

Tackling AMR Through Improved TB Therapies

Tackling drug-resistant tuberculosis (DR-TB) is critical to successfully controlling and combating antimicrobial resistance (AMR). **DR-TB accounts for nearly one third (29%) of all deaths from antimicrobial infection—more than any other disease.** Overall, there are approximately a half million cases of DR-TB each year.

In 2023, the WHO published a policy brief setting the global research agenda for AMR in human health, which highlights several recommendations for the development of tools to combat DR-TB. **TB Alliance is the world's leading developer of new cures for DR-TB, with strategies aligned with WHO's research agenda.** Shared priorities include developing new DR-TB cures that are more effective, safer, cost-effective, and shorter, as well as an increasing focus on ensuring the most vulnerable populations are included in research and benefit from new treatment technologies.

With a new, shorter, safer, and more effective treatment for DR-TB recently introduced and being scaled up, and a regimen development approach that promotes responsible stewardship of new drugs, TB Alliance is spearheading a scientific revolution that could end the distinction between drug resistant and drug-sensitive (DS-TB) TB.

DR-TB accounts for nearly 1/3 of all AMR deaths



A New, Shorter, and Safer Cure for DR-TB

In 2019, TB Alliance earned US FDA approval of its novel drug, pretomanid, explicitly for use as part of the BPaL (“bee-pal”) regimen, which consists of bedaquiline (B), pretomanid (Pa), and linezolid (L). Notably, this drug and drug combination was the first-ever U.S. FDA-approved treatment for extensively drug resistant TB (XDR-TB)—at the time, the most difficult to treat, highly drug-resistant form of TB. This meant the breakthrough would benefit the most vulnerable and highest risk TB patients. **TB Alliance’s BPaL regimen has been shown to cure approximately 90% of patients in six months with an improved safety profile and significantly reduced pill burden (fewer than 750 tablets).**

Previously, treatments for highly drug-resistant TB consisted of up to 14,000 pills administered over 18 months or longer, bearing harsh side effects and low cure rates (34-59%). A reduced treatment duration and pill burden is easier to administer and complete and helps reduce further drug resistance that develops when treatments are given incompletely or discontinued before cure.

To date, BPaL has been approved by 26 regulatory authorities and recommended in the World Health Organization’s guidelines for treating nearly all forms DR-TB. **The introduction of BPaL even prompted a reclassification of XDR-TB.** Given that so much of what was previously considered XDR-TB is now treatable in six months—the same length of duration as DS-TB—the definition of XDR-TB has been changed and constitutes a much smaller percentage of cases.



Developing Regimens, not Drugs, Promotes Responsible Drug Stewardship

Pretomanid and BPaL represent a significant step toward controlling AMR and DR-TB, but even faster-acting, safer, and simpler therapies are required to end TB in all its forms. TB Alliance has next generation regimens under development and remains committed to introducing an ultra-short, “universal” TB treatment regimen for all forms of TB. Both to accelerate the development of these cures; and to promote responsible stewardship of recently introduced cures; TB Alliance’s product development strategy prioritizes developing combinations of drugs, not individual drugs.

The benefits of a regimen-based development approach in pursuit of a universal regimen for new TB cures as it relates to AMR are multifold.

- A fully novel combination of drugs can treat any strain of TB—**erasing the distinction between DR-TB and DS-TB.**
- A fully novel, universal regimen **eliminates the need for drug-susceptibility testing** before treating TB.
- The approval of drugs in combination **protects new drugs against resistance** because specific guidance exists against “exposing” new drugs by using them with other drugs for which there is pre-existing resistance.
- Shorter, simpler cures for TB help improve treatment compliance, **reducing the number of new cases of resistance** that develop when treatment isn’t completed.
- A regimen development approach **accelerates the time it takes for improved treatment combinations**—that can impact AMR—to reach the market.

One day of BPaL vs. one day of traditional treatment for highly drug-resistant TB.

BPaL is Reaching those in Need

- Pretomanid has been approved by 26 regulatory authorities, including the U.S. FDA and European Commission
- Pretomanid has been procured by 70 countries, with 28,000 courses ordered in Q1 2023
- Pretomanid has been made available in more than 150 low- and middle-income countries through the Stop TB Partnership’s Global Drug Facility
- This has been the fastest scale-up of new DR-TB treatment technology in modern history



In the course of the war, shelling damaged TB hospitals. The Chernihiv Regional TB Hospital was subject to attack in 2022, making in-patient care highly challenging.

CASE STUDY

Short, Simple Treatments Enable Successful DR-TB Therapy Amid War in Ukraine

Ukraine was the first high-burden country to adopt the BPaL regimen. A shortened, simplified treatment for DR-TB has been an especially welcome advance for patients who needed treatment amid wartime conditions. As the war began, Ukrainian patients were given the remainder of their full treatment course so the remaining duration of their treatment could be completed remotely. **47 of 50 such patients successfully completed treatment. Overall, more than 90% of Ukrainian patients who completed DR-TB with BPaL 6+ months ago remain TB-free.** These outcomes would have been extraordinarily difficult using the longer, more toxic, and less effective treatments that were in place prior to BPaL. Ukraine’s National TB Program is now moving quickly to scale up access on a nationwide basis.

Despite the ongoing war with Russia, patients on BPaL in Ukraine have been able to continue their treatment even when TB hospitals were under assault.



Read more about the impact of BPaL in Ukraine