PROPOSAL FOR THE ADDITION OF A NEW FORMULATION OF RIFAPENTINE (150 MG SCORED, DISPERSIBLE TABLETS) TO THE WHO MODEL LIST OF ESSENTIAL MEDICINES AND THE WHO MODEL LIST OF ESSENTIAL MEDICINES FOR CHILDREN FOR THE PREVENTION OF TB IN CHILDREN

Applicant: WHO Global Tuberculosis Programme (GTB), Geneva, Switzerland (Tiziana Masini, Sabine Verkuijl, Kerri Viney, Annemieke Brands (WHO/HQ/UCN/GTB/PCD) and Avinash Kanchar (WHO/HQ/UCN/GTB/PCI)).

Persons to contact:

Tiziana Masini, PhD
Email: tmasini@who.int

Avinash Kanchar, MD
Email: kanchara@who.int

Date of submission:

31 October 2024

1. **Summary statement of the proposal**

This application concerns the updating of the forthcoming World Health Organization (WHO) Model List of Essential Medicines (EML) and WHO Model List of Essential Medicines for Children (EMLc) to include a new formulation of rifapentine, namely 150 mg scored, dispersible tablets, to section 6.2.5 Antituberculosis medicines of the WHO EMLs, for use as part of TB preventive treatment (TPT) in children at risk of TB.

Since 2015, WHO recommends treating tuberculosis (TB) infection in populations at higher risk of progression to the disease, within a larger framework of preventive actions outlined under Pillars 1 and 2 of the WHO End TB Strategy *(1)*. At the United Nations High Level Meeting (UNHLM) on TB held in New York in September 2023, Member States committed to scaling up TPT with the goal of providing TPT to approximately 45 million people, including children, between now and 2027.

Children below 5 years who are household contacts of people with bacteriologically confirmed TB have a significantly higher risk of acquiring TB infection and progressing rapidly to TB disease. Children aged under 2 years are also at particularly high risk of progression to severe and disseminated forms of TB with high morbidity and mortality. TPT is strongly recommended in all TB household contacts aged under 5 years once TB disease is ruled out, without any requirement to test for TB infection beforehand *(2)*.

Rifapentine is a core component of short TPT regimens including a three-month regimen of weekly rifapentine and isoniazid (3HP). WHO first recommended the use of 3HP in 2018, but due to lack of evidence, dosing guidance for 3HP was given only for people at risk of TB aged 2 years and above. In general, the cost of rifapentine has been a major barrier to uptake of 3HP. However, thanks to coordinated efforts by several partners, the price of rifapentine and thus, of the 3HP regimen, was significantly reduced in the past few years, making it one of the preferred shorter TPT options throughout the world.

In September 2024, WHO published updated guidelines and an operational handbook on TPT providing dosing guidance for 3HP for people of all ages, including for children under 2 years of age *(2, 3)*. The child-friendly formulation of rifapentine (150 mg scored, dispersible tablet), which became available in November 2023, alongside a child-friendly formulation of isoniazid that was already available, enables appropriate dosing of 3HP for all children across weight-bands, improving the likelihood of adherence to treatment in a particularly vulnerable population.

The negotiated launch price for the child-friendly formulation of rifapentine will be lower than the price of the adult formulation, making 3HP cheaper than alternative TPT regimens available for children. The formulation can be ordered from the Stop TB Partnership Global Drug Facility (GDF) *(4)* or directly from the manufacturer.

2. Consultation with WHO technical departments

N/A

3. Other organizations consulted and/or supporting the submission

The TB Procurement and Market shaping Action Team (TPMAT), a group composed of several stakeholders (including Treatment Action Group, Médecins Sans Frontières and others) and led by GDF was consulted and is supporting this application.

4. Key information summary for the proposed medicine(s)

INN	Rifapentine
ATC code	J04AB05
Indication	TB preventive treatment (TPT)
ICD-11 code	1B14
Strength	150 mg
Dosage form	Dispersible tablet (scored)
EML	Yes
EMLc	Yes

The formulation proposed for inclusion was assessed through the paediatric Quality Target Product Profile Tool available on the WHO website *(5)*. The assessment is available in Annex 1.

5. Listing as an individual medicine or representative of a pharmacological class/therapeutic group

The application is for the inclusion of Rifapentine 150 mg scored, dispersible tablet to the WHO EML and EMLc as an individual medicine.

6. Information supporting the public health relevance

Epidemiological information on disease burden

Tuberculosis is a communicable disease that is a major cause of ill health. In 2023, TB returned to being the world's leading infectious disease killer, surpassing COVID-19. It was also the leading killer of people with HIV and a major cause of deaths related to antimicrobial resistance *(6)*. TB is caused by the bacillus *Mycobacterium tuberculosis*, which is spread when people who are sick with TB expel bacteria into the air, for example, by coughing. The disease typically affects the lungs (pulmonary TB) but can also affect other sites (extrapulmonary TB). About a quarter of the world's population is infected with *M. tuberculosis (7)*, with the lifetime risk of developing TB disease about 5–10% among those infected.

Globally, an estimated 10.8 million people fell ill with TB in 2023, up from 10.6 million in 2022 and 10.3 million in 2021, continuing the reversal of the downward trend that had been sustained for many years up to 2020. Globally, in 2023, TB caused an estimate 1.25 million deaths, down from best estimates of 1.4 million in both 2020 and 2021 and 1.3 million in 2022 and almost back to the 2019 levels. There were an estimated 161 000 deaths from TB among people with HIV *(6)*.

The estimated incidence of TB in children and young adolescents aged below 15 years is 1.25 million per year or 12% of the total TB incidence. Children under 5 years make up 47% of the incidence in this age group. TB-related deaths in children and young adolescents constitute 15% of total mortality due to TB *(6)*.

Proposed indication

TPT is a potent public health intervention to reduce the burden of TB disease. Providing TPT to high-risk individuals has dual benefits. It prevents morbidity and mortality at the individual level and reduces the TB burden by curtailing its transmission from individuals who would otherwise develop TB. TPT reduces the risk of progression from TB infection to TB disease by about 60%, but this can be as high as 90% among certain high-risk groups (such as people living with HIV) *(8, 9)*.

Epidemiological data from the WHO Southeast Asia region, indicate that TPT at scale is an essential intervention if the Sustainable Development Goals targets are to be met. Optimal implementation of TPT alone in certain high-risk groups such as household contacts or people living with HIV has the potential to reduce annual TB incidence rates by 8.3% (95% credible interval [CrI 6.5–10.8] relative to 2015, in the absence of any additional interventions *(10, 11)*.

An investment case on TB screening and TPT was released by WHO in 2024, providing strong economic arguments for policymakers and advocates to raise awareness among the public and government of the true costs of TB and the benefits of prevention. In all four countries included in the modelling, adding TPT to screening for TB disease was found to create efficiencies and maximize health and financial gains. Integrating TPT with TB screening prevents a substantial number of additional TB episodes as well as saving many more lives *(12)*.

Target population(s)

Once TB disease is ruled out, TPT is currently recommended by WHO for household contacts of bacteriologically confirmed pulmonary TB patients, people living with HIV, those with silicosis, those receiving dialysis or anti-tumour necrosis factor treatment, or individuals preparing for haematological or organ transplantation. Depending upon the country context, people with risk factors other than those mentioned above (such as prisoners, non-household close contacts, people with diabetes) can also be considered for systematic screening and TPT.

Children below 5 years who are household contacts of people with bacteriologically confirmed TB have a significantly higher risk of acquiring TB infection and progressing rapidly to TB disease. Children aged under 2 years are also at particularly high risk for severe and disseminated forms of TB with very high risk of morbidity and mortality. TPT is strongly recommended in all TB household contacts aged under 5 years once TB disease is ruled out *(2)*.

At the first UNHLM on TB in 2018, Member States committed to providing TPT to at least 30 million people in the 5-year period 2018–2022 including 6 million people living with HIV, 4

million children aged under 5 years who are household contacts of people with bacteriologically confirmed TB, and 20 million household contacts in older age groups. At the second UNHLM-TB held in 2023, Member States committed to even more ambitious targets, namely providing 45 million people with TPT between 2023 and 2027, with specific targets for people (of all ages) living with HIV (15 million) and household contacts of all ages (30 million, no disaggregated figures for children are available) *(13)*. This translates into providing 90% of people at high-risk of developing TB with TPT by 2027.

Assessment of current use

The global number of people living with HIV and household contacts of people diagnosed with TB who were provided with TPT increased from 1.0 million in 2015 to 3.6 million in 2019. There was then a sizeable reduction to 2.9 million in 2020 and 2021, probably reflecting disruptions to health services caused by the coronavirus (COVID-19) pandemic. There was a substantial recovery to 3.9 million in 2022, above the pre-pandemic level, and a further large increase in 2023 to 4.7 million *(6)*.

The number of people living with HIV (including children) who were enrolled on TPT increased between 2015 and 2019 (reaching a peak of 3.0 million in 2019) before falling in 2020 and subsequently levelling off at about 2 million people per year (with 1.96 million in 2023) Even if TPT coverage for people living with HIV has improved globally since 2015, it still remains well below the new target set at the second UNHLM-TB, where Member States committed to providing TPT to up to approximately 45 million people globally in the 5-year period 2023-2027, including approximately 15 million people living with HIV *(6)*.

Progress towards achieving the first UNHLM targets for TPT coverage (2018-2022) among household contacts has been slow, with only 55% and 10% of the targets for TPT provision in child contacts <5 years and ≥ 5 years being achieved by 2022, respectively.

Even though there has been a particularly noticeable increase in the number of household contacts enrolled on TPT since 2021 - from 0.76 million in 2021 to 2.7 million in 2023 -, TPT coverage for household contacts remains well below the new UNHLM-TB targets, with only 21% of the target being met. Of the 2.7 million household contact provided with TPT in 2023, 23% (667,426) were <5 years and 77% (2.07 million) were ≥5 years. Progress in TPT provision for household contacts aged < 5 years remains slow (+12% compared to 2022), and only 42% of the 1.56 million eligible child contacts aged under 5 received TPT in 2023. For household contacts aged 5 years and above, there was a more significant increase in TPT provision, with a rise of 52% from 2022 *(6)*.

In 2023, 1.0 million people were reported to have started shorter TPT regimens in 86 countries. Among these, 77 countries reported using 3HP.

For TPT among children, the 3 months regimen of daily isoniazid and rifampicin (3HR) has been a preferred TPT option in the past since child-friendly dispersible fixed-dose combinations (FDCs) are widely available and already used for TB treatment, as well as listed on the WHO EMLs. With the availability of a child-friendly formulation of rifapentine, 3HP can be used for TPT in HIV-negative children across weight bands. For children living with HIV, a six-month regimen of daily isoniazid (6H) remains the preferred option until further

data are available. A paediatric formulation of isoniazid that can be used for children is listed on the WHO EMLs.

In the medium to long term, 3HP may become the preferred regimen for all ages. Indeed, due to its shorter duration, improved clinical profile, and programmatic benefits, 3HP is expected to not only replace 6H as the preferred TPT regimen, but also drive overall scale–up of TB prevention programs across ages. The availability of the new child-friendly formulation of rifapentine will enable implementation of 3HP also in younger children.

7. **Treatment details**

The requirements for the identification of people eligible for TPT, the indication and contraindication for its use, and the monitoring associated with the proposed medicine are identical to those of formulations of rifapentine that are already listed on the WHO EMLs.

Rifapentine is used for TPT in combination with isoniazid as a weekly dosage for 3 months (3HP) or a daily regimen for one month (1HP) *(2)*.

The formulation for which this application is being made is targeted for use in the 3HP regimen, which was first recommended for use by WHO in 2018 for people at risk of TB down to 2 years of age. In September 2024, WHO published updated TPT guidelines and an updated operational handbook where dosing guidance for 3HP is provided for people of all ages, including children below 2 years of age *(2, 3)*.

In January-February 2024, evidence from TBTC Study 35 (NCT03730181) was reviewed by the Technical Advisory Group (TAG) on dosing of TB medicines *(14)*. TBTC Study 35 was a dose-finding and safety study of rifapentine and isoniazid as part of the 12-week, once weekly regimen of isoniazid and rifapentine (3HP) in HIV infected and HIV-uninfected children aged 0–12 years with TB infection, including children on efavirenz and dolutegravir. Based on further modelling conducted in early 2024 *(15)*, the TAG advised on updated dosing guidance for 3HP for children of all ages published in the WHO operational handbook on TPT. This modelling was also aimed at matching the dosing used in the trial with new weight bands that the WHO Global Tuberculosis Programme will be implementing in its operational handbooks to standardize dosing across therapeutic areas, with the aim to simplify drug prescribing and administration when treating individual children for multiple diseases and comorbidities *(16)*.

Dosing guidance on rifapentine and isoniazid for the 3HP regimen as published in the WHO Operational Handbook on TPT across weight bands and given available formulations is shown in **Table 1**.

TPT regimens and drug formulations	No. of tablets or quantity of solution by body weight band												
	3–5.9 kg (< 3 months)	3–5.9 kg (≥ 3 months)	6–9.9 kg (< 6 months)	6–9.9 kg (≥ 6 months)	10–14.9 kg	15–19.9 kg	20–24.9 kg	25–29.9 kg	30–34.9 kg	35–39.9 kg	40–44.9 kg	45–49.9 kg	> 50 kg
Three months of weekly rifapentine plus isoniazid (3HP)													
Isoniazid 100 mg dt	0.6 (6 mL[a])	0.7 (7 mL[a])	1	1.5	2.5	3	4.5	4.5	6	6	7.5	7.5	9
Isoniazid 300 mg tab	–	–	–	–	–	1	1.5	1.5	2	2	2.5	2.5	3
Rifapentine 150 mg dt	0.5 (5 mL[d])	0.7 (7 mL[d])	1.5	1.5	2	3	4	4	5	6	6	6	6
Rifapentine 300 mg tab	–	–	–	–	–	1.5	2	2	2.5	3	3	3	3
Rifapentine 300 mg and isoniazid 300 mg FDC tab	–	–	–	–	–	–	–	–	–	–	–	–	3

[a] Solution with a concentration of 10 mg/mL (one 100 mg isoniazid dispersible tablet in 10 mL water)
[d] Solution with a concentration of 15 mg/mL (one 150-mg rifapentine dispersible tablet in 10 mL water)

Table 1. Dosing of rifapentine and isoniazid as part of the three-month tuberculosis preventive treatment regimen of weekly rifapentine and isoniazid (3HP) by weight band *(3)*.

As shown in Table 1, Rifapentine 150 scored dispersible tablets, alongside a 100 mg dispersible tablet formulation of isoniazid that is already available, allow to deliver the required dose of 3HP to children of all ages weighing 3 kg or more. Both isoniazid and rifapentine child-friendly formulations are taste-masked for increased palatability, with the child-friendly formulation of rifapentine having a raspberry-mint flavour when dispersed in water *(17, 18)*.

For children weighing below 10 kg, a joint age- and weight-based approach to rifapentine dosing is indicated to account for age-related differences in drug metabolism (ie, lower drug metabolism resulting in lower clearance in younger children).

WHO promotes the procurement and use of formulations that are appropriate for children, to increase acceptability and promote treatment adherence. Although the Rifapentine Crush study showed that rifapentine adult tablets crushed and suspended in water can be used to dose children without the need for dose adjustments *(personal communication with Professor Anneke Hesseling, study results submitted for publication*), this should be considered only as an interim solution to allow administration of 3HP in children across ages until child-friendly rifapentine tablets are more widely available.

Discussions during the second meeting of the PAediatric Drug Optimization for TB group (PADO-TB) convened by WHO in October 2024 acknowledged that FDCs are preferred from a programme and supply perspective and that the availability of the isoniazid and rifapentine (HP) FDC was a gamechanger for the implementation of the 3HP regimen in adults. A paediatric FDC was not, however, considered as a priority product for development in the short term given several considerations, mainly related to the fact that a 1: 1 FDC would not meet dosing requirements for all ages and weight bands for the 3HP regimen. In fact, the rifapentine: isoniazid ratio differs for people weighing below 30 kg compared to people weighing 30 kg and above. In people weighing 30 kg, a higher dose of rifapentine is needed to reach target exposure, resulting in a 1:1.5 HP ratio, while people weighing 30 kg are given a 1:1 ratio of the two components of the 3HP regimen.

Discussions during PADO-TB2 also took into account that rifapentine is used in the 1HP regimen, which is currently implemented in the IMPAACT 2024 study with a 1:2 ratio of HP for children weighing above 10 kg, based on preliminary modelling work conducted to inform the trial dosing strategy. Additional considerations that the group reflected on when

deciding to prioritize a standalone child-friendly formulation of 3HP over an FDC can be found in the PADO-TB2 report *(19)*.

Rifapentine 150 mg scored, dispersible tablets became available in November 2023, after being approved by the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) Expert Review Panel, making it the first child-friendly formulation of rifapentine available on the market. In 2020, the PAediatric Drug Optimization (PADO) for TB group convened by WHO had prioritized this formulation for development *(19)*. Shortly after, WHO GTB updated the list of TB medicines included in the WHO expression of interest for product evaluation to the WHO prequalification unit to guide manufacturers to prioritize the development of this formulation *(20)*.

Nitrosamine impurities have been an ongoing issue in rifapentine products. The United States Food and Drug Administration (US FDA) and WHO Prequalification have set temporary interim limits for the nitrosamine impurity found in rifapentine (1-cyclopentyl-4-nitrosopiperazine, CPNP) of not more than 20 ppm. This applies to the child-friendly formulation of rifapentine too. Required testing from initial batches from the manufacturer have shown CPNP levels well below the interim level.

8. Review of benefits and harms

The potential benefits and harms of rifapentine have been extensively reviewed and summarised at the time of the original application of the medicine to EML. Rifapentine was approved by EML for inclusion under the core list of TB medicines in 2015 *(21)*.

The effectiveness and potential harms associated with the 150 mg scored, dispersible formulation is not expected to differ from the 300 mg preparation, so long as the tablet is a quality-assured product with proven bioavailability.

WHO guidelines published in 2020 for dosing 3HP were limited to children who weigh ≥ 10 kg and did not include children aged < 2 years of age. Newly available, preliminary data from a trial to fill this evidence gap by studying appropriate, safe of dosing of 3HP in young children, TBTC Study 35, indicated that 3HP can now be proposed for children of all ages.

TBTC Study 35 is a phase I/II dose-finding and safety study of rifapentine and isoniazid in HIV-positive and HIV-negative children with latent TB infection aged 0–12 years (FDA IND # 141932; NCT03730181), which is funded by the US Centers for Disease Control and Prevention through its Tuberculosis Clinical Trials Consortium (TBTC).

Weight-based dosing and dispersible rifapentine trial formulations were used. Children with or without HIV received 12 weekly doses of 3HP under direct observation. Intensive PK sampling was conducted after the first dose and some sampling after the 12th dose. Participants were enrolled by cohorts, cohorts 1 and 2 being enrolled concurrently. An interim analysis was conducted in March 2021 of at least six participants in each cohort for whom data on PK and safety were available. After the first interim analysis, cohorts 3 and 4 were enrolled concurrently at doses based on the modelled PK data obtained from children in cohorts 1 and 2 in the first interim analysis. After the second interim analysis, in August 2022, the rifapentine doses for children <2 years were adjusted according to

the interim analyses of cohorts 3 and 4. The aim was to achieve PK targets derived from the TBTC Study 26 of adult exposures and safety targets, with no more than one grade 3 or higher adverse event related, possibly or definitely, to the study drug (either rifapentine or isoniazid) in each of the mini-cohorts in the interim analyses. The study was conducted at three sites in South Africa, and PK were assays performed at the University of Cape Town.

TBTC Study 35 completed enrolment in December 2023. A total of 64 participants were enrolled at the time of the analysis, achieving the minimum evaluable number of 60 participants. The age range of the participants was 3.4 weeks to 12.9 years; 33 were <2 years, 17 <1 year and 5 ≤ 3 months. Seven children (median age 11 [8–12] years with HIV who were receiving once daily dolutegravir were also included. All the safety criteria were met, and 3HP was safe and well-tolerated by the children).
Evidence from this trial was reviewed by the WHO TAG on dosing in January-February 2024. Additional dosing simulations were conducted to provide dosing guidance for children weighing < 10 kg and aged < 2 years based on the new evidence from TBTC S35, as well as to explore dosing options within the harmonized dose bands to align weight bands for all dosing recommendations. Isoniazid doses and exposure as part of the 3HP regimen were also evaluated.

Additional information on the adult reference targets for rifapentine dose optimization, population paediatric PK model used in TBTC S35 as well as the virtual population used for the simulations, and the formulations considered for 3HP dosing recommendations, are included in *Web Annex A2. Report and background material on dosing recommendations for 3 months of once-weekly isoniazid and rifapentine (3HP) for TPT in children according to current (2020) and newly proposed, harmonized WHO weight bands.*

It should be noted that the recommended approach for determining paediatric doses of rifapentine is to align their exposure as closely as possible with those achieved in adults receiving the same regimen. This approach is aligned with USFDA guidance to industry indicating that extrapolation of efficacy data in adults, in combination with PK and safety data in children can inform clinical use of a medicine in the paediatric population as long as it can be assumed that children have a similar disease progression and response to the intervention when compared to adults.

9. Summary of recommendations in current clinical guidelines

WHO recommendations (2)

The following TB preventive treatment options are recommended regardless of HIV status: 6 or 9 months of daily isoniazid, or a 3-month regimen of weekly rifapentine plus isoniazid, or a 3-month regimen of daily isoniazid plus rifampicin. *(Strong recommendation, moderate-to-high certainty of the estimates of effect).*

The following alternative TB preventive treatment options may be used regardless of HIV status: a 1-month regimen of daily rifapentine plus isoniazid or 4 months of daily rifampicin. *(Conditional recommendation, low to moderate certainty of the estimates of effect)*

10. Summary of available data on comparative cost and cost-effectiveness

The 150 mg scored, dispersible tablet formulation of rifapentine is available from the GDF at a price of 0.138 USD per tab (supplied in blisters packs of 100 tablets). As a result, the 3HP regimen for children is cheaper than alternative TPT regimens. For example, for a child weighing 15 kg, the cost of the 3HP regimen is 6.53 USD while for 3HR and 6INH is 14.18 USD and 16.20 USD, respectively *(4)*. This is the first time that low- and middle-income countries will avoid a higher price per tablet for a pediatric TB formulation.

Recent studies indicate that short-course TPT-containing rifapentine is likely to be cost-effective (compared with no TPT) for contacts younger than 15 years old in almost all TB burden settings and countries with both high and low burdens of HIV *(22)*. Short-course TPT including rifapentine is also projected to be cost-effective for adult contacts in 15 countries and people living with HIV in seven countries, even under conservative cost-effectiveness thresholds. Domestic and external funding agencies should prioritize the expansion of TPT for household contacts of all ages, not just those younger than 5 years—with particular focus on children and adolescents younger than 15 years.

Cost-effectiveness was most favorable for household contacts younger than 5 years ($22 per DALY averted) and contacts aged 5–14 years ($104 per DALY averted) but also fell within conservative cost-effectiveness thresholds in many countries for PLWHA ($722 per DALY averted) and adult contacts ($309 per DALY averted) *(22)*.

11. Regulatory status, market availability and pharmacopoeial standards.

In 2020, after the 150 mg scored dispersible tablet formulation of rifapentine was prioritized for development by the Paediatric Drug Optimization for TB group *(19)* WHO updated the WHO expression of interest for manufacturers to submit products for prequalification *(20)*. Since then, two manufacturers have started the development, with one of them receiving approval by the Global Fund Expert Review Panel in November 2023. Both manufacturers are also currently being assessed for WHO Prequalification *(23)*.

Rifapentine 150 mg scored, dispersible tablet is available on the GDF catalogue *(4)* as well as directly from the manufacturer.

This formulation is also available through an Early Market Access Vehicle (EMAV) of approximately 85,000 patient courses of rifapentine promoted by the UNITAID-funded IMPAACT4TB consortium to catalyse the uptake of the paediatric product *(18)*. Beginning on 1 December 2023, Expressions of Interest (EOI) to the EMAV were accepted on a rolling basis through 30 October 2024 (or when total volume commitment is approved, whichever comes first).

The United States Pharmacopeia Convention (USP) under the USAID-funded Promoting the Quality of Medicines (PQM) programme has issued a product information report to support development of rifapentine *(24)*. Otherwise, rifapentine is not listed in any pharmacopeia to date.

12. References: Comprehensive reference list and in-text citations

1. The End TB strategy. Geneva: World Health Organization; 2015 (https://www.who.int/publications/i/item/WHO-HTM-TB-2015.19).
2. WHO consolidated guidelines on tuberculosis Module 1: prevention - tuberculosis preventive treatment, second edition. Geneva: World Health Organization; 2024 (https://www.who.int/publications/i/item/9789240096196).
3. WHO operational handbook on tuberculosis Module 1: prevention - tuberculosis preventive treatment, second edition. Geneva: World Health Organization; 2024 (https://www.who.int/publications/i/item/9789240097773).
4. Global Drug Facility, Medicines Catalog September 2024. Geneva: Stop TB Partnership, Global Drug Facility; 2024 (https://www.stoptb.org/sites/default/files/2024.10.06_gdf_medicines_catalog_oct_2024.pdf).
5. WHO paediatric quality product profile assessment tool [website]. World Health Organization; 2024 (https://www.who.int/publications/m/item/who-paediatric-quality-product-profile-assessment-tool).
6. Global tuberculosis report 2024. Geneva: World Health Organization; 2024 (https://iris.who.int/bitstream/handle/10665/379339/9789240101531-eng.pdf?sequence=1).
7. Houben RMGJ, Dodd PJ. The global burden of latent tuberculosis infection: a re-estimation using mathematical modelling. PLoS medicine. 2016;13(10):e1002152 (https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002152).
8. Fox GJ, Dobler CC, Marais BJ, Denholm JT. Preventive therapy for latent tuberculosis infection—the promise and the challenges. International Journal of Infectious Diseases. 2017;56:68-76 (https://www.sciencedirect.com/science/article/pii/S1201971216312231).
9. Semu M, Fenta TG, Medhin G, Assefa D. Effectiveness of isoniazid preventative therapy in reducing incidence of active tuberculosis among people living with HIV/AIDS in public health facilities of Addis Ababa, Ethiopia: a historical cohort study. BMC Infectious Diseases. 2017;17(1):5 (https://doi.org/10.1186/s12879-016-2109-7).
10. Nimalan Arinaminpathy NA, Sandip Mandal SM, Vineet Bhatia VB, McLeod R, Mukta Sharma MS, Soumya Swaminathan SS et al. Strategies for ending tuberculosis in the South-East Asian Region: a modelling approach. 2019 (https://www.cabidigitallibrary.org/doi/full/10.5555/20203106395).
11. Mandal S, Bhatia V, Sharma M, Mandal PP, Arinaminpathy N. The potential impact of preventive therapy against tuberculosis in the WHO South-East Asian Region: a modelling approach. BMC Medicine. 2020;18(1):163 (https://doi.org/10.1186/s12916-020-01651-5).
12. Funding a tuberculosis-free future: an investment case for screening and preventive treatment. Geneva: World Health Organization; 2024 (https://www.who.int/publications/i/item/9789240091252).
13. Political declaration on the high-level meeting on the fight against tuberculosis. Geneva: World Health Organization; 2023 (https://www.who.int/activities/preparing-for-the-un-high-level-meeting-on-the-fight-against-tuberculosis--2023).
14. Technical Advisory Group on dosing of TB medicines for adults and children [website]. World Health Organization; (https://www.who.int/groups/technical-advisory-group-on-dosing-of-tb-medicines-for-adults-and-children).
15. WHO operational handbook on tuberculosis. Module 1: prevention - tuberculosis preventive treatment, second edition. Web Annex A. Pharmacokinetics modelling and simulation studies for dosages of 6Lfx and 3HP. Geneva: World Health Organization; 2024 (https://iris.who.int/handle/10665/378537).
16. Simplifying Dosing by Harmonizing Weight-Band-Based Dosing Across Therapeutic Areas in Children - CROI Conference. 2024 (https://www.croiconference.org/abstract/simplifying-dosing-by-harmonizing-weight-band-based-dosing-across-therapeutic-areas-in-children/).
17. Impaact4TB. IMPAACT4TB Paediatric Dispersible flavored 3HP regimen. 2024 (https://www.youtube.com/watch?v=Z49PHP5AEQE).

18. Impaact4TB. Press Release: New Child-Friendly Formulation of Rifapentine for Short Course Tuberculosis Prevention Treatment Now Available as Unitaid and IMPAACT4TB Launch an Early Market Access Vehicle (EMAV) [news release]. 2023/12/11/T07:44:49+00:00: (https://impaact4tb.org/press-release-child-friendly-rpt-short-course-tpt-and-early-market-access/).
19. Paediatric drug optimization for tuberculosis: meeting report, October 2023. Geneva: World Health Organization; 2024 (https://www.who.int/publications/i/item/9789240094826).
20. 22nd Invitation to Manufacturers of Antituberculosis Medicines to Submit an Expression of Interest (EOI) for Product Evaluation to the WHO Prequalification Unit. Geneva: World Health Organization; 2024 (https://extranet.who.int/prequal/news/22nd-invitation-manufacturers-antituberculosis-medicines-submit-expression-interest-eoi).
21. The selection and use of essential medicines. Report of the WHO Expert Committee, 2015 (including the 19th WHO Model List of Essential Medicines and the 5th WHO Model List of Essential Medicines for Children). . Geneva: World Health Organization; 2015 (http://apps.who.int/iris/bitstream/10665/189763/1/9789241209946_eng.pdf).
22. Ryckman T, Weiser J, Gombe M, Turner K, Soni P, Tarlton D et al. Impact and cost-effectiveness of short-course tuberculosis preventive treatment for household contacts and people with HIV in 29 high-incidence countries: a modelling analysis. The Lancet Global Health. 2023;11(8):e1205-e16 (https://doi.org/10.1016/S2214-109X(23)00251-6).
23. FPPs/BTPs under assessment | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control) [website]. World Health Organization; (https://extranet.who.int/prequal/medicines/pipeline/finished-pharmaceutical-products).
24. Promoting the Quality of Medicines (PQM). Product Information Report: Rifapentine. Rockville, Maryland: U.S. Pharmacopeial Convention; 2017 (https://www.usp-pqm.org/sites/default/files/pqms/article/rifapentine-pir-jul2018.pdf).