SIX-MONTH TREATMENTS FOR DRUG-RESISTANT TUBERCULOSIS

An advocacy guide for NFM4

The May 2022 World Health Organization (WHO) rapid communication on forthcoming drug-resistant tuberculosis (DR-TB) treatment guidelines, which will recommend all oral, six-month BPaL/M (bedaquiline, pretomanid, linezolid + moxifloxacin) regimens for treating DR-TB states that:

> The 6-month BPaLM regimen, comprising bedaquiline, pretomanid, linezolid (600 mg) and moxifloxacin, may be used programmatically in place of 9-month or longer (>18 month) regimens, in patients (aged ⩾15 years) with MDR/RR-TB who have not had previous exposure to bedaquiline, pretomanid and linezolid (defined as >1 month exposure). This regimen may be used without moxifloxacin (BPaL) in the case of documented resistance to fluoroquinolones (in patients with pre-XDR-TB). Drug susceptibility testing (DST) to fluoroquinolones is strongly encouraged, but DST should not delay treatment initiation.

This means that countries around the world can start making shorter, safer, and more effective regimens available to people living with DR-TB, which will be a tremendous lifesaving advance in TB treatment and care. Before the development of the BPaL/M regimens, the global treatment success rate for DR-TB was less than 60% with 9-18+ month treatment standards comprising a heavy pill burden per day (as high as 23 pills a day) and often injections. Now, DR-TB can be treated using six-month, all-oral, three- or four-drug regimens (BPaL/M) with reported success rates of approximately 90% in clinical trials.

Currently, no country in the world with a high burden of TB is routinely using BPaL/M regimens programmatically, although South Africa has committed to doing so by the end of 2022. However, as of October 2022, 22 regulatory authorities covering 49 countries have reviewed and approved BPaL/M, and an additional 11 countries have regulatory review in process. To date, at least 14 countries have administered the regimen through operational research or similar programs, with South Africa, Ukraine and Kyrgyzstan implementing BPaL nationally. Forty-one countries and counting have started to procure the regimen, with a cumulative total of ~5,000 treatment courses being shipped worldwide so far. Global Fund resources for the procurement and effective roll-out of BPaL/M regimens could dramatically accelerate and broaden uptake of these new DR-TB treatments.

New BPaL/M regimens are not only life saving, but also cost saving. A 2021 BPaL costing study found the cost per person completing treatment dropped by 50-80% in three diverse countries compared with older treatment regimens. As the usage of BPaL/M regimens expands in response to updated WHO guidelines, economies of scale are expected to make the regimen even more affordable.

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Key arguments and messages to leverage in country dialogue discussions

If you experience push back or get questions in response to your ask for funding requests to prioritize the adoption and roll out of the BPaL/M regimens, **use these key messages and arguments** to bolster your voice:

- The new all oral 6-month BPaL/M regimens for treating DR-TB are more effective, safer, shorter and more affordable alternatives to older regimens.
  - Old standard treatments for DR-TB can involve painful injections, which come with a plethora of possible side effects, ranging from aches and pains to depression to irreversible hearing loss. Novel BPaL/M regimens are proven to be safer, with **more manageable side effects** than old treatments.
  - The global treatment **success rate** has been 60% or lower with older 9+ month treatment standards. Now, six-month, all-oral, three or four drug BPaL/M regimens consistently report success rates of approximately 90%.
  - Introducing BPaL/M regimens will be substantially **cost saving** to National TB Programs and people affected by the disease. A study published in PLOS Global Public Health showed that the new regimen could save governments up to US$740 million annually, which is enough to fund almost another year's worth of DR-TB treatments globally. Savings are driven by the costs of medicines, the shortened duration of treatment, and the resulting lower healthcare and personal costs, including fewer monthly follow-ups and lab-based treatment monitoring tests.

- ***Pushback:*** "**WHO guidelines** on the new regimen haven't been issued yet and we plan to wait to see those before acting."
  - ***Response:*** "The WHO issued a rapid communication recommending the programmatic use of BPaL/M in May 2022. The Global Fund also currently recommends the scale up of this regimen. Official WHO guidelines are anticipated before the end of 2022, and it is essential to start planning now."

- ***Pushback:*** "Before we move to full programmatic implementation of new regimens, we want to run a pilot project in our country first."
  - ***Response:*** "WHO and the Global Fund recommend rapid introduction of innovations in treatment as priority actions to accelerate progress towards TB targets. If plans for a pilot are already underway, planning for scale up as part of the process and learning from other countries' experiences would maximize impact and efficiency.

- ***Pushback:*** "Country clinical guideline updates and the initiation of new treatments at programmatic scale take time. Local approval processes mean what you are asking simply can not happen rapidly."
  - ***Response:*** Based on the COVID-19 experience, we know that country clinical guidelines and new treatment can be adopted much faster when there is political will and focus. We can and must do the same by rapidly rolling out new TB treatments like BPaL/M now."

- ***Pushback:*** "But BPaL/M isn't recommended yet for children?"
  - ***Response:*** "Studies are underway, and until we know how to safely administer BPaL/M to children, the Global Fund can support programs to administer other shorter, all-oral regimens that are recommended by the WHO for the treatment of children with DR-TB. The WHO rapid communication says that "BPaL/M may be used in people aged ≥15 years. While the work continues to optimize treatment for children, people aged ≥15 must not be denied access to shorter treatment regimens."

Hear from people living with DR-TB who have been treated with BPaL/M

Besik's Story

Mapalesa's Story

Click on the images to watch the videos

Additional Resources

The science backing up BPaL/M first started with TB Alliance's Nix-TB trial, which showed BPaL was capable of curing 90% of people with DR-TB using just three drugs given for 6-months. To limit toxic effects of linezolid and improve patients' quality of life, subsequently TB Alliance conducted the ZeNix trial which was published recently (September 2022) in the New England Journal of Medicine and showed the dose of linezolid could be reduced to 600mg to improve tolerability and safety of the BPaL regimen without compromising its efficacy. In parallel, MSF partnered with global leaders in medical research to conduct TB PRACTECAL; a phase 2/3 randomized controlled clinical trial to evaluate BPaL-based regimens for people with rifampicin-resistant/multidrug-resistant TB (RR-/MDR-TB). TB-PRACTECAL found the six-month BPaL regimen with or without moxifloxacin (BPaLM) to be safe and effective in comparison to the World Health Organization standard of care. Final results from TB-PRACETCAL were presented at the 2022 Union Conference.

If you have any questions about BPaL/M, including about its use in your country, do not hesitate to reach out to:

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