

NATIONAL TUBERCULOSIS ELIMINATION PROGRAMME

Guidance document on shorter one-month daily isoniazid and rifapentine (1HP) regimen option for TB Preventive Treatment

Forward:

This is a technical and operational guidance document on shorter one month daily isoniazid and rifapentine (1HP) TPT regimen option for implementation in age group ≥ 13 years. The guidance is presented as an addendum to and should be referred in context of the Guidelines for Programmatic Management of TB Preventive Treatment in India 2021.

Evidence for 1HP:

- A large randomized, open label trial¹ compared the efficacy and safety of the shorter 1HP regimen and reported that 1HP regimen is noninferior to 9 month daily isoniazid regimen (9H) in PLHIV from high TB prevalence area or had evidence of TB infection.
 - 3,000 patients were followed for a median of 3.3 years.
 - Treatment completion was significantly higher in 1HP compared to 9H (97% versus 90%, $p < 0.001$).
 - Serious adverse event occurred 6% and 7% in the group given 1HP and 9H respectively. Although lower in 1HP, the difference was not significant ($p = 0.07$).
 - TB incidence was reported to be 0.65 and 0.67 per 100 person-years in the group given 1HP and 9H respectively. The rate of difference in 1HP was -0.02 per 100 person-years; upper limit of 95% confidence interval was 0.30).
- WHO’s guidelines on TPT also recommends 1HP as alternative option for the use across all disease burden settings and target populations including PLHIV.²

TPT target group, strategy, and treatment options:

Target population	Strategy	Treatment option
<ul style="list-style-type: none"> • People living with HIV <ul style="list-style-type: none"> ○ PLHIV adults and children >12 months irrespective of ART initiation status ○ Child living with HIV age <12 months in contact with active TB • Household contact below 5 years of pulmonary* TB patients 	TPT to all after ruling out active TB disease	<ul style="list-style-type: none"> • 1HP (1 month of daily isoniazid and rifapentine – 28 doses) in person ≥ 13 years <p style="text-align: center;">Or</p> <ul style="list-style-type: none"> • 3HP (3 months of weekly isoniazid and rifapentine – 12 doses) in person
<ul style="list-style-type: none"> • Household contacts 5 years and above of pulmonary* TB patients (testing would be offered whenever available) 	TPT among TBI positive# after ruling out TB disease	







¹ Swindells S, Ramchandani R, Gupta A et. al. BRIEF TB/A5279 Study Team. One Month of Rifapentine plus Isoniazid to Prevent HIV-Related Tuberculosis. N Engl J Med. 2019 Mar 14;380(11):1001-1011. doi: 10.1056/NEJMoa1806808. PMID: 30865794; PMCID: PMC6563914.

² World Health Organization. WHO operational handbook on TB: Module 1 – TB Preventive Treatment, 2020

<ul style="list-style-type: none"> • Other risk group <ul style="list-style-type: none"> ○ Children/adult on initiation of immunosuppressive therapy or anti-TNF treatment, ○ Person with silicosis, ○ Patient on dialysis, ○ Person considered for organ or haematologically transplantation 	TPT after ruling out TB disease among TBI positive	<p>older than 2 years</p> <p>Or</p> <ul style="list-style-type: none"> • 6H (6 months of daily isoniazid – 180 doses)[§] <p>Or</p> <ul style="list-style-type: none"> • 3RH (3 months of daily rifampicin and isoniazid - 84 dosages) in age group < 15years
<ul style="list-style-type: none"> • Household contacts of multi drug resistant TB (MDR-TB) patients with fluoroquinolone (FQ) sensitive 	TPT after ruling out TB disease among TBI positive	<ul style="list-style-type: none"> • 6Lfx (6 months of daily levofloxacin)
<ul style="list-style-type: none"> • Household contacts of Isoniazid mono/poly resistant TB (Hr-TB) patients with rifampicin (R) sensitive 	TPT after ruling out TB disease among TBI positive	<ul style="list-style-type: none"> • 4R (4 months of daily rifampicin)

* bacteriologically confirmed pulmonary TB patients will be prioritized for enumeration of the target population for TPT; # Chest X-ray (CXR) and testing for TB infection would be offered wherever available, but TPT must not be deferred in their absence; § fixed-dose combination of Isoniazid + Pyridoxin (B6) + Cotrimoxazole (CPT) is a preferred formulation in PLHIV

Recommended dosages of 1HP

Regimen	Dose by age and weight band				
1HP – one month of daily rifapentine plus isoniazid (28 doses)	Age ≥ 13 years (regardless of weight band):				
	Isoniazid: 300 mg/day				
	Rifapentine: 600 mg/day				
	Formulations:				
	No. of pills	HP FDC (Isoniazid 300mg + Rifapentine 300mg)	Rifapentine 300mg	Isoniazid 300mg	Rifapentine 150mg
	2 pills				
OR					
3 pills					
OR					
5 pills		--			

1HP as a TPT treatment options

	1HP
Medicines	Isoniazid + Rifapentine
Duration	1 month
Interval	Daily
Number of doses	28
Pregnancy	Not known
Interaction with ART	Contraindicated: – All PIs, NVP/NNRTIs, TAF Use with – TDF, EFV (600mg), DTG, RAL (without dose adjustment)
Adverse Drug Reactions	Hepatotoxicity, hypersensitivity reaction, rash, GI upset, orange discolouration of body fluids
Absorption	Peak concentration is increased with given with a meal.

Special situation

- **TPT among people who use drugs:** people taking 3HP, 3RH, 4R or 1HP with Opioid Substitution Therapy (OST) should be closely monitored for signs of opiate withdrawal and other adverse events. Increasing the dose of methadone or buprenorphine when taking rifamycin can lessen the risk of withdrawal.

Management of interruptions

Treatment interruptions with 1HP should be managed as is done in case of 6H, 6Lfx and 4R.

TPT regimen	Duration of interruption	Management steps
1HP	Less than 1 weeks	<ul style="list-style-type: none"> • If more than 23 (80%) doses out of 28 expected doses in the regimen were taken, no action is required, just complete the remaining doses. • If less than 23 (80%) doses out of 28 expected doses in the regimen were taken, resume treatment immediately upon return and add the missed doses to the total treatment duration to complete the course within a maximum of 6 weeks from the first dose.
	More than 1 weeks	<ul style="list-style-type: none"> • If more than 7 consecutive doses were missed, consider restarting the complete course of 1HP regimen. • If more than 7 doses were missed intermittently, resume preventive treatment immediately upon return and add the missed doses to the total treatment duration to complete the course within a maximum of 8 weeks from the first dose. • If adherence to 1HP is not possible, consider discontinuing it and offering 3HP or an alternative daily regimen

Treatment outcomes:

- **Treatment completion with 1HP:** 80% of recommended dose (23/28) consumed within 133% of planned TPT duration (40 days) for 1HP.

Regimen	Total duration in months	Expected number of dosages	80% of recommended dosages (days)	Extended time for treatment completion (days) (treatment duration + 33% additional time)
1HP (daily)	1	28	23	40

- **Loss to follow up in 1HP:** TPT interrupted by person for 10 consecutive days for 1HP.
- There is no difference in definitions of treatment failed, died, TPT discontinuation due to toxicity and not evaluated. Refer Guidelines for Programmatic Management of TB Preventive Treatment in India 2021

Recording and reporting:

Ni-kshay is the real-time case-based information management and surveillance system for TB in India. Records of enrolment, screening, TB diagnosis or TBI tests, treatment information, adverse event, dispensation etc. should be recorded in Ni-kshay TPT module. The operational aspects in terms of data entry points, health facility/ field level staff to perform the data entry can be referred in table 12.1 in the guidelines for programmatic management of TB preventive treatment. All the PLHIV eligible for TPT should be enrolled in Ni-kshay and follow-up through Ni-kshay TPT module. The data manager at the ART Centre (ARTC) should be responsible for complete entry of TPT care cascade in Ni-kshay under the guidance of ARTC In-charge.

The TPT care cascade monitoring is possible through 'TB Preventive Treatment dashboard' available in Ni-kshay.