Short-course treatment to prevent tuberculosis: 3HP

One-quarter of the world's population is infected with the bacterium that causes tuberculosis (TB), a disease that kills more than 4,000 people per day. People can have TB in their body but not be contagious, not show any symptoms and remain healthy. This is called latent TB infection. The problem is that without treatment, many people with latent infection can develop active TB. And once they have active TB, they are at risk of death and are infectious to their close contacts—such as their children, other family members and co-workers—who are at high risk of getting TB.

By treating the TB infection, we are able to prevent active TB. Treatment for TB infection, known as TB preventive therapy (TPT), has been available since the 1960s, yet very few people who should get TPT receive it. And because current regimens require daily treatment for at least six months, many who start treatment may fail to complete a full, effective course. The good news is that we now have new, shorter treatment options for people with latent infection.

What is 3HP?

3HP is a short-course TPT regimen that combines two antibiotics used to treat TB—isoniazid and rifapentine—taken only once a week for 12 weeks.

- **Components:** 900 mg isoniazid (H) + 900 mg rifapentine (P), separate tablets
- **Dosing:** once weekly
- **Duration:** 12 weeks
- **Target populations:** people living with HIV and household contacts over two years, regardless of HIV status.

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### Co-administration of 3HP and dolutegravit (DTG)

In July 2018, the WHO released updated interim guidance on first- and second-line ART regimens including DTG-based regimens as a preferred first-line ART for adults, adolescents and all infants and children with approved DTG dosing. The WHO guidelines acknowledged the clinical and programmatic advantages of DTG including improved tolerability, lower potential for drug interactions, shorter median time to viral suppression and a higher genetic barrier to resistance.

Countries are now choosing DTG-regimens as the preferred first-line ART due to superior efficacy, tolerability and higher threshold for resistance compared to efavirenz-containing regimens. The fixed-dose combination tablet of TLD—tenofovir (TDF), lamivudine (3TC) and DTG—is now available at a price affordable to low- and middle-income countries; prices are expected to further decrease as generic manufacturers increase production. PEPFAR has also recommended the regimen for all of its supported-countries.

In 2018, a study carried out in South Africa by the Aurum Institute and the Johns Hopkins University School of Medicine looked at the safety and pharmacokinetics of giving 3HP with DTG. Researchers enrolled 60 adults with HIV, who received DTG for eight weeks, then began 3HP; after completion of 3HP, all participants were followed for four more weeks. **Overall, co-administration of DTG and 3HP was well-tolerated, safe and does not appear to require any dose-adjustment for DTG.**
What do the guidelines say?

In 2018, the World Health Organization (WHO) released new guidelines for the treatment of TB infection, which recommend the use of 3HP for people living with HIV as well as HIV-uninfected adults and children at risk of developing active TB.

3HP is already approved for the treatment of TB infection by the U.S. Food and Drug Administration and is recommended by the U.S. Centers for Disease Control and Prevention. The Aurum Institute and its partners will also be pursuing regulatory approval of 3HP products in project countries. In high-TB burden countries where rifapentine is not yet registered, an importation waiver to use rifapentine will be obtained through the Stop TB Partnership’s Global Drug Facility.

For people living with HIV/AIDS, 3HP is safe to give with efavirenz-based antiretroviral therapy (ART) as well as with dolutegravir, which is becoming part of the first-line drug to treat HIV in many high-burden TB countries.

What are the advantages of 3HP?

- The 12-dose regimen reduces treatment time to three months, compared to at least six months for isoniazid.
- It requires weekly doses compared to daily doses with isoniazid.
- Shorter treatment regimens have been shown to have higher completion rates.
- There are lower rates of hepatotoxicity with 3HP than with daily doses of isoniazid.
- It places less of a burden on TB and HIV programs compared to at least six months of daily isoniazid.
- Modeling studies indicate that 3HP is cost-effective, reducing the economic burden of TB control efforts.

Who is not recommended for treatment with 3HP?

- Children under two years of age, as proper dosage is not yet known.
- Patients taking certain drugs that interact with 3HP such as protease inhibitors for HIV.
- Persons presumed infected with M. tuberculosis that is resistant to isoniazid and/or rifampin.
- Until the results of ongoing studies evaluating the safety of 3HP in pregnant women are available, caution should be exercised in using 3HP for pregnant women.
- Women who are unwilling or unable to use contraception. As 3HP decreases hormonal contraceptive levels, women must be advised to use barrier methods such as condoms or diaphragms.
- Patients who had prior adverse events or hypersensitivity to isoniazid or rifampin or rifapentine.

Advantages of 3HP

- Shorter—3 months weekly vs. 6 months daily
- Less liver toxicity
- Fewer side effects
- Greater adherence

For more information, visit www.impact4TB.org or contact: impact4tb@auruminstitute.org

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Increasing Market and Public health outcomes through scaling up Affordable Access models of short Course preventive therapy for TB