**To** Honorable Minister of Health Name of the minister

Ministry of Health

Government of (Your Country)

**Cc** TB Programme Head, (Your Country)

Other Senior Government Official stakeholder in TB Programme in Your Country

Date

**Open letter re: Injection-free drug-resistant TB treatment with bedaquiline**

Dear Hon. Minister (Name),

As civil society organizations, community groups, TB survivors, researchers, clinicians, and other partners committed to ending the tuberculosis (TB) epidemic in (Your Country), we commend you for the recent advances in addressing tuberculosis (TB) in (Your Country) and the bold steps taken so far to end TB. We write today to urge you to move quickly to update guidelines, procurement, and training in (Your Country) to make bedaquiline a core agent in the treatment for rifampicin-resistant TB (RR-TB), replacing injectable agents. Our request follows recently updated World Health Organization (WHO) recommendations, and a wealth of evidence on the benefit of the drug bedaquiline versus the harmful effects of the injectable agents.

TB continues to be a major health emergency in (Your Country). Our country had an estimated **(your country data)** people fall ill with TB in 2016, with **(your country data)** new cases of RR-TB.[[1]](#footnote-1) Of note, only (Number) persons in (Your Country) have been offered treatment with bedaquiline. One of the biggest challenges with TB is diagnosis of people affected by TB and ensuring that they are put on the right treatment. According to the Global TB Report 2017, only one in five persons with RR-TB was started on treatment. Treatment success remains low at a bleak 54% globally.

In July 2018, South Africa took a major step towards improving cure rates and the quality of life of people with RR-TB when it recommended an injection-free, bedaquiline-based regimen for ALL patients with RR-TB. This decision was based on their experience offering bedaquiline to more than 11,000 people with MDR-TB, which showed that using bedaquiline was associated with a 41% increase in treatment success and a three-fold reduction in mortality,[[2]](#footnote-2) results in cost savings for the health system,[[3]](#footnote-3) and can be used to replace the dangerous injectable agents that are currently a core part of DR-TB treatment but can result in serious adverse events in over 60% of those who receive them.[[4]](#footnote-4)

Shortly after, a WHO guideline group reviewed a large body of evidence on the safety and efficacy of RR-TB treatments, and concluded that the core RR-TB treatment regimen should rely on bedaquiline, plus levofloxacin/moxifloxacin, and linezolid. Capreomycin and kanamycin are no longer recommended, given their association with increased risk of treatment failure and relapse. Amikacin should only be considered when a regimen cannot otherwise be constructed, if drug susceptibility testing (DST) confirms susceptibility, and if quality audiometry is ensured (streptomycin is to be considered only if amikacin cannot be used, and if phenotypic DST confirms susceptibility).[[5]](#footnote-5)

We request the Health Ministry to follow South Africa’s lead and WHO recommendations by ensuring that bedaquiline replaces the injectable medicines that currently form part of (Your Country) recommended RR-TB treatment regimen. This includes moving swiftly to update guidance, revise procurement, and conduct trainings for implementation of the newly WHO-recommended injectable-free regimen. In updating guidelines, it is important to ensure that oft neglected populations benefit from injectable-free regimens, including:

* **people with HIV**—bedaquiline is safe for people with HIV, though it cannot be used with some antiretrovirals. People on efavirenz-based regimens in need of bedaquiline should switch to nevirapine- or integrase inhibitor-based regimens. Lopinavir/ritonavir increases bedaquiline levels, though it’s not clear if adjustments are necessary.
* **pregnant women**—research on RR-TB treatment in pregnancy is limited, but bedaquiline is likely to be one of the safest options for RR-TB treatment during pregnancy.[[6]](#footnote-6) Pregnant women with RR-TB can and should be given bedaquiline.
* **people who need multiple newer drugs or who need treatment with newer drugs for more than six months**—many people with RR-TB will need multiple newer drugs (bedaquiline and delamanid together), and/or the use of them for over six months. Emerging evidence suggests that giving bedaquiline for over six months, or giving bedaquiline and delamanid together, is safe and associated with good outcomes.[[7]](#footnote-7),[[8]](#footnote-8)
* **children** **and adolescents**—bedaquiline should be used in children aged 12 and older, as they metabolize the drug similarly to adults. As paediatric studies of bedaquiline are ongoing in children under 12, we request the Health Ministry to ensure an appropriate injectable-free regimen for children under 12, who are particularly vulnerable to hearing loss. For children under 12 years old with less severe disease, the Health Ministry should drop the injectable without replacement in line with 2016 World Health Organization recommendations for children.[[9]](#footnote-9) For children under 12 years with more severe forms of disease, the Health Ministry should replace the injectable with delamanid—which has been shown to be very safe, and its paediatric use is recommended by the World Health Organization.[[10]](#footnote-10)

Patients with RR-TB are suffering from painful injectables and permanent hearing loss from injectables, when safer, more effective evidence-based treatment options exist. We look to the (Your Country) Government to right the course by taking the necessary actions and provide the strong leadership to uphold the right of every person affected by TB to access drugs that will cure them and not leave them with permanent disability.

We look forward to your response by (date—recommend two weeks from sending), and are committed to supporting the ministry and the TB programme in providing the highest quaity care and ending TB in (Your Country). For further information, kindly contact (Name), (Organisation Name), on (Contact No.), or email at (email address)

Respectfully submitted,

1. http://www.who.int/tb/country/data/profiles/en/ [↑](#footnote-ref-1)
2. Schnippel K et al. Effect of bedaquiline on mortality in South African patients with drug-resistant tuberculosis: a retrospective cohort study. Lancet Respir Med 2018. http://dx.doi.org/10.1016/S2213-2600(18)30235-2 [↑](#footnote-ref-2)
3. Ionescu AM et al. Bedaquiline- versus injectable-containing drug-resistant tuberculosis regimens: a cost-effectiveness analysis. Expert Rev Pharmacoecon

   Outcomes Res. 2018 doi: 10.1080/14737167.2018.1507821. [↑](#footnote-ref-3)
4. Reuter A et al. The devil we know: is the use of injectable agents for the treatment of MDR-TB justified? Int J Tuberc Lung Dis. 2017 doi:10.5588/ijtld.17.0468. [↑](#footnote-ref-4)
5. http://www.who.int/tb/publications/2018/WHO\_RapidCommunicationMDRTB.pdf [↑](#footnote-ref-5)
6. Jaspard M et al. Bedaquiline and linezolid for extensively drug-resistant tuberculosis in a pregnant woman. Emerging Infectious Diseases 2017: <https://wwwnc.cdc.gov/eid/article/23/10/16-1398_article>. [↑](#footnote-ref-6)
7. Ferlazzo G et al. Early safety and efficacy of the combination of bedaquiline and delamanid for the treatment of patients with drug-resistant tuberculosis in Armenia, India, and South Africa: a retrospective cohort study. Lancet Infect Dis. 2018 [↑](#footnote-ref-7)
8. Guglielmetti L et al. Long-term outcome and safety of prolonged bedaquiline treatment for multidrug-resistant tuberculosis.Eur Respir J. 2017 doi: 10.1183/13993003.01799-2016. [↑](#footnote-ref-8)
9. http://apps.who.int/iris/bitstream/handle/10665/250125/9789241549639-eng.pdf?sequence=1 [↑](#footnote-ref-9)
10. http://www.who.int/tb/publications/Delamanid\_interim\_policy/en/ [↑](#footnote-ref-10)