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## A.34 Pretomanid - 200 mg tablet

MSF strongly supports the application from Global Alliance for TB Drug Development for the inclusion of pretomanid (Pa) 200 mg tablet in the Complementary List of Section 6.2.5 "Antituberculosis medicines" in the Essential Medicines List (EML) as an individual medicine administered as part of a combination regimen with bedaquiline (B) and linezolid (L), with or without moxifloxacin (M), designated BPaLM/BPaL, for the treatment of patients ≥14 years old with multidrug-resistant tuberculosis (MDR-TB) or rifampicin-resistant tuberculosis (RR-TB).

The 2020 WHO "Consolidated Guidelines on Tuberculosis, Module 4: Treatment - Drug-Resistant Tuberculosis Treatment" recommended that a treatment regimen lasting 6 to 9 months, composed of bedaquiline, pretomanid, and linezolid (BPaL), may be used under operations research (OR) conditions in MDR-TB patients with TB that is resistant to fluoroquinolones, who have either had no previous exposure to bedaquiline and linezolid or have been exposed for no more than 2 weeks[1].

The WHO "Rapid Communication: key changes to the treatment of drug-resistant tuberculosis" published in May 2022 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 months) 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 fluoroquinolone (in patients with pre-XDR-TB). Drug susceptibility testing (DST) to fluoroquinolones is strongly encouraged, but should not delay treatment initiation[2].

The 2022 update to the WHO "Consolidated Guidelines on Tuberculosis, Module 4: Treatment - Drug-Resistant Tuberculosis Treatment", suggests the use of a 6-month treatment regimen composed of bedaquiline, pretomanid, linezolid (600 mg) and moxifloxacin (BPaLM) rather than the 9-month or longer (18-month) regimens in MDR/RR-TB patients[3].

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[1] WHO consolidated guidelines on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment. Geneva: World Health Organization; 2020. https://www.who.int/publications/i/item/9789240007048

[2] Rapid communication: key changes to the treatment of drug-resistant tuberculosis. Geneva: World Health Organization; 2022 https://www.who.int/publications/i/item/WHO-UCN-TB-2022-2

[3] WHO consolidated guidelines on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment, 2022 update. Geneva: World Health Organization; 2022. https://www.who.int/publications/i/item/9789240063129

In August 2019, pretomanid in combination with bedaquiline and linezolid was approved by the Food and Drug Administration (FDA) for treating a limited and specific population of adult patients with extensively drug resistant, treatment-intolerant or nonresponsive multidrug resistant pulmonary TB.

In July 2020, pretomanid in combination with bedaquiline and linezolid was approved by the European Medicines Agency (EMA) for treating adults with drug-resistant tuberculosis: extensively drug-resistant (resistant to at least 4 antibiotics used for treating tuberculosis, including the standard antibiotics isoniazid and rifampicin); multi-drug resistant (resistant to isoniazid and rifampicin) and when antibiotics used for this form of tuberculosis do not work or cause unacceptable side effects.

Pretomanid is also approved in an additional 20 countries.

In November 2020, pretomanid was prequalified by WHO for a first generic manufacturer. Two more manufacturers should be able to supply quality-assured pretomanid tablets before end of 2023.

MSF has been using pretomanid in its programs since 2022. Currently, pretomanid is used in MSF programs in Belarus, Uzbekistan, Sierra Leone, Pakistan and Tajikistan.

MSF urges the 24th Expert Committee on the Selection and Use of Essential Medicines to include pretomanid, in the Complementary List of Section 6.2.5 “Antituberculosis medicines”, in the WHO Model List of Essential Medicines, as an individual medicine administered as part of BPaLM/BPaL regimen, for the treatment of patients ≥14 years old with multidrug-resistant tuberculosis or rifampicin-resistant tuberculosis.

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