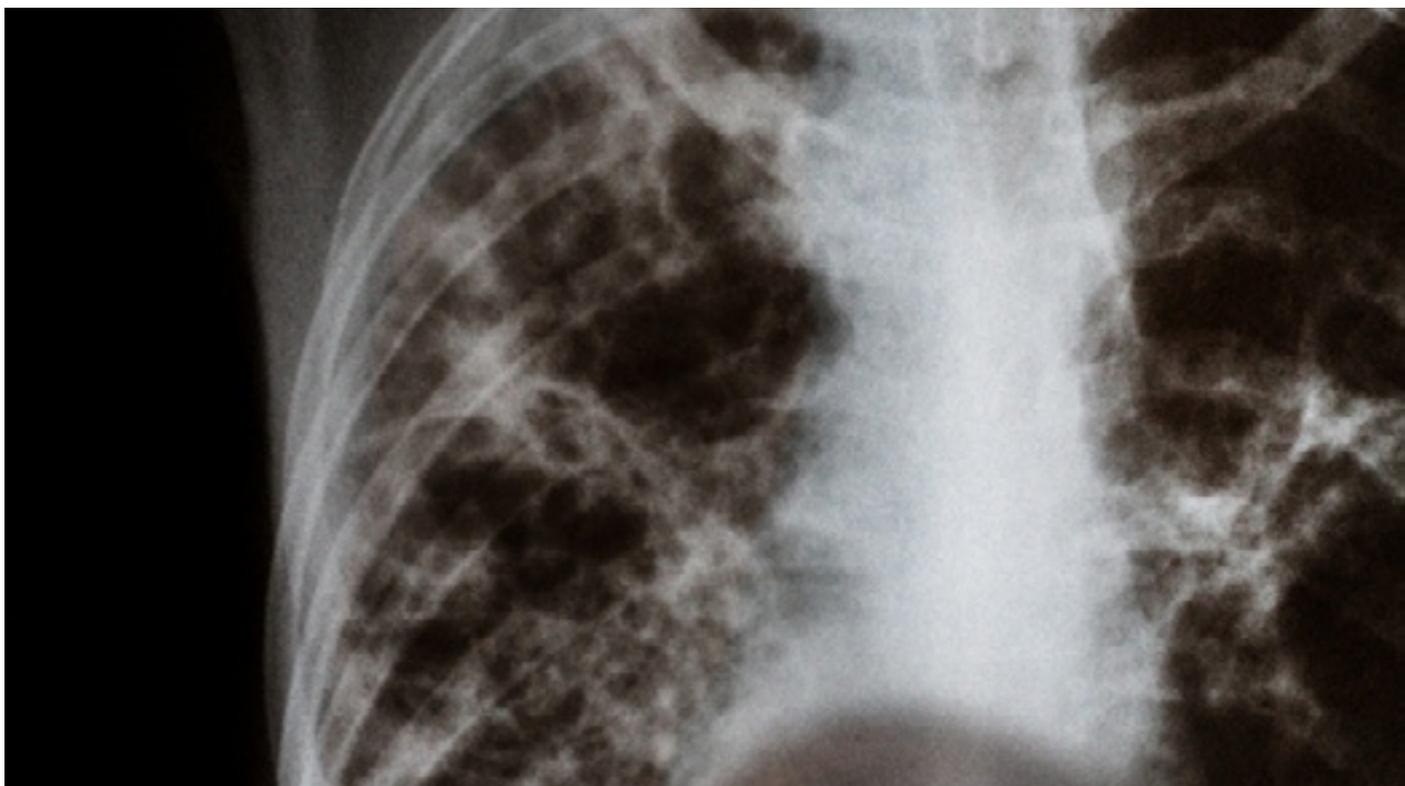


MONITORING COMPASSIONATE USE OF
NEW DRUGS FOR TUBERCULOSIS



RESIST-TB

Research Excellence to Stop TB Resistance



MONITORING COMPASSIONATE USE OF **NEW DRUGS FOR TUBERCULOSIS**

Compassionate Use (CU) programs have been utilized for new cancer and HIV drugs to provide access to lifesaving drugs prior to regulatory approval. The rise of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) have generated a growing need for CU for TB drugs. Two of these new drugs, bedaquiline and delamanid, represent two new classes of anti-TB medication. Although approved by US and European regulators, registration in high-

burden MDR-TB countries is lagging. Thus, the vast majority of the 480,000 persons who develop MDR-TB each year will need to gain access to them through CU. In 2014 and 2015, RESIST-TB monitored CU of new drugs for MDR-TB and XDR-TB, aiming to address an urgent need to document patient demand, advocate for new or existing CU programs to meet this demand, and identify solutions so that patients may be able to access valuable treatments through CU.

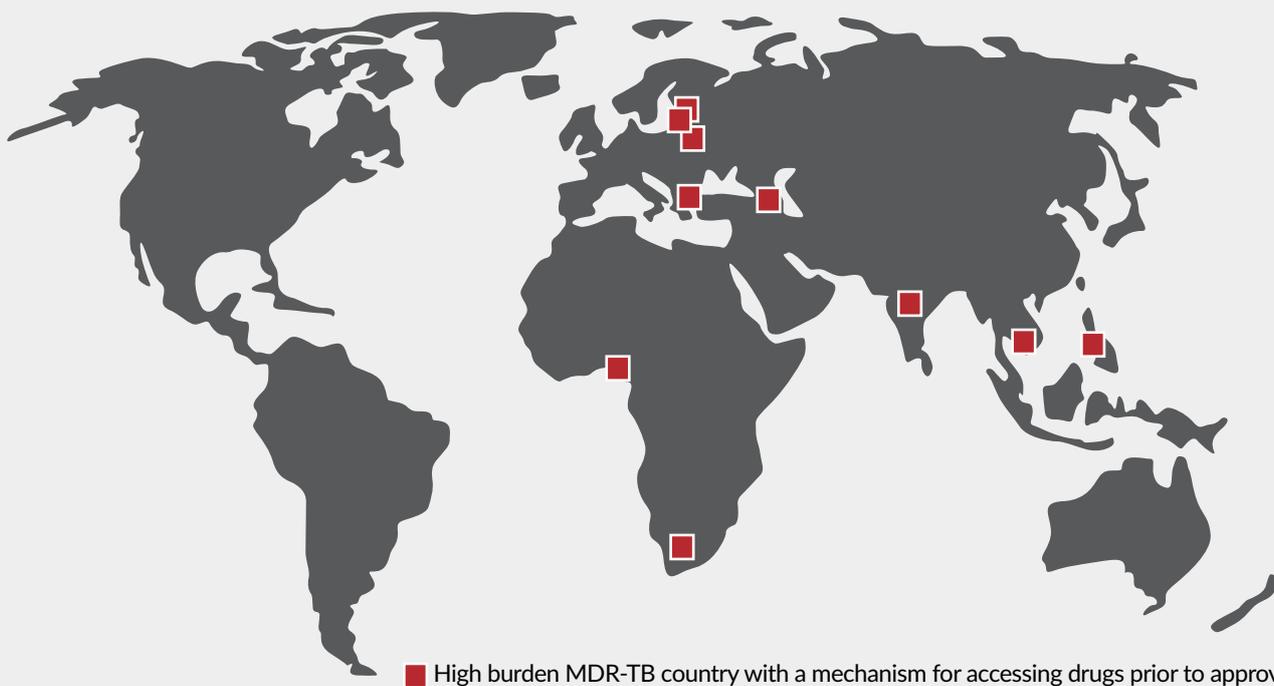
MECHANISMS FOR COMPASSIONATE USE IN THE 27 HIGH BURDEN MDR-TB COUNTRIES

10

Countries with a mechanism for pre-approval access to drugs including compassionate use, expanded access, or access on a named-patient basis

17

Countries without an existing mechanism for pre-approval access to drugs or where a determination could not be made



INVESTIGATING COMPASSIONATE USE OR OTHER PRE-APPROVAL MECHANISMS IN THE 27 HIGH BURDEN MDR-TB COUNTRIES

Through a systematic internet search of regulatory authority websites and interviews with key persons working in countries of interest, we determined approximately 37% of high burden MDR-TB countries had an existing

mechanism or process for providers to request the use of a drug prior to regulatory approval. These countries included Armenia, Belarus, Bulgaria, Estonia, India, Latvia, Nigeria, Philippines, South Africa, and Vietnam.

Survey on experiences accessing new TB drugs through CU

To better understand the experience of providers and advocates attempting to access new TB drugs through CU or similar mechanisms, we distributed a survey to key providers and advocates working with MDR-TB patients. The survey aimed to gather data on the number of patients who would benefit from treatment with delamanid or bedaquiline and the number of patients that have successfully accessed these treatments.

The survey also collected data on what potential roadblocks deter access to these drugs under CU and how advocacy efforts could contribute to increasing access to treatment.

SURVEY RESPONSES

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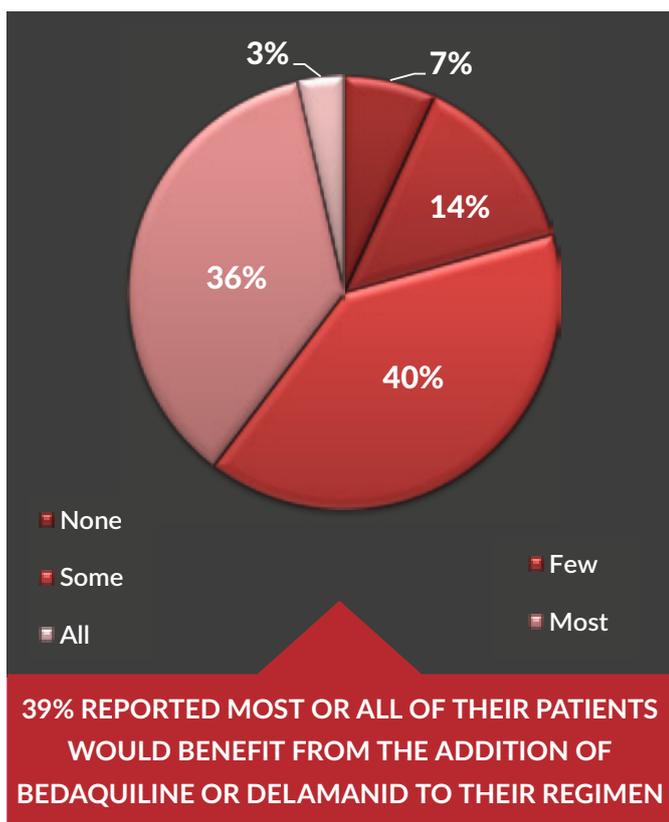
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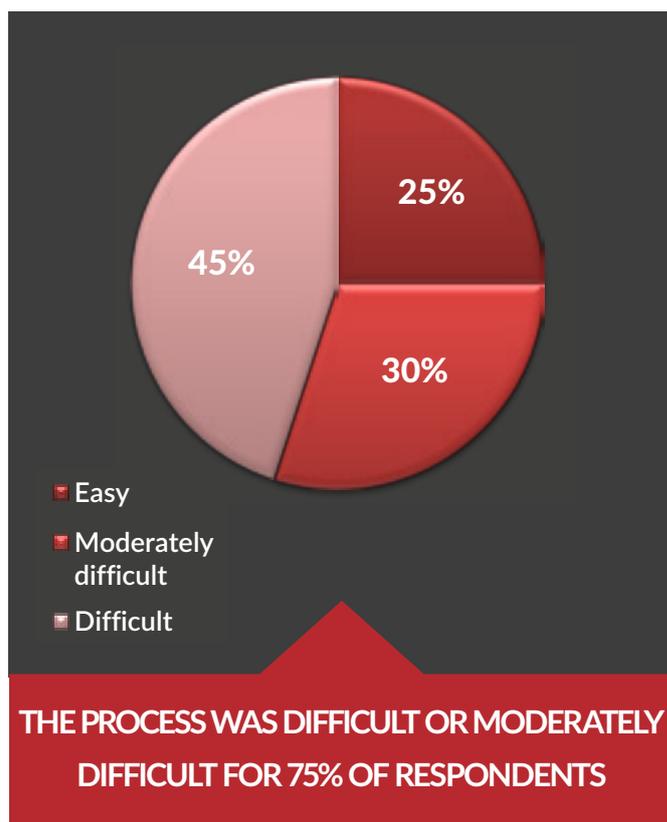
CHARACTERISTICS OF SURVEY RESPONDENTS

Between July and December 2015, 59 providers and advocates in 28 countries shared their thoughts and experiences attempting to gain access to new TB drugs prior to regulatory approval in their respective countries. Of the 27 high burden MDR-TB countries, 19 were represented among survey respondents. Over 75% of respondents provided care in the public sector, 14% in the private sector, and 10% in both the public and private sectors. Half of respondents reported caring for less than 100 DR-TB patients per year and 27% reported caring for over 500 MDR-TB and XDR-TB patients per year. Respondents represented a variety of types of organizations, including research institutions and academia, technical agencies and non-profit organizations, and national or state organizations.



RESPONDENT PERSPECTIVES AND EXPERIENCES OF PRE-APPROVAL ACCESS

Approximately 19% of respondents reported they did not know whether the country they were reporting on allowed access to investigation drugs prior to regulatory approval, highlighting the dearth of information available on mechanisms such as compassionate use. One-quarter of respondents reported they had not attempted to access new TB drugs through pre-approval mechanisms such as compassionate use. The most common reasons for not doing so included believing



the process was too complex, not having administrative support to handle required documentation, and believing one had to have a relationship with pharmaceutical companies in order to do so. Of the 75% of respondents who had attempted to gain access, three-quarters reported that the process was difficult or moderately difficult. Over half of these providers and advocates utilized compassionate use, 20% attempted access through an expanded access program, 18% used waivers, and 9% enrolled or attempted to enroll patients in clinical trials.

RESPONDENT SUCCESS ACCESSING NEW TB DRUGS

Respondents reported they attempted to gain access to bedaquiline for a cumulative 1175 patients. The outcome of the attempt was reported for only 50%: 544 patients successfully received bedaquiline and 40 patients did not. Success rates were greatest in the Africa (96%), Europe (95%), and Americas (83%) WHO regions, and lowest in the South-East Asia region (68%).

Respondents reported access to delamanid was attempted for 180 patients, of which 70 successfully accessed delamanid and 17 did not. Success rates were greatest in the Africa (81%), Europe (84%), and South-East Asia (82%) WHO regions, and lowest in the region of the Americas (0%).

ACCESS TO BEDAQUILINE

Successful	544	40
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ACCESS TO DELAMANID

Successful	70	17
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The amount of time between application and receipt of investigational drugs varied. Some respondents received drugs within one month of application, while others did not receive drugs for up to three years. Significant delays of over six months were reported in countries in the Western Pacific, Europe, and Africa regions. Legal barriers to importation were cited as a major cause of delay.

Respondents described many barriers to gaining access to new TB drugs, including difficulty acquiring background drugs because they were also unregistered or prohibitively expensive. They noted the same process used to access bedaquiline or delamanid had to be used to acquire background drugs when they were not registered in the country.

To aid in the process of accessing drugs prior to regulatory approval, respondents suggested creating streamlined processes, support networks for consultations, and country-level legislative changes.

BARRIERS TO PRE-APPROVAL ACCESS

- Background regimen considered too weak
- Drugs for background regimen not available in country
- Delamanid denied due to history of bedaquiline use
- Importation delays
- Lack of information on process
- Application and documentation lengthy
- Country-specific legislative hurdles
- Denied in pediatric patients

SUGGESTED FACILITATORS TO PRE-APPROVAL ACCESS

- Streamlined, electronic process for application
- Support for providers and advocates from international agencies to navigate registration and importation processes
- Creation of small stocks of drugs in-country that can be released upon approval
- Country legislation changes to fast track registration
- Transparency from companies on eligibility
- Clinical committees available for consultation

THIS PROJECT WAS MADE POSSIBLE BY SUPPORT FROM



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