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AN ACTIVIST'S GUIDE TO RIFAPENTINE

FOR THE TREATMENT OF TB INFECTION

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FOR THE TREATMENT OF TB INFECTION

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I. INTRODUCTION AND BACKGROUND

This guide summarizes information on rifapentine, an important drug for treating **tuberculosis (TB) infection**. Treatment of TB infection is referred to as TB preventive therapy (TPT) and is one of the most powerful ways to prevent TB. If left untreated, TB infection can develop into active TB disease, the form of TB that makes people sick and is capable of being transmitted from one person to another. Yet only a very small proportion of the people who may benefit from TPT receive it.

Rifapentine belongs to a class of drugs called **rifamycins** and is the backbone of newer short-course TPT. When combined with a second TB drug, isoniazid, rifapentine forms the **3HP** regimen (taken once weekly for 12 weeks) and the **1HP** regimen (taken once a day for one month). The 3HP and 1HP regimens offer shorter alternatives to the older standard of care, called isoniazid preventive therapy (IPT), in which people take isoniazid every day for between six and 36 months.

TPT has two major goals: 1) protect people who are already infected with the TB bacterium from falling ill with active TB disease, and 2) shield people who are uninfected but at risk of TB exposure from getting infected in the first place. Preventive therapy is one of the best ways to keep individuals and families safe from TB, which in turn helps communities become—and remain—TB free.

We wrote this guide to provide people at risk of TB, as well as their family members and caregivers, with the knowledge they need to make an informed choice about whether to take rifapentine-based TPT. For this choice to be meaningful, rifapentine must be available, accessible, and affordable, so this guide suggests actions people can take to promote equitable access to rifapentine. We need to give more people access to newer TPT regimens like 3HP and 1HP if we hope to end TB in our families and communities.

II. THE EFFICACY OF RIFAPENTINE-BASED TB PREVENTIVE THERAPY

Large, multicountry clinical trials have established the efficacy of the 3HP and 1HP regimens in preventing TB disease. PREVENT-TB, a phase III clinical trial conducted by the U.S. Centers for Disease Control and Prevention, evaluated the efficacy of 3HP against nine months of daily isoniazid (9H). The trial enrolled over 8000 participants and found that

KEY TERMS

TB INFECTION, sometimes referred to as latent TB infection (LTBI), is caused by infection with *Mycobacterium tuberculosis*.

RIFAMYCINS are a class of antibiotics that includes the drugs rifampicin, rifapentine, and rifabutin. They share a similar chemical structure and method of action.

KNOW YOUR TPT REGIMENS:
When abbreviating TB drug regimens, **H** = isoniazid; **P** = rifapentine; and **R**= rifampicin (sometimes called rifampin).

- **3HP** = 12 weeks of isoniazid and rifapentine taken together once a week
- **1HP** = one month of isoniazid and rifapentine taken together once a day
- **3HR** = three months of isoniazid and rifampicin taken together once a day
- **4R** = four months of daily rifampicin
- **IPT** = isoniazid taken daily for six, nine, 12, or up to 36 months

3HP was **noninferior** to (no worse than) 9H in preventing TB disease.[1] Participants taking 3HP were more likely to complete treatment than those on 9H.

PREVENT-TB also assessed the effectiveness of 3HP in nearly 400 people living with HIV (PLHIV) and over 900 adolescents and children as young as two years old. Among PLHIV, 3HP was noninferior to 9H in preventing TB disease, and people taking 3HP were more likely to complete treatment.[2] Based on when the study started, participants with HIV in the trial were not on antiretroviral therapy (ART). Today, TPT should always be offered together with ART (read "*What about people living with HIV?*" below.) Children taking 3HP in the PREVENT-TB study also did well and were more likely to complete treatment than those receiving 9H.[3]

The BRIEF-TB trial, conducted by the AIDS Clinical Trials Group at the U.S. National Institutes of Health, evaluated the efficacy of 1HP compared with 9H. This phase III trial enrolled 3000 adults living with HIV and assessed safety, treatment completion, and efficacy over three years of follow-up.[4] The trial found that 1HP was noninferior to 9H in preventing TB and death from either TB or unknown cause. Participants taking 1HP were significantly more likely to complete treatment than those on 9H. Further studies to assess whether 1HP is effective in other populations, including HIV-negative people, children, and pregnant women, are planned.

3HP and 1HP look efficacious in clinical trials, but do they work in the real world? Yes! Programmatic experience with 3HP in the **United States**, Australia, Taiwan, Pakistan, and other places indicates that the regimen is safe, is well accepted by most people who take it, and has higher completion rates than IPT.[5,6] Evaluations of 1HP among PLHIV in program settings will begin soon.

III. THE SAFETY OF RIFAPENTINE-BASED TB PREVENTIVE THERAPY

Rifapentine-based TPT is safe and well tolerated. Across studies, 3HP appears to pose less risk of **hepatotoxicity** than IPT, and the BRIEF-TB trial suggests 1HP is also less hepatotoxic.[7,8] A systematic review of 15 studies comparing 3HP to other TPT regimens (mostly 9H) found that 3HP has "equal safety and effectiveness" to other preventive regimens.[9] A separate analysis looking at the efficacy and toxicity of various TPT regimens reached similar conclusions about the safety and efficacy of 3HP.[10] Compared with IPT, rifamycin-based TPT may carry a higher risk of **hematologic toxicity**.

Overall, 3HP is safe enough for people to take themselves (self-administration). Some programs recommend that people taking 3HP have a monthly visit with a health care worker to identify any adverse events and receive adherence support.[11]

Rare adverse events called hypersensitivity reactions have been reported in both clinical trials and programmatic use of rifapentine.[12] These reactions are often characterized by **flu-like symptoms**. There are some reports of people experiencing **hypotension** or **syncope** after taking 3HP. Hypersensitivity episodes are uncommon and usually resolve quickly after medication is stopped without any long-term effects. In some cases, people experiencing hypersensitivity have been hospitalized.

NONINFERIORITY means that the intervention is no worse than the control by a prespecified amount (called a noninferiority margin).

One study of 3HP in **16 U.S. TB programs** reported a higher treatment completion rate than observed in the PREVENT-TB trial (see Sandul A, et al.).

HEPATOTOXICITY, or liver toxicity, occurs when drugs or other chemicals damage the liver.

HEMATOLOGIC TOXICITIES are those that affect the blood and its components (e.g., anemia).

FLU-LIKE SYMPTOMS can include fever, chills, headaches, dizziness, and fatigue.

HYPOTENSION is abnormally low blood pressure.

SYNCOPE is a temporary loss of consciousness due to a fall in blood pressure.

In the PREVENT-TB trial, 3.5% of participants who received 3HP had a hypersensitivity reaction, with many occurring several hours after taking the third 3HP dose (i.e., in the third week of the 12-week treatment course).[13]

Hypersensitivity may be linked to the intermittent, once-weekly dosing schedule of 3HP.[14] The cause of these reactions is unknown—they could be due to rifapentine, isoniazid, or the combination of the two. Several TB drugs can cause hypersensitivity. Flu-like symptoms have been observed with intermittent, high-dose rifampicin and, less commonly, with isoniazid. People taking 3HP should be informed about the small risk of experiencing hypersensitivity and taught to recognize its signs (flu-like symptoms) and contact a health care provider immediately if experiencing them.

Like other rifamycin class drugs, rifapentine interacts with many medications for other conditions. In addition, there are some important things to consider when using 3HP in special populations such as pregnant individuals, children, and people who use drugs.

What about people living with HIV? Rifapentine is safe to use in PLHIV, but interactions between rifapentine and certain antiretrovirals must be managed (or avoided altogether either by using other TPT options or by switching antiretroviral regimens). 3HP and 1HP are safe to use with efavirenz- and raltegravir-based ART. Many countries will soon transition from efavirenz- to dolutegravir-based first-line therapy (i.e., the TLD regimen composed of dolutegravir, lamivudine, and tenofovir disoproxil fumarate). A recent study assessed the safety and **pharmacokinetics** (PK) of giving 3HP with dolutegravir (see box). Importantly, PLHIV in areas where malaria or severe bacterial infections are common should receive 3HP together with **cotrimoxazole**.

What about children and young people? 3HP can be given to adolescents and children as young as two years of age. The drug has not yet been studied in children under two years; however, a study looking at safety and optimal dosing of 3HP in this age group will begin in 2019. The study is using a child-friendly formulation of 3HP developed by Sanofi that dissolves in water and tastes like mango. While waiting for the results of this study, infants and children under two years who need TPT can receive either 3HR or six months of isoniazid (6H). Kids with HIV on efavirenz-based ART can take 3HR, which is available in a child-friendly, water-dispersible formulation. 6H is preferred for children with HIV taking nevirapine, lopinavir-ritonavir, or dolutegravir because it does not require ARV dose adjustments. Isoniazid also comes in a child-friendly dispersible tablet. Until Sanofi's pediatric 3HP product becomes available, even children over two years may prefer 3HR or 6H if they have trouble swallowing pills, due to the 3HP regimen's high pill burden (see "*Rifapentine Dosing Information*" below).

What about pregnant individuals? Pregnancy increases the risk of TB infection progressing to active TB disease. Rifapentine is currently not recommended for use in individuals who are pregnant. This is due to a lack of data on the safety of giving rifapentine during pregnancy. Research is underway to fill this critical knowledge gap.[15] Until then, pregnant individuals at risk of TB can take IPT, though when to start IPT—during pregnancy or after delivery—requires careful consideration. The World Health Organization (WHO) recommends that pregnant women with HIV take IPT, although the only clinical trial of IPT in this population

PHARMACOKINETICS involves studying what the body does to a drug by looking at things like how a drug moves throughout the body or how the concentration and distribution of a drug changes across space and time.

COTRIMOXAZOLE is an antibiotic that consists of two drugs—trimethoprim and sulfamethoxazole—and is taken by PLHIV to prevent serious bacterial infections such as pneumonia or toxoplasmosis.

found more **adverse pregnancy outcomes** among women who took IPT during pregnancy compared with those who did so after delivery.[16] Anyone who receives IPT during pregnancy or in the postpartum period should be closely monitored, especially since the risk of hepatotoxicity is higher during pregnancy and following birth.[17] Rifampicin is also safe in pregnancy, and some clinicians prefer to use rifampicin-based TPT (e.g., 4R). Which TPT regimen to take, and when to start treatment, should be decisions made together by pregnant individuals and their health care providers after openly weighing all the risks and potential benefits.

ADVERSE PREGNANCY OUTCOMES include things like preterm delivery, low birth weight, fetal demise, and congenital anomalies (birth defects).

Individuals who wish to avoid pregnancy should know that rifapentine (like other rifamycins) decreases the effectiveness of hormonal contraceptives.[18] These individuals should consider using a different, or additional, form of contraception when taking rifapentine-based TPT.

What about people being treated for hepatitis C virus (HCV)?
Rifamycins, including rifapentine, are not recommended for use together with many of the direct-acting antiretroviral drugs (DAAs) used to treat HCV.[19] This is because rifamycins can decrease the concentration of HCV drugs to **subtherapeutic levels**. People with HCV should consult with their health care providers about starting rifapentine-based TPT either before or after completing treatment for HCV.

The body processes many DAAs in the liver using enzymes such as cytochrome P450. These enzymes play a major role in drug metabolism and are induced by rifamycins, resulting in faster metabolism and lower drug levels.

SPOTLIGHT: GIVING 3HP WITH DOLUTEGRAVIR-BASED HIV TREATMENT

In March 2019, investigators from the Johns Hopkins Center for TB Research and the Aurum Institute presented results from a phase I/II study assessing the safety and PK of coadministering 3HP and dolutegravir. The study enrolled 60 adults with HIV who were given dolutegravir-based ART (TLD) and 3HP.

The study sought to answer two questions: 1) Is it safe to take 3HP with dolutegravir-based ART? 2) If yes, does the dose of dolutegravir need to be adjusted? Answering these questions is important because dolutegravir and 3HP each have their advantages over alternative ART and TPT regimens, and so many HIV and TB programs will want to use them together. At the same time, rifamycins such as rifapentine can speed up the body's metabolism of ARVs, including dolutegravir, which could require increasing the dose of dolutegravir to maintain viral suppression of HIV while taking the two treatments together.

1. Safety results: Coadministering 3HP with dolutegravir was safe, with very few adverse events reported. There were no deaths. All 60 participants completed a full course of 3HP.
2. PK results: Rifapentine reduced dolutegravir concentrations, but not by a clinically meaningful amount, so all participants received the standard dose of dolutegravir (50 mg once a day) without adjustment. All participants saw their HIV remain virally suppressed while taking 3HP. One participant had a detectable HIV viral load reading, but this occurred four weeks after completing 3HP and was judged to be unrelated to rifapentine.

Main takeaway: 3HP can be safely used with dolutegravir-based ART without adjusting dolutegravir doses. With these results, national governments should feel confident introducing 3HP into HIV programs, and donors, including the President's Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund, should support countries in procuring 3HP for TPT as an essential part of the HIV clinical care package.

What about people who use drugs (PWUD)? PWUD have a higher prevalence of TB infection and incidence of TB disease.[20] Rifapentine has not been systematically studied in PWUD. However, rifampicin is known to reduce exposures to **opioid substitution therapies** (OST) such as methadone and buprenorphine.[21] In some people, this results in opiate withdrawal. For this reason, people taking 3HP with OST should be closely monitored for signs of opiate withdrawal and other adverse events. Increasing the dose of methadone or buprenorphine when taking rifamycins can lessen the risk of withdrawal. IPT is safe to use in PWUD, although careful monitoring for liver toxicity is important.[22] Drug use should never be taken as a blanket rationale for denying someone TPT; it is the responsibility of health care providers to proactively manage drug-drug interactions for PWUD in a safe way.

OST is a type of harm reduction intervention for drug use. OST treats opioid dependence by replacing opioids (like heroin) with prescribed drugs that can manage or reduce opioid cravings and prevent sudden withdrawal.

IV. RIFAPENTINE DOSING INFORMATION

Rifapentine is currently available as 150 milligram (mg) tablets.

- In the **3HP** regimen for adults, 900 mg of rifapentine is taken with 900 mg of isoniazid (which comes in 300 mg tablets), along with a vitamin B6 supplement. That means each dose of 3HP requires taking 10 pills (see illustration).
- In the **1HP** regimen for adults, 600 mg of rifapentine is taken with 300 mg of isoniazid together with vitamin B6. That means each dose of 1HP requires taking six pills.

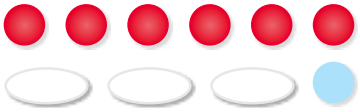
ILLUSTRATION: Per-Dose Pill Count of 3HP and 1HP by Different Formulations of Rifapentine and Isoniazid

3HP = 900 mg isoniazid (INH) with 900 mg rifapentine (RPT), plus vitamin B6
1HP = 300 mg of INH with 600 mg of RPT, plus vitamin B6

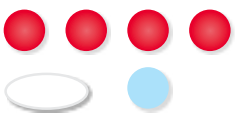
= Rifapentine (RPT) = Isoniazid (INH) = Vitamin B6 = INH/RPT

Pill count with tablets of INH = 300 mg and RPT = 150 mg

3HP



1HP



Pill count with an INH/RPT fixed-dose combination (INH 300 mg, RPT 300 mg)

3HP

1HP

Lowering the pill burden of 3HP and 1HP would improve acceptability by making it easier for people to take every dose in full. Several generic drug manufacturers are developing new formulations of rifapentine that would reduce pill burden by offering rifapentine as a 300 mg tablet or by putting 300 mg of rifapentine and isoniazid together in a fixed-dose combination (FDC).

When to take rifapentine: if possible, people should take rifapentine with food, since taking the drug with a meal (especially one with some fat) increases the **bioavailability** of rifapentine.

BIOAVAILABILITY is the amount of a drug that enters circulation after being taken and is therefore able to have an active effect.

Don't be surprised: rifapentine tablets are red in color, and people taking rifapentine may notice their urine, sweat, or tears turn red or orange. This effect is harmless and will disappear soon after finishing treatment.

V. ACCESS TO RIFAPENTINE

Rifapentine is an old drug, first discovered in the 1960s. This means that any **patents** on rifapentine have long expired.[23] Despite this long history and lack of intellectual property barriers, access to rifapentine is constrained by its high price, limited number of quality-assured suppliers, and lack of registration beyond a few countries (see table on p. 7).

PATENTS are a type of intellectual property, a kind of 'right of ownership' that allows the owners of a patented product to exclude others from making or selling it for a period of time.

Until recently, Sanofi was the only quality-assured supplier of rifapentine. This monopoly has contributed to the high price of the drug. In early 2019, a generic manufacturer based in India applied to receive WHO prequalification for a 3HP FDC.[24] At least one other generic manufacturer is expected to seek prequalification for a rifapentine product soon. The introduction of **quality-assured** generic formulations of rifapentine should improve the drug's availability, accessibility, and affordability by introducing competition among multiple suppliers. But ensuring that rifapentine becomes equitably accessible to all who may benefit from this essential TB prevention drug will require vigilance and action on the part of activists.

A **QUALITY-ASSURED** drug is one that has been evaluated and approved by a stringent regulatory authority (e.g., the Food and Drug Administration, the European Medicines Agency or the WHO prequalification program.)

VI. TAKE ACTION! KEY ADVOCACY MESSAGES

TB preventive therapy saves lives. There is no doubt that TPT saves lives, prevents illness, and averts suffering. Some of the strongest proof comes from the TEMPRANO trial, which studied IPT among PLHIV in Cote d'Ivoire. Participants receiving IPT had a 37% reduction in mortality, independent of whether they were also on ART, with those on both IPT and ART enjoying the greatest protection against severe disease and death.[25] Several million TB deaths could have been avoided if IPT had been rolled out worldwide when WHO recommended its programmatic use in 2008.[26] Short-course rifapentine-based TPT may have an even greater potential to save lives. *Activists should demand that TPT be offered to all people at risk of TB and raise awareness of TPT among TB-affected communities so that people demand access to TPT as their right.*

TABLE: RIFAPENTINE PRODUCTS ON THE MARKET AND IN LATE-STAGE DEVELOPMENT

Which companies make rifapentine?	What rifapentine product(s) do they make?	What does rifapentine cost?	Where is rifapentine registered for treatment of TB infection?
Sanofi	RPT 150 mg tablet	**In the United States:** RPT 150 mg = $24/24-tablet blister pack This equates to $72 for the RPT in a full course of 3HP **Via the Global Drug Facility:** RPT 150 mg = $15/24-tablet blister pack This equates to $45 for the RPT in a full course of 3HP	As of March 1, 2019, Sanofi had registered rifapentine in the United States (2014), Taiwan (2017), Hong Kong (2017), the Philippines (2018), Thailand (2018), Indonesia (2018), and South Africa (2018). This encompasses 4 out of 30 high-TB-burden countries and 3 out of 30 high-TB/HIV-burden countries. In addition, Sanofi has filed rifapentine for registration in India.
Sanofi	Water-dispersible 3HP FDC tablet for children (150 mg INH, 150 mg RPT) Water-dispersible RPT standalone tablet for children (100 mg RPT)	*Under evaluation in a clinical trial; not yet on the market*	NA
Generic Supplier 1	3HP FDC tablet (300 mg INH, 300 mg RPT)	*WHO PQ and Global Fund ERP endorsement pending (WHO PQ submission February 2019; accepted for Global Fund ERP review March 2019)*	NA
Generic Supplier 2	RPT 300 mg tablet	*In development; WHO PQ submission expected in 2019*	NA

ERP = Global Fund Expert Review Panel for Pharmaceutical Products; FDC = fixed-dose combination; INH = isoniazid; mg = milligram; NA = not available; PQ = WHO prequalification; RPT = rifapentine

Notes:
1. Rifapentine is also registered in Chile, although this product is not made by Sanofi.
2. Rifapentine is produced in China, although this product is not quality assured.

Rifapentine is an essential TB medicine and the cornerstone of new TPT regimens. All countries should have guidelines for TPT that include 3HP (and 1HP following its endorsement by WHO). Countries must rapidly update guidelines when data on using 3HP during pregnancy and in children aged 0–2 years become available. Guidelines should respond to **ongoing research** to develop even safer and shorter regimens. International donors, particularly the Global Fund and PEPFAR, should financially support countries' scale-up of rifapentine-based TPT as a routine and integral part of TB and HIV programs. *Activists should hold country governments and donor agencies accountable for implementing rifapentine-based TPT in line with global guidelines and evolving scientific evidence.*

The price of rifapentine must fall! The high price of rifapentine set by Sanofi is a major impediment to its widespread use in the short term. Equitable and sustainable access to rifapentine will depend on substantial price reductions. Based on what it costs to manufacture rifapentine, and assuming sufficient volumes of sales, 3HP could cost as little as $10 per patient (and should cost no more than $15 per patient at lower volumes). To reach this more affordable price point, several things must happen:

Want more information on **ONGOING RESEARCH** on rifapentine-based TPT? Read TAG's 2018 TB Prevention Pipeline Report! www.pipelinereport.org

Major **PUBLIC FUNDERS** of rifapentine development efforts include the U.S. Centers for Disease Control and Prevention, the U.S. National Institutes of Health, the U.S. Agency for International Development, Unitaid, and the European and Developing Countries Clinical Trials Partnership.

1. Additional suppliers must enter the market. The expected market entry of at least two generic manufacturers is a sign that Sanofi's monopoly on quality-assured rifapentine will end. All suppliers must price rifapentine within reach of TB programs.
2. Volumes must rise, and buyers should work together to pool demand and negotiate lower prices. Pooling procurement by purchasing rifapentine via the Global Drug Facility (GDF) would help consolidate demand and create the positive, predictable market dynamics that would encourage the price to fall as volumes rise.
3. *Activists should support the entry of generic manufacturers; push Sanofi and generic companies to set a fair price for the drug; build community demand for rifapentine; and encourage governments to pool demand by buying rifapentine through the GDF.*

Rifapentine is a global public good. The high price of rifapentine is especially indefensible considering that **public funding** underwrote the vast majority of research behind 3HP and 1HP. Sanofi is not the original innovator behind rifapentine. Traded from one pharmaceutical company to the next over five decades, "rifapentine has had many private owners and mostly public benefactors."[27] The public has a right to benefit from public investments in science. Sanofi and other manufacturers therefore have an obligation to make rifapentine accessible to all, in a manner that honors the drug's status as a global good developed primarily with public resources. *Activists should hold Sanofi and generic manufacturers accountable for pricing rifapentine affordably and registering the drug widely.*

Provision of TPT must always be based on human rights and respect for persons. Whether to take TPT (or not) must always be an individual choice made with full information and without coercion. By definition, people with TB infection are not sick and therefore do not pose any risk to others. The risk of TB infection progressing to TB disease is much higher for some groups, such as PLHIV, very young children, and people who have just recently acquired infection. In general, however, only 5–10% of people with TB infection will develop active TB at some point in their lifetime. Treatment always carries some risk of side effects, so understanding the individual risk/benefit tradeoff of taking TPT is necessary to make an informed decision. The WHO TB Ethics Guidance clearly states that taking TPT should never be compulsory.[28] *Activists should raise awareness of rifapentine-based TPT, share knowledge of how to prevent TB in communities, and ensure TB prevention efforts are based on human rights and respect for individual decision-making.*

VII. OVERCOMING RESISTANCE TO IMPLEMENTING TPT

Activists will hear many excuses for not implementing TPT. Some common excuses for not using TPT are outlined below, along with the evidence and arguments that activists can use to overcome them.

EXCUSE: There isn't a good test for TB infection, or for predicting who with infection will progress to active TB disease, so we don't know whom to treat with TPT.

RESPONSE: WHO guidelines do not require a test for infection before starting PLHIV or child household contacts less than five years old on TPT.[29] These two groups face a much higher risk of TB, making the risk/benefit tradeoff favor TPT, even without testing for infection. It is true that current tests for TB infection are imperfect and expensive and come with several important caveats, the biggest being that they do not directly measure infection or the risk of progression to active TB. (Current tests for TB infection include tuberculin skin tests [TSTs] and interferon-gamma release assays [IGRAs].) Therefore, testing should never be a barrier for offering TPT to PLHIV and young children. For other groups, a test for infection does two useful things: 1) a test result may help individuals decide whether to take TPT, and 2) a positive test may help clinicians identify people who are more likely to benefit from TPT (generally speaking, those with a positive test benefit more from TPT than those without). Active TB disease must always be ruled out before starting TPT in all people, regardless of HIV status or age.

EXCUSE: Taking TPT encourages the development of drug-resistant TB.

RESPONSE: There is no evidence that TPT promotes the development of drug-resistant TB. A review of six trials of rifamycin-based TPT regimens (e.g., 3HP, 3HR) found no statistically significant increased risk of rifamycin resistance in people taking these regimens compared with people taking TPT without a rifamycin or placebo.[30] Similarly, a review of 13 IPT studies published since 1951 found no significantly increased risk of isoniazid-resistant TB among people receiving IPT versus placebo.[31] The vast majority of drug-resistant TB arises from inadequate treatment of active TB disease. Rather than withhold TPT out of fear of drug-resistant TB, TB programs should 1) ensure all people starting TPT are first screened for active TB; 2) promote treatment completion by offering short-course TPT options like 3HP; and 3) diagnose and treat all people with drug-resistant TB to halt its spread.

EXCUSE: TB programs are overwhelmed with treating active TB. TPT will divert attention and resources away from TB treatment.

RESPONSE: Treatment versus prevention is an old, tired, and false conflict. We must abandon the austerity mindset that tells TB programs they can do only one thing at a time. This either/or mentality traps TB-affected communities in a false economy of partial solutions. Denying people interventions like TPT that are proven to reduce suffering is a violation of the human rights to health and scientific progress. When considering different TB interventions, we need to adopt a both/and mindset. Today, TB programs must do more than diagnose and treat active disease. TB programs should actively identify TB in the community (active case finding), perform contact tracing after diagnosing someone with TB, offer TPT to contacts of people with TB, and support people taking TPT to complete treatment.

A TB program that focuses only on diagnosis and treatment of active disease is living up to only part of its human rights and public health responsibilities.

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