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Sentinel Project on pediatric drug-resistant tuberculosis

ZERO child deaths from DR-TB

BRIEF UPDATE ON BEDAQUILINE

New WHO "meeting report" discusses evidence on the use of bedaquiline in adolescents treated for MDR-TB

On March 13, 2017, the World Health Organization issued a "meeting report" that contained information on a series of Guideline Development Group meetings that happened in June and September of 2016. In this meeting report, evidence on the use of bedaquiline in 537 individuals treated for MDR-TB disease—including 39 adolescents ages 12 to 17 years—was presented. In addition, the group reviewed data from a mortality study done in South Africa comparing persons who had received bedaquiline-containing regimens versus those who had not.

The evidence reviewed by the group found that no new safety events were documented among the 39 adolescents who received bedaquiline, although they noted the number of adolescents included in the review was small. The South African mortality study included in the review found that no adolescents who received bedaquiline-containing regimens died, compared to 7.4% of adolescents in the group who did not receive bedaquiline in their treatment regimens (47 out of 630).

The World Health Organization also clarified in their "meeting report" that bedaquiline should be used in adults who do not qualify for shortened MDR-TB regimens.

Although the Guideline Development Group felt that data on the use of bedaquiline in adolescents were "insufficient to make any recommendations," they did note in their "Frequently Asked Questions" document that "It is conceivable that selected patients may require changes to their MDR-TB regimen based on a limited number of effective medicines remaining. In such cases, the decision to use bedaquiline is entirely at the discretion of the clinical practitioner treating the patient and should include patient informed consent in writing and active TB drug safety monitoring (aDSM) and proper management of adverse events as per conditions for bedaquiline use." However, there is no indication that adolescent children have different bedaquiline pharmacokinetics compared to adults or are at increased risk of bedaquiline related adverse effects.

ZERO DEATHS

in 39 adolescents who were treated for MDR-TB with bedaquiline-containing regimens

When making recommendations about new drugs we must bear in mind that there are limited safety and efficacy data available on both the recently recommended shortened regimens and many of the second-line drugs that are widely used in the adolescent population. Therefore, given that available data on the use of bedaquiline in adolescents suggest no increased toxicity compared to adults,

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and in light of the South African mortality data, the Sentinel Project on Pediatric Drug-Resistant Tuberculosis proposes recommendations to clinical providers and national TB programs.

WE RECOMMEND:

1. Bedaquiline should be used among adolescents age 12 to 17 years who do not qualify for the shortened regimens;
2. Bedaquiline continue to be provided as a treatment option for adolescents with resistance or intolerance to second-line agents, given the high rates of adverse events reported with the use of other second-line medications, especially the injectable agents;
3. Guidelines on the use of bedaquiline be updated to allow for the use of bedaquiline in adolescents where treatment options are limited, provided there is informed consent provided by the patient and his or her care provider; and
4. Data on the safety of bedaquiline in adolescents continue to be collected as part of active drug safety monitoring and management under program conditions and as part of observational research in addition to the formal dosing and safety studies being done on bedaquiline in adolescents.

Of note, bedaquiline is now available through a compassionate use program for adolescents ages 12 to 17 years. To access bedaquiline via Janssen's compassionate use program, submit written requests to JanssenMAc@its.jnj.com. Please note this program is currently only accepting requests for adolescents. Janssen's compassionate use program is no longer open to adults, since the drug has been on the market for several years, and is freely available through the Global Drug Facility (GDF) for any Global Fund-eligible country. More information is available at StopTB.org.

For additional information on the use of newer drugs—including bedaquiline and delamanid—or shortened regimens in children and adolescents, please contact The Sentinel Project at Sentinel_Project@hms.harvard.edu.

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