# *Fighting Tuberculosis*

**GRI Standards:**

N/A

## EXECUTIVE SUMMARY

Along with HIV/AIDS and malaria, tuberculosis (TB) is one of the most widespread infectious diseases in the world and is one of the top 10 causes of death. To achieve the strategic objectives of tuberculosis elimination, the new WHO recommendations aim to accelerate the detection and to improve the results of tuberculosis treatment by using a new rapid diagnostic test and a shorter and less costly treatment regimen. Sanofi is a key historical partner as it is the first company to manufacture rifampicin, the cornerstone of tuberculosis treatment. Today, Sanofi remains at the forefront by developing new treatment options for tuberculosis. Sanofi is working with external partners to shorten the duration of treatment for latent and active tuberculosis. Besides, one of the main areas of intervention is prevention, particularly through the treatment of latent tuberculosis.

# TABLE OF CONTENTS

# 1. Context

Tuberculosis (TB) is the second biggest infectious disease killer after COVID-19. This contagious disease, caused by the bacterium Mycobacterium tuberculosis, is spread through respiratory droplets. The COVID-19 pandemic has reversed years of progress in providing essential TB services and reducing TB disease burden. The most obvious impact is a large global drop in the number of people newly diagnosed with TB and reported.

This fell from 7.1 million in 2019 to 5.8 million in 2020, an 18% decline back to the level of 2012 and far short of the approximately ten million people who developed TB in 2020.

Best estimates for 2020 are 1.3 million TB deaths among HIV-negative people (up from 1.2 million in 2019) and an additional 214,000 among HIV-positive people (up from 209,000 in 2019), with the combined total back to the level of 2017.

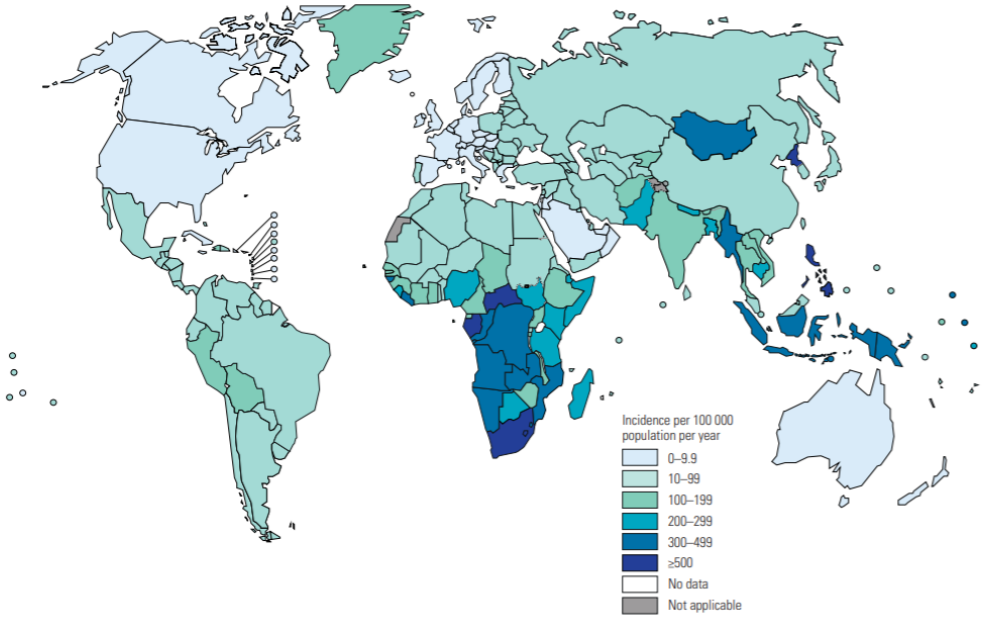


Figure 1: Estimated TB Incidence Rates, 2019

*SOURCE - WHO: GLOBAL TUBERCULOSIS REPORT 2020, FIG. 4.4, PAGE 35*
*https://www.who.int/publications/i/item/9789240013131*

In addition, a quarter of the world's population - currently estimated to affect 1.7 billion people worldwide - is infected with latent TB: they have no symptoms, are not contagious and most do not know they are infected. Without treatment, 5% to 15% of these people – 85 million to 170 million people globally – will develop active TB, the form which makes people sick and can be transmitted from person to person.

HIV infection makes people up to 37 times more likely to fall ill with the active disease.

## 1.1. THE END TB STRATEGY: A GLOBAL STRATEGY TO END THE GLOBAL TB EPIDEMIC

In September 2018 was the first United Nations High Level meeting (UN-HLM) on tuberculosis. This meeting was a significant step forward by governments and all partners engaged in the fight against TB. The outcome was a political declaration agreed by all United Nations Member States, in which existing

commitments to the Sustainable Development Goals (SDGs) and WHO's End TB Strategy were reaffirmed, and new ones added.

The political declaration included four new global targets:

- treat 40 million people for tuberculosis disease in the five-year period from 2018 to 2022;
- reach at least 30 million people with TB preventive treatment for a latent TB infection in the five-year period from 2018 to 2022;
- mobilize at least $13 billion annually for universal access to TB diagnosis, treatment and care by 2022; and
- mobilize at least $2 billion annually for TB research.

## 1.2. MAJOR CHALLENGES TO SIMPLIFY TREATMENT AND FIGHT RESISTANT STRAINS

Standard treatment for TB consists of a combination of antibiotics taken daily, usually for six months: two months of treatment with four antibiotics, followed by four months with two antibiotics.

When administered properly, the treatment for TB is generally highly effective. However, for many patients it is difficult to comply with six months of treatment. Poor compliance not only puts the patients at risk of treatment failure, it also creates conditions that encourage the development of antibiotic-resistant bacteria.

Efforts are needed to simplify TB treatment by reducing the treatment duration.

Preventive TB therapy takes one to 36 months and uptake is low. Research shows that patients are far more likely to complete shorter treatment courses.

Strains of *Mycobacterium tuberculosis* that are resistant to conventional treatments have begun to appear in the 80s. In 2019, 465,000 incident cases of rifampicin resistant TB were observed. It is therefore crucial to stop the progression of resistance and to develop new treatments.

*For more information, see:* https://www.who.int/tb/publications/global_report/en/.

# 2. Sanofi Global Health

Sanofi aims to contribute to the objective to end the epidemics of tuberculosis by 2030, as per goal 3, target 3.3 of the Sustainable Development Goals.


Sanofi was the first company to manufacture rifampicin, a key antibiotic for the treatment of Tuberculosis that was isolated in 1957 by scientists at Lepetit Research Laboratories in Milan (Italy), now part of Sanofi.

The Company remains one of the key producers of this component in all drug-susceptible tuberculosis (DS-TB) treatments. Several of the Company's manufacturing facilities have developed and are currently producing a range of antibiotics to treat TB, which are distributed in many countries.

In 2011, rifapentine, a member of the rifamycin family, was shown by the US Centers for Disease Control and Prevention (CDC) to have the ability to simplify considerably the treatment of latent TB (LTBI)[1]. The proposed development of rifapentine offers the prospect of simpler and shorter latent TB treatments, with the aim of improving patient compliance. A rifapentine-based regimen shortens treatment to 12 weekly doses in combination with another medicine, isoniazid. The World Health Organization (WHO) recommends

[1] T.R. Sterling, M.E. Villarino, A.S. Borisov, et al. (2011). "Three Months of Once-Weekly Rifapentine and Isoniazid for M. tuberculosis Infection." *New England Journal of Medicine*, 365, pp.2155-66.

the use of this regimen for treatment of latent TB infection in people living with HIV and contacts of TB cases of any age.

# 3. Actions

## 3.1. SIMPLIFYING TUBERCULOSIS TREATMENT

Fixed-dose combinations of drugs are recommended by WHO and greatly simplify TB treatments by reducing the number of pills to be ingested. Sanofi's current efforts are focused on endeavoring to simplify and shorten the course of treatment for non-resistant TB, both for LTBI and DS-TB.

In November 2014, the US Food and Drug Administration approved the indication of treatment of LTBI for rifapentine in combination with isoniazid, with a regimen of weekly rifapentine+isoniazid for three months (12 doses).

Since then, rifapentine is also approved for LTBI indication in several other geographies mainly in low- and middle-income countries.

This new regimen, the 3HP regimen, is recommended in the WHO Guidelines on the Management of Latent Tuberculosis Infection released in October 2014. Rifapentine has been included on the Essential Medicines List since April 2015. Moreover, in January 2017, rifapentine was granted WHO prequalification.

## 3.2. FINDING SOLUTIONS WITH OUR PARTNERS

The development of rifapentine is carried out in close collaboration with the CDC in Atlanta (United States), which coordinates an international group of researchers and clinicians.

In October 2020, The Tuberculosis Trials Consortium (TBTC) from the Centers for Disease Control and Prevention (CDC) announced results from the "Rifapentine-containing treatment shortening regimens for pulmonary tuberculosis" study (TBTC Study 31). This found that a four-month regimen that included high-dose rifapentine and moxifloxacin was non-inferior to the current six-month standard TB treatment regimen, with equivalent TB-free rates achieved in each arm 12 months after starting treatment.

In addition, a pivotal and long-awaited trial on short-course treatment for the prevention of tuberculosis (TB) in children has opened in South Africa in 2019. The goals of this phase I/II trial are to evaluate the safety of giving rifapentine in combination with isoniazid to prevent TB in children, and to establish the dose at which rifapentine should be administered. The United States Centers for Disease Control and Prevention (CDC) execute the study with financial support provided by both CDC and UNITAID. Sanofi donates the medicines used in the study.

## 3.3. IMPROVING EDUCATIONAL EFFORTS ON LATENT TUBERCULOSIS INFECTION

Treatment of TB infection and preventing the development of active disease is essential to TB elimination worldwide.

Detecting and treating TB infection, however, presents unique challenges for those working to end TB. Recognizing this, Sanofi and The Union have developed a new open-access online training course to help clinicians, healthcare workers and national TB program managers to better identify and successfully treat LTBI.

This new online training program is designed to meet the needs of National TB Program (NTP) staff; National AIDS Program (NAP) staff; clinicians (specialists, pediatricians, pneumologists, general practitioners, nurses) working with TB and/or HIV patients and other high-risk groups; and health care workers at all levels.

*For more information, see the:*

- *English version*
- *French version*
- *Spanish version*

In parallel, Sanofi developed and launched a new global website fully dedicated to latent tuberculosis infection. Because information and adherence are essential to combat the disease, the key objectives of this website are to raise awareness on tuberculosis prevention and to educate patients, their families and more largely the general public on this huge public health issue.

Patients will find simple information to understand the importance of treating LTBI, and at the end eliminate TB.

*For more information, see: https://www.ltbi.com/.*