World Health Organization

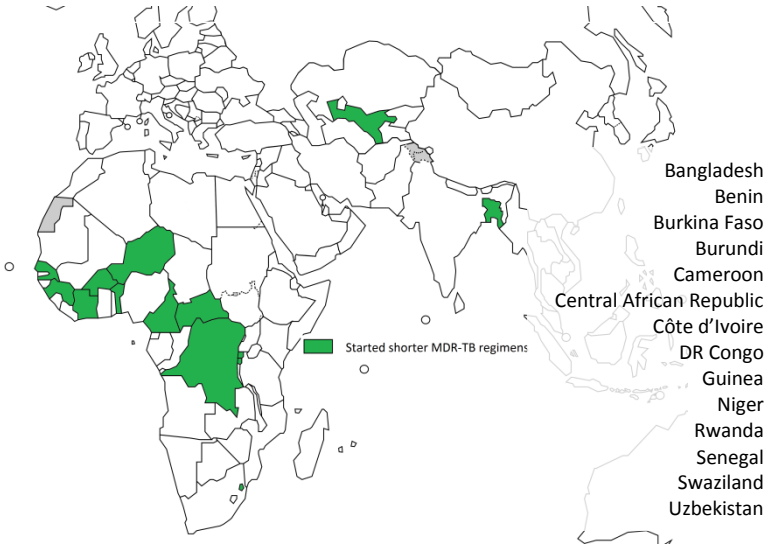
THE SHORTER MDR-TB REGIMEN

BACKGROUND

- Multidrug-resistant tuberculosis (MDR-TB) represents a public health crisis and a global health security risk, carrying grave consequences for those affected.
- In 2015, there were an estimated 480 000 new cases of multidrug-resistant TB (MDR-TB) and an additional 100 000 people with rifampicin-resistant TB who were also newly eligible for MDR-TB treatment.
- MDR-TB and rifampicin resistant TB (MDR/RR-TB) cannot be treated with the standard 6-month course of first-line medication which is effective in most TB patients. Patients with MDR/RR-TB are treated with a different combination of second-line drugs, usually for 18 months or more.
- Attempts to reduce the length of MDR/RR-TB regimens and to use a combination of drugs which is tolerable have been ongoing for several years through various studies. A standardized treatment regimen lasting less than 12 months has been used in a number of countries (see map), with promising results in selected patients
- Based on data from these studies, WHO updated its treatment guidelines for drug-resistant TB in May 2016 and included a recommendation on the use of a shorter MDR-TB regimen under specific conditions.
- This new recommendation is expected to benefit the majority of patients with MDR/RR-TB worldwide; however, there are serious risks for worsening resistance if the regimen is used inappropriately (e.g. in XDR-TB patients).
- WHO encourages ongoing and future randomized controlled clinical trials to strengthen the evidence base for shorter and more effective regimens.

For more information please visit: www.who.int/tb

Countries using the shorter MDR-TB regimen
(in addition, Ethiopia, Mongolia, South Africa and Viet Nam are participating in the clinical trial)



FEATURES OF THE SHORTER MDR-TB REGIMEN

- Standardized shorter MDR-TB regimen with seven drugs and a treatment duration of 9-12 months
- Indicated conditionally in MDR-TB or rifampicin-resistant-TB, regardless of patient age or HIV status
- Monitoring for effectiveness, harms and relapse will be needed, with patient-centred care and social support to enable adherence
- Programmatic use is feasible in most settings worldwide
- Lowered costs (<US$1,000 in drug costs/patient) and reduced patient loss expected
- Exclusion criteria: 2nd line drug resistance, extrapulmonary disease and pregnancy.

REGIMEN COMPOSITION

4-6 Km-Mfx-Pto-Cfz-Z-$H_{high\text{-}dose}$-E / 5 Mfx-Cfz-Z-E

Km=Kanamycin; Mfx=Moxifloxacin; Pto=Prothionamide;
Cfz=Clofazimine; Z=Pyrazinamide;
$H_{high\text{-}dose}$= high-dose Isoniazid; E=Ethambutol

WHO RECOMMENDATION

ON THE USE OF THE SHORTER MDR-TB REGIMEN

In May 2016, WHO issued a conditional recommendation on the use of the shorter MDR-TB regimen. A flow chart outlining selection of patients on the shorter MDR-TB regimen is presented below.

CHOOSING THE MDR-TB TREATMENT REGIMEN IN PATIENTS WITH CONFIRMED RIFAMPICIN-RESISTANT OR MDR-TB

CRITERIA: Do any of the following apply ?

- ✓ Confirmed resistance or suspected ineffectiveness to a medicine in the shorter MDR-TB regimen (except isoniazid resistance)
- ✓ Exposure to ≥1 second-line medicines in the shorter MDR-TB regimen for >1 month
- ✓ Intolerance to ≥1 medicines in the shorter MDR-TB regimen or risk of toxicity (e.g. drug-drug interactions)
- ✓ Pregnancy
- ✓ Extrapulmonary disease
- ✓ At least one medicine in the shorter MDR-TB regimen not available in the programme

NO

Shorter MDR-TB regimen

Intensive phase
Duration: 4-6 months
Composition: 4 second-line drugs

Continuation phase
Duration: 5 months
Composition: 2 second-line drugs

Supported by selected first-line TB drugs

FAILING REGIMEN, DRUG INTOLERANCE, RETURN AFTER INTERRUPTION >2 MONTHS, EMERGENCE OF ANY EXCLUSION CRITERION

YES

Longer ("Individualized") MDR-TB regimens

Intensive phase
Duration: up to 8 months
Composition: 4 or more second-line drugs

Continuation phase
Duration: 12 months or more
Composition: 3 or more second-line drugs

Supported by selected first-line TB drugs

KEY TERMS

- TB bacteria resistant to the medicines used in its treatment occur in countries all over the world. Drug resistance is fuelled by inadequate treatment; once TB bacteria acquire drug resistance they can spread from person to person in the same way as drug-susceptible TB.
- **Rifampicin-resistant TB (RR-TB)** is caused by TB bacteria that are resistant to at least rifampicin, one of the most effective anti-TB medicines. These patients need second-line treatment similar to MDR-TB patients.
- **Multidrug-resistant TB (MDR-TB)** is caused by TB bacteria that are resistant to at least isoniazid and rifampicin, the two most effective anti-TB drugs. These patients need second-line treatment.
- **Extensively drug-resistant TB (XDR-TB)** is a form of MDR-TB that is also resistant to any fluoroquinolone and any of the second–line anti-TB injectable agents (i.e. amikacin, kanamycin or capreomycin).