April 6, 2023

To: Secretary of the Expert Committee on the Selection and Use of Essential Medicines
Medicines Selection, IP and Affordability (MIA)
Department of Health Products Policy and Standards (HPS)
World Health Organization
By email via emlsecretariat@who.int

Re: Statement in support of including pretomanid in the World Health Organization Model List of Essential Medicines

Dear Colleagues:

I am writing to you to express the U.S. BPaL Implementation Group (BIG)'s strong support for the proposal of the TB Alliance to include the antituberculosis medication, pretomanid 200mg tablets, in the World Health Organization (WHO) Model List of Essential Medicines (EML). BIG is a collaboration of over 100 medical providers from U.S. state and local tuberculosis programs, academic medical centers, private practice, and community health centers who provide care to individuals with tuberculosis (TB). As such, we have extensive experience treating persons who have TB resistant to at least rifamycins (RR-TB) or who are unable to tolerate rifamycins due to severe adverse reactions or drug interactions.

As you know, the WHO currently recommends the use of BPaL (Bedaquiline, pretomanid and linezolid) or BPaL plus moxifloxacin (BPaLM) to treat people suffering from MDR/RR-TB or MDR/RR-TB with additional resistance to fluoroquinolones (pre-XDR-TB). These recommendations stem from the results of at least three clinical trials and several observational studies demonstrating that these pretomanid-based regimens offer better outcomes, higher tolerance, remarkably shorten the duration of treatment, and thus significantly improve quality of life for people with MDR/RR-TB. This all oral, 6-month BPaL(M) regimen with a proven cure rate of 90% has transformed treatment for RR/MDR-TB globally.

Since August 2019, the U.S. FDA has approved the use of pretomanid in BPaL, and the U.S. Centers for Disease Control and Prevention (CDC) has also issued recommendations for its use in clinical practice (https://www.cdc.gov/tb/topic/drtb/bpal/default.htm). Over the past three plus years, U.S. providers have utilized pretomanid in more than 150 patients as part of the BPaL or BPaLM regimen, becoming the new U.S. standard of care. Based on the U.S experience, patients treated with this regimen experience fewer adverse events and interruptions during treatment, such that patients can more quickly resume their activities of daily living, work, education, social interactions, and other areas of productivity essential to human existence. It is anticipated that this regimen will be used to save countless lives and avoid the significant and often permanent toxicity associated with traditional treatments for RR/MDR-TB. With concern of emerging resistance to bedaquiline, inclusion of pretomanid in a TB treatment regimen may be even more essential given its dual action to rapidly kill actively replicating *M. tuberculosis* organisms and also to sterilize semi-dormant persister organisms required for a durable cure.

We thus strongly support the inclusion of pretomanid 200mg tablets on the WHO EML.

If you need additional information in support of this application, please do not hesitate to contact me.

Sincerely,

Connie Haley

Connie A. Haley, MD MPH
on behalf of the U.S. BPaL Implementation Group
Connie.haley@medicine.ufl.edu
615-598-6411