



# SHORT, ALL ORAL DR-TB REGIMEN

# **SESSION 3: SHORTER DR-TB REGIMEN**

- **Drug-Resistant TB (DR-TB)** is caused when the TB bacteria are resistant to at least one of the first-line TB medications - isoniazid (INH), rifampin (RIF), ethambutol (EMB), and pyrazinamide (PZA).
- **Causes of drug resistance**
  - Mutation in the TB bacteria that makes a drug ineffective
  - Exposure to someone with DR-TB
  - Inadequate or poorly administered treatment regimen allows drug resistant mutants to become the dominant strain - e.g., interruptions or premature discontinuation of treatment, or poor patient adherence
  - Appropriately administered drugs have not achieved necessary drug levels to deal with all population of mycobacteria
  - Weak TB services can lead to delay in detection and effective treatment of drug resistance

# TYPES OF DRUG RESISTANT TUBERCULOSIS

- **RR-TB:** TB bacteria that are resistant to rifampicin (R).
- **Multidrug-resistant TB (MDR-TB):** TB bacteria that are resistant to two of the most important TB drugs, **rifampicin (R) and isoniazid (INH)**.
- **Pre-XDR-TB:** TB caused by Mycobacterium tuberculosis strains that fulfil the definition of MDR/RR-TB and which are also resistant to any fluoroquinolone.
- **XDR-TB:** TB caused by Mycobacterium tuberculosis strains that fulfil the definition of MDR/RR-TB and which are also resistant to any fluoroquinolone and at least one additional Group A drug\*

\* The Group A drugs are: **Lfx, Mfx, Bdq, Lzd**.

- Challenges
  - Fewer treatment options
  - Higher treatment cost
  - Adverse drug reaction
  - Psychological stress
  - Increased mortality rate
- Thorough counselling on the diagnosis and treatment are necessary along with having a support network. Peer-to-peer support is also beneficial.

## New WHO Clinical Guidelines

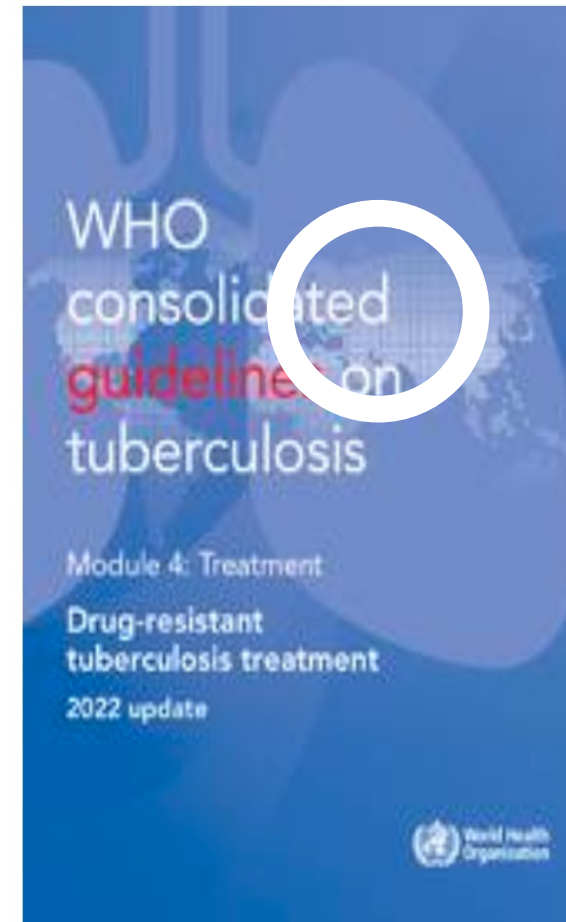
*“WHO suggests the use of the 6-month treatment regimen composed of bedaquiline, pretomanid, linezolid (600 mg) and moxifloxacin (BPaLM) rather than 9-month or longer (18-month) regimens in MDR/RR-TB patients.” (p.18)*

*“...in cases of documented resistance to fluoroquinolones, BPaL without moxifloxacin would be initiated or continued” (p.26)*

Almost all people with drug-resistant TB could be treated with a six-month, all-oral, highly effective therapy under programmatic conditions.

Two BPaL-based regimens:

- **BPaLM:** Bedaquiline, pretomanid, linezolid, and moxifloxacin
- **BPaL:** Bedaquiline, pretomanid, linezolid



# DRUG RESISTANT TB TREATMENT OPTIONS

| Regimen  | MDR/RR-TB fluoroquinolone susceptible   | Pre-XDR-TB           | XDR-TB | Extensive pulmonary TB | Extrapulmonary TB  | Age <14 years |
|--|---|----------------------|--------|------------------------|--|---------------|
| <b>6-month BPaLM/BPaL</b>  | Yes (BPaLM)   | Yes (BPaL)           | No     | Yes                    | Yes – except TB involving CNS, miliary TB and osteoarticular TB              | No            |
| <b>9-month all-oral</b>  | Yes   | No                   | No     | No                     | Yes – except TB meningitis, miliary TB, osteoarticular TB and pericardial TB | Yes           |
| <b>Longer individualized 18-month</b>                                | Yes <sup>a</sup> /No  | Yes <sup>a</sup> /No | Yes    | Yes                    | Yes  | Yes           |
| Additional factors to be considered if several regimens are possible | Drug intolerance or adverse events  |                      |        |                        |  |               |
|  | Treatment history, previous exposure to regimen component drugs or likelihood of drug effectiveness |                      |        |                        |  |               |
|  | Patient or family preference  |                      |        |                        |  |               |
|  | Access to and cost of regimen component drugs   |                      |        |                        |  |               |

BPaL: bedaquiline, pretomanid and linezolid; BPaLM: bedaquiline, pretomanid, linezolid and moxifloxacin; CNS: central nervous system; MDR/RR-TB: multidrug- or rifampicin-resistant TB; TB: tuberculosis; XDR-TB: extensively drug-resistant TB.

<sup>a</sup> When 6-month BPaLM/BPaL and 9-month regimens could not be used.



# COVENTIONAL TREATMENT VS BPaL | BPaLM

| Details              | Conventional Regimen   | BPaL              | BPaLM             |
|----------------------|--|-------------------|-------------------|
| Efficacy             | Approximately 60%  | Approximately 90% | Approximately 90% |
| Duration             | 9-18 months  | 6 months          | 6 months          |
| Number of Pills      | Between 2828 - 4898 pills<br>(depending on body weight and duration) | 564 pills         | 746 pills         |
| Number of Injections | 85-130 injections  | None              | None              |
| Hearing Loss         | Yes  | No                | No                |
| Kidney Failure       | Yes  | No                | No                |



- Highly cost saving
  - Potential health systems savings of USD 740 million per year
  - Potential savings of 40-75% for MDR-TB treatment and up to 90% for pre-XDR-TB treatment
  - Reduction in cost of follow-up due to lower duration

- Countries such as Indonesia, Kyrgyzstan, Myanmar, Nigeria, Pakistan, Philippines, South Africa, Tajikistan and Ukraine have already planned to start programmatic use of BPaL from late 2023/early 2024 onwards

# BPaL USER EXPERIENCE

***“I am feeling very good now – I am not sick anymore”***

– Mariia, BPaL OR patient from Kyiv



***“BPaL was my only hope ... It really was a miracle”***

– Anna Christina, BPaL OR patient from Manila



***“... since the beginning of the treatment I’ve been feeling like I’m healing fast”***

– Saikal, Kyrgyzstan

***“I really want to get well fast, so BPaL is better for me”***

– First patient enrolled on BPaL in the Philippines

***“When I took it, my health was improving each and every day”***

– Panganai, ZeNix patient from Johannesburg



***“I’m happy about how this research program helped me”***

– Mapalesa, ZeNix patient from Johannesburg

**THANK YOU!**