

## Bedaquiline –A new drug against multidrug-resistant tuberculosis

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### Abstract

The infectious diseases have taken a toll on the rapidly multiplying population of the developing countries. The top three killers being HIV AIDS, TB and malaria. The total number of deaths due to TB is really a cause of concern since a well laid national program is running in most of these countries. However, even in the presence of clear guidelines to treat TB, there has always been a gradual rise in the new cases with few exceptions in some of these resource-constrained countries. The issue becomes graver when the problem of drug-resistant TB also comes into the picture. In the present article, the authors highlight the introduction of the new drug i.e., Bedaquiline in India to counter the problem of multidrug-resistant TB.

**Keywords:** Bedaquiline, Drug; Drug-resistant, TB; Tuberculosis.

### Introduction

The problem of tuberculosis (TB) is known to mankind for long; however, till date, not much progress has been made in the direction to eliminate TB.<sup>1</sup> TB is caused by *Mycobacterium tuberculosis* and is transmitted by aerosols.<sup>2-4</sup> WHO reported around 480000 multidrug-resistant TB (MDR-TB) cases in 2014 with about 300000 being pulmonary MDR-TB cases and about half of all these from the three highly populated countries, i.e. India, China and the Russian Federation.<sup>5</sup> The situation in countries like India is not good with India having a major share in the TB load of the world with the highest number of incidences and a very high mortality.<sup>3,4,6-8</sup> Since 1990 the country is also facing the burgeoning issue of the drug-resistant TB.<sup>3</sup> MDR-TB is a man-made problem with the prevalence of MDR-TB in new cases around 3.5% and in retreatment cases around 20.5%.<sup>3</sup> In India, the TB control is done through the Revised National Tuberculosis Control Programme (RNTCP). The RNTCP is functioning through its DOTS and DOTS-Plus strategies for the TB control. However, even in the presence of a well-organized program the hope to eliminate TB looks like a distant dream. The Government of India has taken this situation seriously and had introduced a new drug Bedaquiline (BDQ) on 21<sup>st</sup> March 2016 to be included as a conditional access in the existing treatment of the programmatic management of drug-resistant tuberculosis (PMDT) for the MDR-TB cases.<sup>8</sup>

Thus, after Rifapentine which was approved in 1998, BDQ (previously known as TMC207) becomes the first new antitubercular drug to be approved for human use.<sup>8-10</sup> The drug is effective against drug sensitive, MDR, Pre-XDR, and XDR strains of *M. tuberculosis* in vitro.<sup>10</sup> Also, post approval of Rifampicin which happened more than four decades ago; BDQ became the first anti-TB drug with a novel mechanism of action.<sup>8,10</sup> BDQ is a unique drug that has been specially introduced for the treatment of MDR-TB along with other anti-TB

drugs.<sup>8,10</sup> The effects of BDQ on *M. tuberculosis* are unaffected even in the presence of resistance to other anti-TB drugs, like Ethambutol, Isoniazid, Rifampicin, Streptomycin, and Moxifloxacin.<sup>8,11</sup> The drug had given good results in the countries where it was already a part of the MDR-TB regimen and thus similar results are expected from India as well.<sup>9</sup>

### Why a new drug?

The introduction of BDQ is really important as the present situation of DR-TB cases is really scary due to the long duration of treatment, high pill load, the toxicity of drugs with adverse drug reactions, and a very expensive overall treatment.<sup>5</sup> The psychological impacts of TB on the social, mental and physical prosperity of the patient are well documented.<sup>12</sup> In this context, the inclusion of a novel drug like BDQ with reports of the early culture conversion gives a hope to reduce the total duration of the DR-TB course.<sup>4</sup>

### Where it was started and who was included?

The drug was launched in the year 2016 on the World TB day and was introduced at six tertiary care sites all over India.<sup>5</sup> Post introduction the drug was rolled over throughout the country as an extended access.<sup>5,8</sup> In New Delhi the drug was added to the existing MDR-TB regimen at two DOTS-Plus sites, thus covering a total 15 districts of the Delhi state.<sup>5,8</sup>

The drug was given as an add-on to the existing MDR-TB regimen.<sup>8</sup> Only pulmonary MDR-TB cases more than 18 years of age were started on this new regimen after a compulsory minimum fifteen days stay at the DOTS-Plus site.<sup>5</sup> The comprehensive inclusion and exclusion criteria for BDQ are explained elsewhere.<sup>5</sup>

### Dosage

On the basis of patient's tolerance and after consulting the treating physician at the DOTS-Plus site the BDQ would be added to the MDR-TB regimen along

with other second-line anti-TB drugs. A per oral dose of 400mg/day for first two weeks, followed by an alternate day dose of 200mg/day for the next 22 weeks.<sup>5,8</sup> With a cutoff limit of the maximum dose does not exceed 600mg/week.<sup>13</sup> Post completion of 24 weeks with BDQ, MDR-TB regimen would continue as per the recent PMDT guidelines.<sup>5,8,14</sup>

### Adverse effects

The drug was found to be linked with certain adverse drug reactions (ADR) and thus regular monitoring along with the immediate management of these adverse events was imperative. The ADR due to BDQ is reported in detail elsewhere.<sup>5,8,13,14</sup> Collaboration with the private practitioners and other public and private hospitals was also done so that the ADR's would be managed without any time lag.<sup>5</sup> Besides, the drug was also given to the private practitioners under 'compassionate use'.<sup>5</sup> And thus the importance of dissipation of healthcare information about this new drug is very important and so is the responsibility of government and private agencies.<sup>15-17</sup>

### Implications for resource-poor countries like India

The introduction of a novel drug in an asset restricted nation like India could pay rich dividends. TB is a public health problem and in a country where the per capita income is less and the public health sector is weak owing to the poor contribution of the government's annual budget on health sector the BDQ may serve as an important tool against the MDR-TB.<sup>18</sup> Besides, with the introduction of Delamanid (another new anti-TB drug) the importance of newer tools to fight TB has given hope to the policymakers about the elimination of TB by 2025.<sup>19,20</sup>

### Conclusion

The introduction of BDQ to a pre-defined MDR-TB treatment is an important step in TB care. The present condition of DR-TB cases is handicapped by a very high mortality and loss to follow-up cases, thereby resulting in a growing number of cases in India. The overall results from this inclusion will be definitely important in the context of the future of drug-resistant TB care in a resource-limited country. Besides, the implications of this drug might also help in reducing the total duration of the MDR-TB regimen in the future, which will surely be a boon to the patients.

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