T-11020/36/2005/NACO (ART)-Part 2
Government of India
Ministry of Health and Family Welfare
National AIDS Control Organization
(Care, Support and Treatment Division)

6th & 9th Floor, Chandralok Building
36, Janpath, New Delhi
Dated: 20.05.2024

To,
The Project Director,
All State AIDS Control Societies

Subject: Revised guidance on Tuberculosis Preventive Therapy for PLHIV under NACP -reg.

As you are aware, the risk of developing active TB disease among People Living with HIV (PLHIV) is higher than those without HIV infection. Therefore, to prevent the progression of latent TB infection to active TB disease among PLHIV, TB Preventive Therapy (TPT) is provided, after ruling out active TB, through ART centers under the National AIDS Control Programme (NACP), in alignment with National TB Elimination Programme (NTEP) guidelines and recommendations of Technical Resource Group on ART. Guidance on TPT for PLHIV have been updated recently in view of availability of shorter and more effective TPT regimens under NTEP.

The revised guidance on TPT for different groups of PLHIV is as below:

S.N.	PLHIV category	Preferred TPT regimen	Remarks
1.	PLHIV who are 13 years of age and older	INH & Rifapentine daily for 28 days **(1HP)**	Dose modification of Dolutegravir is **not required** with '1HP'.
2.	PLHIV less than 13 years of age	INH daily for six months **(6H)**	
3.	Pregnant & Breastfeeding Women living with HIV	INH daily for six months **(6H)**	
4.	PLHIV on Protease Inhibitor(PI) based ARV regimens	INH daily for six months **(6H)**	
5.	PLHIV having contact with Drug-Resistant Tuberculosis (DRTB)	4 months daily Rifampicin **(4R)** for contacts of TB patients with INH mono/poly resistance & Rifampicin susceptible OR 6 months daily Levofloxacin **(6 Lfx)** for contacts of TB patients with MDR/ Rifampicin Resistance & Fluoroquinolone susceptible	Proper documentation of history for TB among family members/close contacts and drug resistance of index TB patient should be done.
6.	PLHIV less than 13 years of age who have successfully completed treatment for TB disease	INH daily for 6 months **(6H)** (Secondary Prophylaxis)	For PLHIV who are 13 years of age and older and have successfully completed treatment for TB disease, immediate TPT as secondary prophylaxis is **not required.**

In this regard, the specific action points at State level are as follows:

a) SACS to calculate the following:
   - Estimate category-wise number of PLHIV who will be eligible for different TPT regimens
   - Facility wise currently available stock of TPT

b) Prepare annual indent to be given to respective State TB Officers for various TPT regimens for each ART center

c) SACS to support ARTC in rational usage of currently available stocks of Isoniazid as TPT

d) States to plan phased implementation of '1HP' for PLHIV who are more than 13 years of age, in consultation with respective State TB Officer

e) Capacity building of ART center staff will be undertaken

Detailed technical guidance of NTEP on '1HP as TPT' is enclosed for reference. SACS is requested to coordinate with the State TB officers for the supply of various TPT regimens, based on facility-wise requirement and to ensure implementation of the above guidance at all ART centres in the State.

It is informed that this guidance for ART centres supersedes previous guidance on TPT for PLHIV under NACP.

For any clarification, please email to nacocst@googlegroups.com

Yours sincerely,

Chinmoyee Das
20/12/2024

(Dr. Chinmoyee Das)
HoD-CST Division, NACO

Enclosure: *"Guidance document on shorter one-month daily isoniazid and rifapentine (1HP) regimen for TB Preventive Treatment"* issued by NTEP

Copy to:

- Joint Director CST/CST in-charge, SACS
- PD- CoE/PCoE
- All ART centres

Copy for information to:

- PPS to AS & DG, NACO
- PS to JS, NACO
- Heads of Programme divisions, NACO
- Deputy Director General, Central TB Division
- Additional Commissioner, Central TB Division

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 trial[1] 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:

<table>
<tr><th>Target population</th><th>Strategy</th><th>Treatment option</th></tr>
<tr><td>• People living with HIV
○ 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</td><td>TPT to all after ruling out active TB disease</td><td rowspan="2">• 1HP (1 month of daily isoniazid and rifapentine – 28 doses) in person ≥ 13 years
Or
• 3HP (3 months of weekly isoniazid and rifapentine – 12 doses) in person</td></tr>
<tr><td>• Household contacts 5 years and above of pulmonary* TB patients (testing would be offered whenever available)</td><td>TPT among TBI positive# after ruling out TB disease</td></tr>
</table>

[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

• **Other risk group** ○ 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	older than 2 years Or • 6H (6 months of daily isoniazid – 180 doses)[$] Or • 3RH (3 months of daily rifampicin and isoniazid - 84 dosages) in age group < 15years
• **Household contacts of multi drug resistant TB (MDR-TB) patients with fluoroquinolone (FQ) sensitive**	TPT after ruling out TB disease among TBI positive	• 6Lfx (6 months of daily levofloxacin)
• **Household contacts of Isoniazid mono/poly resistant TB (Hr-TB) patients with rifampicin (R) sensitive**	TPT after ruling out TB disease among TBI positive	• 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

<table>
<tr><th>Regimen</th><th>Dose by age and weight band</th></tr>
<tr><td>1HP – one month of daily rifapentine plus isoniazid (28 doses)</td><td>
Age ≥ 13 years (regardless of weight band):
Isoniazid: 300 mg/day
Rifapentine: 600 mg/day

Formulations:
<table>
<tr><th>No. of pills</th><th>HP FDC (Isoniazid 300mg + Rifapentine 300nmg</th><th>Rifapentine 300mg</th><th>Isoniazid 300mg</th><th>Rifapentine 150mg</th></tr>
<tr><td>2 pills</td><td>  </td><td>  </td><td></td><td></td></tr>
<tr><td>OR</td><td></td><td></td><td></td><td></td></tr>
<tr><td>3 pills</td><td></td><td>  </td><td>  </td><td></td></tr>
<tr><td>OR</td><td></td><td></td><td></td><td></td></tr>
<tr><td>5 pills</td><td></td><td>--</td><td>  </td><td>  </td></tr>
</table>
</td></tr>
</table>

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	• 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	• 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.