

# PRODUCT BRIEF

## Paediatric-friendly rifapentine and isoniazid for 3HP TB preventive treatment (TPT)

### TB prevention and short-course TPT for children

Children, especially those under the age of 5, who are infected with TB are at a higher risk of progressing from TB infection to TB disease, when compared to adults. Children who are household contacts of an infectious TB patient, HIV infected, malnourished, or have any other underlying health condition have a higher risk of progression. Given the higher risk and the potential for developing severe forms of the disease, it is crucial to evaluate and provide TPT to children as appropriate to prevent progression to TB disease.

**The World Health Organization (WHO) recommends TB preventive treatment (TPT) for children and adolescents at high risk including:**



**Children aged < 5** who are household contacts of people with bacteriologically confirmed pulmonary TB who are found not to have TB disease  
(Strong recommendation)



**Children and adolescents aged 5 and above** who are household contacts of people with bacteriologically confirmed pulmonary TB who are found not to have TB disease (Conditional recommendation)



**Children 12 months and older living with HIV** who are considered unlikely to have TB disease if they live in a setting with high TB transmission, regardless of contact with TB (Strong recommendation)



**Infants aged < 12 months** living with HIV who are in contact with a person with TB and who are unlikely to have TB disease  
(Strong recommendation)



**Adolescents living with HIV** who are unlikely to have TB disease, including those on antiretroviral treatment, pregnant women, and those who have previously been treated for TB.  
(Strong recommendation)



**All children living with HIV** who have successfully completed treatment for TB disease (Conditional recommendation)

- Exclusion of TB disease should be based on appropriate clinical evaluation or according to national guidelines
- TPT should be provided even if TB infection testing is unavailable
- TPT should be offered as part of a comprehensive package of HIV prevention and care

## Available rifapentine - based short course TPT regimens for children and adolescents

There are currently two shorter rifapentine-based TPT regimens recommended by WHO: 3HP, a three-month oral treatment taken once weekly recommended for children and adults aged 2 years and above; and 1HP, a 28-day oral treatment taken once daily recommended for adults and adolescents aged 13 years or older. Rifapentine is taken in combination with isoniazid (H) in both 3HP and 1HP regimens. The HP drug ratio in the two regimens is different, refer to WHO operational handbooks for dosing.

Evidence from TBTC Study 35 for 3HP in children <2 years and to review dosing guidance for 3HP in all children, has been generated and will be reviewed by the WHO Technical Advisory Group on dosing in Q1 2024. The IMPAACT2024 study, that is ongoing, is expected to generate evidence for dosing of people at risk of TB aged below those <13 years for 1HP.

Other WHO recommendations for TPT include 3 months of daily Isoniazid and Rifampicin (3HR), 4 months of Rifampicin (4R)<sup>1</sup> or 6-9 months of daily isoniazid (6H, 9H). 6/9H remains important for CLHIV on most ART regimens in the absence of data from DOLPHIN Kids on DTG and rifapentine DDIs. Levofloxacin (Lfx) can be used in children and adolescents exposed to MDR-TB.

## Rifapentine and Isoniazid products for children and adolescents

Palatable tablets of both medicines are available, that can be dispersed in water and are therefore easier to administer to children. This allows for more accurate dosing compared to crushing adult tablets.



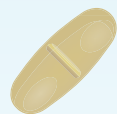
Rifapentine 150mg scored dispersible tablet  
(GF ERP approved, under review by WHO PQ)  
– taste-masked for increased palatability

**\$1.38**  
per 10 pack



Isoniazid 100mg scored dispersible  
(WHO Prequalified)  
– taste-masked for increased palatability  
Already in use

**\$8.95 - \$9.16**  
per 100 pack



Isoniazid 100mg scored dispersible tablet  
(under development)  
– taste-masked for increased palatability

**\$3.00**  
per 100 pack<sup>2</sup>

<sup>1</sup>Although there is a conditional recommendation, there is currently no suitable child-friendly option for 4R.

<sup>2</sup>Contingent upon successful development and regulatory approval

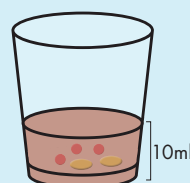
## About the new RPT 150mg scored dispersible tablet (Lupin)





- Functionally scored tablet to provide 75mg dose increments
- Disperses rapidly in a small volume of water (about 10ml)
- Taste masked with raspberry mint flavoring
- Stability data generated at ICH Zone IVb conditions (30°C/75% Relative Humidity (RH))
- Proposed shelf-life: 24 months
- Proposed Packaging:
  - o Aluminum strips (10ct and 28ct)
  - o Aluminum/Aluminum blister (10ct and 12ct)
  - o PVC/PVDC blister with Aluminum lidding foil (10ct)
- Can be ordered via the Stop TB Partnership Global Drug Facility (GDF) or other country procurement mechanisms directly from the manufacturer



## Pediatric dosing and pricing

**3HP = 12 weekly doses**  
**Ages 2-14**



Weight Band	Weekly Dose	Regimen Price
10 – 15 kg	3x INH 100mg DT + 2x RPT 150mg DT 	\$6.53
16 – 23 kg	5x INH 100mg DT + 3x RPT 150mg DT 	\$10.34
24 – 30 kg	6x INH 100mg DT + 4x RPT 150mg DT 	\$13.07
31kg+	7x INH 100mg DT + 5x RPT 150mg DT 	\$15.80

### Evidence for 3HP use in children and adolescents

- 3HP is as effective as isoniazid-only treatment for the prevention of TB in individuals aged 2 to 17 years. 3HP has been associated with higher treatment completion rate and was found to be safe. (Villarino et al., 2015)
- DOLPHIN Kids - PK and Safety of 3HP and DTG in CLHIV: Results expected in 2025
- Among HIV-infected persons (2 years and above), 3HP was as effective and safe for the treatment of TB infection as 9H, and better tolerated. (Sterling et al., 2016) The WHO currently recommends 3HP for children living with HIV on Efavirenz based regimens
- 3HP and 1HP are cost effective in comparison to no TPT in TB high-burden countries (Ryckman et al., 2023)

### Summary of Paediatric friendly TPT regimens

Regimen	Duration	Dosing schedule	Formulations	Regimen price <sup>3</sup> (example for a 15kg child)
3HP	3 months	Weekly	INH 100mg DT + RPT 150mg DT	\$6.53
3HR	3 months	Daily	INH 50mg/RIF 75mg FDC DT	\$14.18
4R	4 months	Daily	RIF 150mg capsule	\$15.42
6H or 9H	6 or 9 months	Daily	INH 100mg DT	\$16.20- \$24.30

<sup>3</sup>Based on GDF Catalog, October 2023