STAGE 1: Exposure
TB Bacilli are inhaled into the lungs of an healthy person via droplets sneezed, coughed or spat by another person who is ill with TB.

STAGE 2: TB germs are found in the lungs but are inactive. This is known as TB INFECTION.

STAGE 3: Immune system unable to contain the TB Bacilli which escapes into the rest of the lungs - and possibly other parts of the body causing disease. This is known as ACTIVE TB DISEASE.
1HP is a combination of 2 drugs, rifapentine and isoniazid, which are taken daily for 28 days to get rid of TB infection.
What is TB infection?

Not everyone infected with Tuberculosis (TB) immediately develops TB disease. Some people go on to have a dormant form of TB that can be reactivated over time or when the immune system is suppressed. This form is called TB infection, and treating it will prevent the person from getting active TB.

Is treating TB infection effective?

Strong evidence shows that the treatment of TB infection (with isoniazid or rifampicin monotherapy, or in combination with other drugs) is effective in preventing progression to active TB disease in adults and children. There were an estimated 10 Million new cases of tuberculosis (TB) and around 1.6 million people died from TB in 2021 (including 187,000 people with HIV). The World Health Organization (WHO) has set ambitious targets for reducing TB incidence and mortality in the next 10–20 years, with an aim to eliminating TB by 2035. Elimination of TB, however, cannot be considered without discussion of TB infection, its diagnosis and treatment. 1.8 billion people are estimated to have and are at risk of developing TB in their lifetime.
Is treatment of TB infection necessary?

Yes, it is extremely important to treat TB infection, particularly in those at high risk of progression to active TB disease, as it can avert the suffering and catastrophic economic costs associated with developing active TB disease.

Does TB preventive treatment (TPT) promote resistant TB?

No! The fact that TPT might promote resistance is a myth that has prevented programs and individuals from accessing life-saving TB preventive treatment.

There are a few reasons why the development of resistance is extremely unlikely:

• TPT is used for patients who do not currently have active TB
• Active TB can be quickly and easily excluded using simple screening algorithms
• Individuals with TB infection have a small number of slowly replicating bacteria in complexes in the lung. These “hidden” bacteria are at low risk of selecting for drug-resistance
• Most resistance arises from suboptimal treatment of active disease, hence preventing active disease may be beneficial for resistance overall
• Multiple trials have failed to find scientific evidence of a significant association between TB drug-resistance and the use of isoniazid or rifamycins for TPT
What is 1HP?

1HP is a short-course Tuberculosis Preventive Treatment (TPT) regimen which is endorsed by the WHO. It combines Isoniazid (H) and high dose rifapentine (P) once daily for 28 days. 1HP is associated with significantly lower hepatotoxicity and higher rates of treatment completion than isoniazid preventive treatment.

Is 1HP superior to IPT?

There is no evidence that 1HP is more effective than IPT, but studies have shown 1HP to be non inferior to IPT and other shorter regimens such as rifampicin alone or rifampicin/isoniazid in preventing progression to active disease. There is evidence, however, to show that 1HP is less toxic to the liver than IPT regimens, although the risk of systemic drug reactions is increased among those taking 1HP.

There is strong evidence to show that people taking shorter regimens such as 1HP are much more likely to complete their course of treatment than people taking IPT.
Is 1HP cost-effective?
While 1HP is expensive in the short-term, the shorter duration of treatment and higher rates of treatment completion make it more cost-effective in the long-term.

Could (and should) 1HP be used for a wider population?
Evidence to support rollout to a wider population such as health care workers and prisoners is very limited at present. The superiority of 1HP (and other shortened regimens) with regard to treatment completion makes it a very attractive option, particularly for use in correctional facilities and other dynamic or unpredictable environments.

28 day of 1HP vs 180 days (six months) of TPT
Fewer doses, shorter duration, better adherence
What about children?
Children above the age of 13 years can have 1HP. They can use the same dose used by adults. There is ongoing research about the use of 1HP in children below the age of 13 years.

What about pregnant women?
1HP is not recommended in Pregnancy.

EVERY DAY
ONCE A DAY
FOR 28 DAYS
How is 1HP used?

1HP is the shortest of several available regimens recommended for treating TB infection.

It consists of a once daily dose of rifapentine and isoniazid, taken at the same time for 28 days.

1HP is made up of 300mg Isoniazid (INH) + 600mg Rifapentine (RPT)

### Dosing of rifapentine and isoniazid for treatment of TB infection (1HP)

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Formulation</th>
<th>Patients &gt; 13 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Option 1 - Singles</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>300 mg</td>
<td>1</td>
</tr>
<tr>
<td>Rifapentine</td>
<td>300 mg</td>
<td>2</td>
</tr>
<tr>
<td>Isoniazid - Rifapentine</td>
<td>300 mg / 300 mg</td>
<td></td>
</tr>
</tbody>
</table>
Who can take 1HP?

Persons with no active TB disease and none of the following contra-indications, can be started on 1HP:

- Age 13 years and above
- Active Hepatitis (acute or chronic)
- Regular & heavy alcohol use
- Peripheral Neuropathy
- Women of child-bearing age who are wishing to conceive or not able to use barrier methods for contraception
- Pregnancy or breastfeeding
- Protease Inhibitor based antiretroviral therapy

Individuals at higher risk of peripheral neuropathy should be offered vitamin B6 (pyridoxine) supplementation with 1HP; if B6 is not available this should not delay starting a course of 1HP.

How should 1HP be administered?

Self administered therapy should be provided by clinicians. Patients should be educated on the symptoms of TB and side effects. Directly observed therapy is however not required for 1HP administration.
How to handle a missed dose

- Encourage a daily routine of taking medications. If a patient misses one or more days, they can take 1HP immediately and go back to their normal daily routine.
- If they miss a dose for more than 3 days:
  - They can continue until all 28 doses have been taken.
- The 28 dose course should be finished by 8 weeks which provides some leeway for missed doses.
- 28 doses in 8 weeks can also be counted as sufficient, although not ideal.
Monitoring

Patients taking 1HP should be monitored at monthly visits to assess tolerability and adherence.

**Essential components of the visit are:**

- Screen for active TB
- Screen for pregnancy
- Screen for AEs and assess tolerability
- Assess adherence and provide support as appropriate
- Assess for new medications that can interfere with 1HP
Adverse Events

Clinicians should educate patients about possible adverse events, and instruct patients to use a symptom checklist (see below) and medication intake log.

- Patients should be evaluated to assess adherence and treatment-associated adverse events.
- It is important that AEs are recorded and reported wherever possible.
- Minor adverse events are likely to occur in small proportion of individuals. Serious adverse events rarely occur and hence both the health care provider and patient should be vigilant and manage such events proactively.
- Because 1HP is a preventive treatment used to cure persons with no active disease, the risk of AEs should be especially minimized. Important AEs associated with 1HP are mostly drug reactions but some may be due to drug interactions with other medicines.
- In addition, active TB and pregnancy during 1HP treatment require special attention.
Counselling for Adverse Events

- Red/orange discoloration of urine and other body fluids such as sweat and tears while taking 1HP is normal and completely harmless. Individuals should be alert to the following symptoms:
  - Rashes accompanied by fever and chills. Gastrointestinal upset like vomiting, diarrhoea and abdominal cramps.
  - Weakness, fatigue, loss of appetite, persistent nausea (early symptoms of liver injury)
  - Symptoms of active TB (weight loss, night sweats, fever, cough)

Persistent fatigue, nausea and fever.

Rifapentine may cause your urine (pee), saliva, tears, or sweat to appear an orange-red colour.

normal
Management of Adverse Events

If an AE occurs while a patient is taking 1HP, they should be advised not to take any further doses until an assessment is made of the severity and nature of the AE.

Assessment should include:

- Screen for active TB
- Past history
- History of the AE: type, onset and duration, severity
- Relevant physical examination

Management of the AE should always be guided by the clinical judgement. Suggested management:

- Severe drug reactions: seek urgent supportive care
- Mild/moderate drug reactions: reassurance, symptomatic relief, further assessment

Pregnancy or active TB while on 1HP requires discontinuation of the drug.

- Pregnancy: discontinue 1HP
- Active TB: discontinue 1HP and start TB treatment
In the absence of specific information regarding 1HP and anti-malarials, the only guidance that can be offered currently is:

- If a patient is diagnosed with malaria but is not yet on TPT, decisions regarding 1HP initiation should be delayed until the episode of malaria has resolved.
- If a patient is diagnosed with malaria while on 1HP, the patient should be treated for malaria and clinically monitored according to national guidelines to ensure that the malaria is cured. At this stage, there is insufficient evidence to indicate that doses need to be adjusted.
- If a patient has malaria recrudescence while on 1HP, and the patient should be retreated for malaria according to national guidelines. The 1HP regimen should be withheld only if the new treatment also includes a drug with known interactions with rifamycins. In that case, 1HP can be restarted once the episode of malaria is resolved.
- If a patient meets diagnostic criteria for severe malaria (impaired consciousness, low blood glucose, high bilirubin/jaundice, bleeding, anemia, kidney failure and parasitemia >10%) while on 1HP, the 1HP regimen should be withheld and the patient should be urgently treated according to national guidelines. 1HP should be recommenced only once the episode of malaria is fully resolved.

Recording and Reporting

- Routine pharmacovigilance procedures should be used for AEs associated with 1HP, where possible and according to national guidelines.
- At sentinel sites, AEs should additionally be reported according to the evaluation protocol.
Drug-drug Interactions with Principles of Rifamycin same for 1HP

When two drugs are given together, there can be a change in either of the drug’s effect on the body. A drug-drug interaction (DDI) can increase or decrease the action of either or both drugs, or can be the cause of adverse events. Drug reactions are usually mild and self-limiting, but occasionally they can be severe.

Rifapentine can cause a decrease in the activity of many drugs that pass through the cytochrome enzyme system. Caution should be exercised when co-administering 1HP with hormonal contraceptives, ART that includes protease inhibitors, some anti-seizure medicines as well as anti-malarials.
Note the following:

- Alternate forms of contraception should be used (barrier methods) when taking 1HP.
- If malaria is diagnosed during 1HP treatment, the malaria treatment might be less effective. If malaria does not resolve, patients should be re-treated according to country guidelines. If a patient is receiving malaria treatment, they should hold off on taking their 1HP dose for that week and resume once the malaria course is completed.
- Patients taking a protease inhibitor for HIV should not receive 1HP. An alternate regimen containing efavirenz, dolutegravir, or raltegravir can be safely used instead.
- Please consult the brief “drug-drug interactions” available at https://www.impaact4tb.org/library/ for further information on potential interactions, or consult a pharmacist.