Treatment Action Group

Secretary of the Expert Committee on the Selection and Use of Essential Medicines
Department of Essential Medicines and Health Products
World Health Organization
20 Avenue Appia
CH-1211, Geneva 27, Switzerland

19 May 2021

Re. Statement of support for the addition of a fixed-dose combination of rifapentine and isoniazid to the World health Organization Model List of Essential Medicines

Dear Expert Committee:

The Treatment Action Group (TAG) and the undersigned civil society and community-based partners submit this letter **in support** of adding a fixed-dose combination of rifapentine (300 mg) and isoniazid (300 mg) to the World Health Organization (WHO) Model List of Essential Medicines (EML) for the treatment of tuberculosis (TB) infection in adults (hereinafter the 300/300 HP FDC).

The organizations endorsing this letter represent a diverse constituency of civil society and community-based actors working to expand access to evidence-based regimens for preventing TB, the world's leading infectious cause of death second only to COVID-19. We note that the fixed-dose combination described in this application combines two existing drug agents, each of which is individually listed on the EML (rifapentine since 2015 and isoniazid since 1977). It is our view that TB preventive treatment (TPT) regimens that combine rifapentine and isoniazid represent the current highest attainable standard of care for the prevention of TB disease. The 3HP regimen involves taking 900 mg of rifapentine and 900 mg of isoniazid once a week for 12 weeks. The 1HP regimen consists of taking 600 mg of rifapentine and 300 mg of isoniazid daily for one month.

3HP and 1HP are each listed as recommended regimens in WHO guidelines.[1] Importantly, communities affected by TB have expressed a clear preference for 3HP and 1HP as shorter, more tolerable alternatives to lengthier courses of isoniazid preventive therapy (IPT). In addition to the shorter treatment duration, communities cite the lower risk of liver toxicity associated with 3HP and 1HP as a major reason to prefer rifapentine-based TPT to IPT.

The 300/300 HP FDC submitted for consideration in this application is particularly well suited for 3HP dosing. Until recently, the pill burden of 3HP limited its acceptability. The advent of a 300/300 HP FDC would reduce the pill count of each 3HP dose from 10 pills under existing

[1] World Health Organization. WHO consolidated guidelines on tuberculosis: Module 1: Prevention—Tuberculosis preventive treatment. Geneva: World Health Organization; 2020.

formulations to 4 pills.[2] Communities have heralded this reduction in pill burden as a major step forward.[3] Among other possibilities, a 300/300 HP FDC will be easier to incorporate within differentiated service delivery models of TB/HIV co-management. An FDC may also make it easier for people to take each dose of 3HP with minimal supervision, an important consideration as national TB programs shift TPT services toward multi-month dispensing as part of health system adaptations to COVID-19.

We acknowledge that the current price of rifapentine may limit the affordability of the 300/300 HP FDC before the Committee. However, it is important to couch affordability concerns in the broader context of rifapentine accessibility. Rifapentine and isoniazid are each separately off patent.[4] While Sanofi applied for patents on two 300/300 HP FDC formulations for adults and children, civil society won a major concession when in 2020 Sanofi initiated a process of abandoning all of the patent applications on combinations of rifapentine and isoniazid in all countries where they were filed.[5] Furthermore, Sanofi has committed "not to reinstate any of the patents/applications, and not to initiate any action against any party who would like to manufacture the specific formulations of the combinations once covered by Sanofi's two patent families, before the abandonments become effective under the relevant national patent regulations."[6]

Free of patent barriers, the availability and affordability of rifapentine/isoniazid FDC formulations should improve as additional suppliers enter the market. Adding an FDC of rifapentine and isoniazid to the EML will send an important signal to manufacturers to enter this space. Aside from Macleods Pharmaceuticals, the current supplier of the 300/300 HP FDC, we are aware of at least one other manufacturer preparing to supply this product.

Thank you for the opportunity to share our views on the importance of including a 300/300 HP FDC on the WHO EML. If you need additional information on our support of this application, please contact Mike Frick, TAG TB project co-director at mike.frick@treatmentactiongroup.org.

Respectfully submitted,

---

[2] Using existing formulations of rifapentine 150 mg and isoniazid 300 mg, each dose of 3HP requires taking 6 rifapentine tablets, 3 isoniazid tablets, and 1 vitamin B6 tablet for a total of 10 tablets. See calculations in: Treatment Action Group. An activist's guide to rifapentine for the treatment of TB infection. New York: Treatment Action Group; 2020. https://www.treatmentactiongroup.org/publication/an-activists-guide-to-rifapentine-for-the-treatment-of-tb-infection/

[3] Community movements across Africa, Asia, and South America celebrate roll-out of short-course, patient-friendly TB preventive therapy [Press Release]. 16 February 2021. https://www.treatmentactiongroup.org/statement/community-movements-across-africa-asia-and-south-america-celebrate-roll-out-of-short-course-patient-friendly-tb-preventive-therapy/

[4] Treatment Action Group. Isoniazid/rifapentine (3HP) access roadmap and patent landscape. New York: Treatment Action Group; 2020: https://www.treatmentactiongroup.org/publication/isoniazid-rifapentine-3hp-access-roadmap-and-patent-landscape/.

[5] See record of correspondence between TAG and Sanofi on 3HP patents, available here: https://www.treatmentactiongroup.org/letter/letter-to-sanofi-ceo-calling-for-patent-withdrawals-on-critical-tb-drugs/.

[6] Ibid.

Mike Frick, *on behalf of*

1. Treatment Action Group (USA) [Lead signatory]
2. ARK Foundation (India)
3. Coalition of Women Living with HIV and AIDS/COWLHA (Malawi)
4. Facilitators of Community Transformation/FACT (Malawi)
5. Ghana TB Voice Network (Ghana)
6. Jointed Hands Welfare Organization (Zimbabwe)
7. Journalists Association Against AIDS/JournAIDS (Malawi)
8. KHANA (Cambodia)
9. Pamoja TB Group (Kenya)
10. Sankalp Rehabilitation Trust (India)
11. Stop TB Partnership-Kenya (Kenya)
12. Stop TB Partnership–Zimbabwe (Zimbabwe)
13. TB Proof (South Africa)
14. Women, Law and Development Association/MULEIDE (Mozambique)