those who are G6PD normal.
- Patients with ANY sign of AHA should go to the nearest health facility
- You need to take extra time to explain AE to patients with low / medium G6PD activity.

Any questions?