

“Call to Action” To Accelerate Access to DR-TB Drugs: 2016 Update

June 3, 2016

On March 10th, 2015, Médecins Sans Frontières (MSF), ACTION Global Health Advocacy Partnership, SWIFT Response Project, Treatment Action Campaign (TAC), Treatment Action Group (TAG), and 83 other humanitarian, public health, civil society and medical organizations issued a call to action for the global TB community in order to urgently improve access to the two new drugs used to treat multidrug-resistant tuberculosis (MDR-TB), bedaquiline and delamanid (<http://www.msfacecess.org/content/call-action-accelerate-access-dr-tb-drugs>). The purpose of this update, over a year after that call, is to inform the concerned community about general progress in the introduction of these two new medications in TB programs worldwide, and to report specifically on the requests made in the original call to action.

DR-TB STAT: Formation and Progress

One primary request in the call to action was the formation of a consortium to monitor and support the progress of new drug introduction. In late April, 2015, at the joint meeting of the Global Drug Resistance Initiative (GDI) and Global Laboratory Initiative Joint Partners Forum convened at the World Health Organization (WHO), the formation of such a consortium was openly debated. Members called for the recognition of the DR-TB Scale-up Treatment Action Team (DR-TB STAT)—which had already begun operating with support from MSF, Partners In Health (PIH), TAG, and the SWIFT Response Project—as an official task force of the GDI. While the core members of the GDI debated this, DR-TB STAT held the first of what would become monthly calls with key stakeholders involved in new drug introduction, including National TB Programs, implementing partners, technical assistance groups, drug suppliers, donors, and members of affected TB-communities. In July 2015, the DR-TB STAT task force was officially recognized and funded by the GDI and the chair of DR-TB STAT was made a core member of the GDI.

DR-TB STAT calls happen each month. These calls are open to all interested parties, last for 1 hour, discuss overall progress in new drugs introduction globally, follow up of any items from previous call or country situations then focus on the situation in 2 countries. The goal of these calls is to understand the situation on the ground in each of these countries, discuss any barriers to new drug introduction, actively problem solve with all involved stakeholders and provide ongoing support to countries for the optimal introduction of these new MDR-TB drugs. DR-TB

STAT has convened eleven calls have been held since May of 2015, and have discussed the following countries: China, Georgia, Haiti, India, Indonesia, Lesotho, Kenya, Mexico, Mozambique, Papua New Guinea, Peru, the Philippines, Russia, Swaziland, South Africa, Vietnam. One monthly call was devoted to the introduction of delamanid after the February 2016 announcement that this drug would now be available through the Global Drug Facility. DR-TB STAT maintains a website with monthly progress reports (<http://drtb-stat.org/about/>), presented an update at the Union conference in Cape Town and has published an article about progress and challenges in new drug introduction in Emerging Infectious Diseases (http://wwwnc.cdc.gov/eid/article/22/3/15-1430_article).

The DR-TB STAT task force was reviewed by the Stop TB Partnership's Board in November of 2015 and given a mandate to continue operating for another 12 months. Although funding for the task force ended in January of 2016, the group was able to continue its work through in-kind support from a number of partners, including PIH, MSF, TAG, and the SWIFT Response Project. DR-TB STAT is due to receive additional funding from the GDI sometime in June or July of 2016.

For additional questions or suggestions about the DR-TB STAT Task Force, or to contribute to it, please contact the current chairperson, Dr. Jennifer Furin (jenniferfurin@gmail.com).

Progress on new drug introduction

There has been some general progress in the introduction of new drugs in program settings. In July, 2015, there were 482 patients on bedaquiline under program conditions. As of May 1, 2016 there were 3566 persons who were receiving or had received bedaquiline under program use and an additional 766 who had received the drug under compassionate use/expanded access conditions. When the DRTB STAT was formed in April 2015 there were less than 600 people receiving bedaquiline outside of clinical trials. Of note, more than 2000 of these patients were from South Africa. For delamanid, there were 219 persons who were receiving or had received delamanid under program conditions—largely through a donation of 400 courses given by Otsuka to MSF—and numbers on access through compassionate use were not made available from the company but are estimated at more than 250 individuals – In April 2015 there were less than 50 patients who were receiving delamanid in programmatic use. Of note, it is estimated that there are between 33,000 and 67,000 persons living with MDR-TB worldwide who would benefit from access to the new drugs following current WHO recommendations. Thus, while there were notable improvements in access to bedaquiline, the initial situation prompting the “Call to Action” remains of concern.

There were several specific requests made in the “Call to Action” and progress in each of these will be described below:

- 1. Quickstart:** Ensure 500 patients are started on routine regimens which include BDQ by July 2015, and 500 patients started on routine regimens which include DLM by January 2016.

As of August 1, 2015, there were 482 patients on BDQ as part of routine treatment; the goal of 500 was reached in September, when 634 patients were receiving BDQ under program conditions. The goal of 500 patients on DLM under program conditions by January 2016 has not been met, with less than half that number on treatment as of May 1, 2016.

- 2. Optimal DR-TB treatment:** Technical assistance provided for 25 countries by 2016 and 52 countries by 2017 for drafting implementation plans; implementation plans are adopted by 25 countries by 2016 and 52 countries by 2018; and BDQ and DLM are routinely used by 20 countries by end of 2016 and 52 countries by end of 2019. Key repurposed drugs (especially linezolid and clofazimine) should be on the national Essential Medicines List (EML), and countries and national TB programmes (NTPs) should be using these drugs.

Technical assistance on the introduction of new drugs has been provided for at least 40 countries as of May 1, 2016. This technical assistance is largely supported by USAID through a number of its partner agencies (including KNCV, MSH/SIAPS), by the Global Drug Facility, and by groups such as MSF, PIH, IRD, as part of their UNITAID endTB project. DR-TB STAT also provides direct support to countries in all regions of the world. The Global Fund directly supports the provision of technical assistance in many of the countries using new drugs.

Bedaquiline is currently used routinely in 18 countries plus the European Union, with plans for routine use to begin in additional 3 countries by June 1, 2016ⁱ. Delamanid is routinely used in the European Union, Japan, and South Korea and is also being used in Georgia, Armenia, Belarus, and South Africa through both the donation made to MSF and routine procurement of the drug from the GDF.

- 3. Regulatory status:** BDQ and DLM dossiers are submitted for registration in 25 countries by beginning of 2016 and 52 countries by 2017; and drugs are registered, or import waivers are in place, by 2016.

As of May 1, 2016, BDQ has been registered in 12 countries plus the European Union, including the high-burden countries of India and South Africaⁱⁱ. Dossiers have been submitted to an addition 17 countriesⁱⁱⁱ, including the high-burden countries of China, Indonesia, and Vietnam. DLM has been registered in Japan, South Korea, Hong Kong, and the European Union and is not registered in any high-burden countries. Dossiers have been submitted for registration in the Philippines, Indonesia, Turkey and Vietnam.

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- 4. Pharmacovigilance (PV):** The consortium supports a flexible approach for countries implementing BDQ (such as sentinel PV), proposes a set of standardised data for monitoring and reporting on adverse events, and works towards a supranational body to collect and analyse data.

In June of 2015, the WHO convened a meeting of experts in pharmacovigilance and an agreement was made to support a flexible approach for countries implementing new drugs that is now termed “Active Drug Safety Monitoring and Management” or aDSM. It was also agreed that the endTB sites would serve as sentinel Cohort Event Monitoring sites. The updated WHO guidelines can be found at <http://www.who.int/tb/publications/aDSM/en/>.

- 5. Procurement:** Forecasting of drugs is completed; procurement strategies are developed for 52 countries by 2018; and, the turnaround time between ordering and drug delivery is reduced.

The Global Drug Facility has been a strong participating member of the DR-TB STAT task force and is currently working with programs to optimize forecasting and develop flexible tools. Together with USAID they have developed a mechanism for expedited shipping of BDQ and have covered shipping costs for a number of countries. They reached an agreement with Otsuka for DLM in February 2016 and are now the sole suppliers of DLM for Global Fund eligible countries. They have also added BDQ and DLM to their rotating stockpiles to ensure reduced drug delivery times. They provide monthly updates on the number of orders for BDQ and DLM placed with the GDF to the DR-TB STAT task force. As of May 1, 2016, there were 4080 orders placed for BDQ and 567 for DLM.

Although there has been some progress made in access to the new MDR-TB drugs BDQ and DLM, there is still a significant gap in ensuring these drugs reach the people who need them most. The slow pace of DLM roll out is especially concerning, this is due to a lack of mechanism to procure the drug until February 2016 as well as the lack of registration of the drug in high-burden countries. DR-TB STAT will continue to strive not only to monitor the progress in access to these medications on a global level but to collaborate with all involved stakeholders to support countries, providers, and persons living with MDR-TB in the optimal use of these medications.

How to join DR-TB STAT

DR-TB STAT is open to any interested person. If you would like to join the team and our monthly calls, please email Jennifer Furin (jenniferfurin@gmail.com) and Laura Vaughan (lvaughan@pih.org)

To sign on to the “Call to Action” please go to <http://www.msfacecess.org/content/call-action-accelerate-access-dr-tb-drugs>

Figure 1: Monthly Progress in Use of BDQ and DLM under Program Conditions

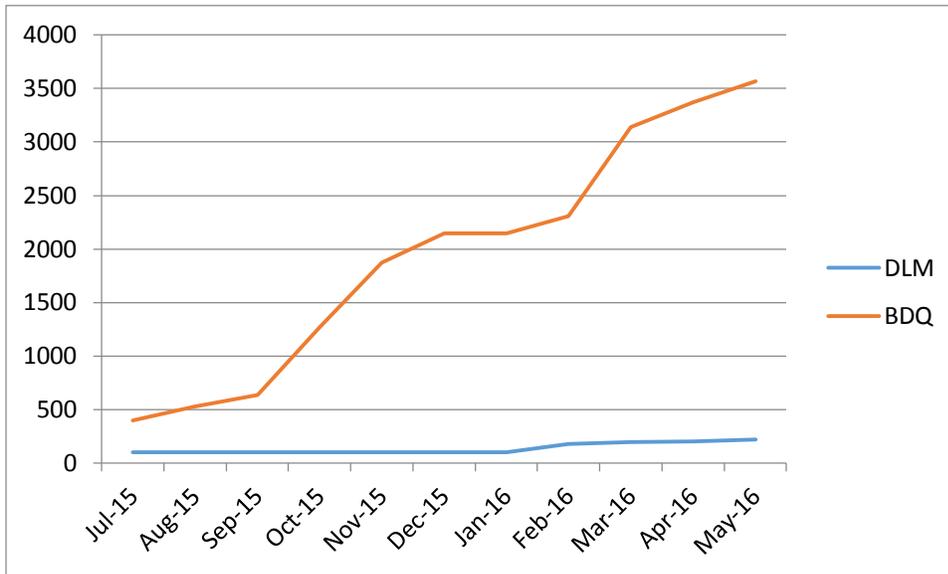


Figure 2: Monthly Progress in Use of BDQ and DLM compared with Conservative Estimate of Need

ⁱ The following countries are using BDQ under program conditions: Armenia, Belarus, Canada, Georgia, Haiti, Indonesia, Kazakhstan, Kenya, Lesotho, Nigeria, North Korea, Papua New Guinea, Peru, Russia, South Africa, Tanzania, Swaziland, the United States, and Viet Nam. The three countries expected to start using BDQ are Bangladesh, India, and the Philippines.

ⁱⁱ BDQ has been registered in Armenia, the European Union, India, Macau, Peru, Philippines, Russia, South Africa, South Korea, Taiwan, Turkmenistan, the United States, Uzbekistan

ⁱⁱⁱ Dossiers have been submitted in Azerbaijan, Bangladesh, Belarus, China, Colombia, Hong Kong, Indonesia, Kazakhstan, Mexico, Moldova, New Zealand, Tanzania, Thailand, Uganda, Viet Nam. Of note, a dossier submitted in Kyrgyzstan was rejected on the basis that there was no phase III data. Additionally a joint application has been submitted for the following countries via a WHO pilot project for collaborative registration: Burundi, Cameroon, Ethiopia, Ghana, Kenya, Nigeria, Tanzania