

South African National Department of Health

NATIONAL ESSENTIAL MEDICINES LIST COMMITTEE

DELAMANID – MDR/RR-TB

Medicine details

Medicine Class	No
Medicine/s name INN:	Delamanid
Medicine/s (ATC5):	J04AK06
Indication (ICD-10 code):	U50.0, U50.2, U50.20, U50.21, U50.5
SAHPRA Approved	Yes
Dosage form/s	Tablet
Route of administration/s	Oral
Patient population	Children, adolescents and adults (including pregnant or breastfeeding women) with multidrug-resistant/rifampicin-resistant tuberculosis (RR-MDR/RR-TB)
Prevalence and/or incidence of condition	In 2024, the estimated prevalence of MDR/RR-TB among TB cases in South Africa was 3.6% in new cases and 17% in previously treated cases. The estimated burden of MDR/RR-TB was 14,000 incident cases, corresponding to an incidence of 21 per 100,000 population per year. ¹
Level of Care	Primary Healthcare
Prescriber level	Doctor prescribed

Current Standard of Care

Delamanid is included in the National TB Programme guidelines for the management of MDR/RR-TB.¹ Delamanid, in combination with other anti-TB medicines, is used as part of individualised treatment regimens for MDR/RR-TB in children, adolescents, adults and pregnant or breastfeeding women not eligible for BPAL-L. Delamanid, in combination with other anti-TB medicines, is used as part of individualised rescue regimens for bedaquiline-resistant TB in children, adolescents, adults and pregnant or breastfeeding women.

Executive Summary

- Delamanid is included in the National TB Programme Guidelines and is used, in combination with other appropriate anti-TB medicines, as part of individualised or rescue regimens for children, adolescents, adults, and pregnant or breastfeeding women with MDR/RR-TB not eligible for BPAL-L or with bedaquiline-resistant TB.
- Delamanid has not been formally evaluated by the NEMLC. The development of updated Tuberculosis Standard Treatment Guidelines (STGs) in 2025/2026 required consideration of its inclusion in the Essential Medicines List (EML).
- Given the widespread programmatic use of delamanid in South Africa since 2019, it was not considered an efficient use of resources to undertake a full de novo evidence review to support inclusion in the EML. Instead, a limited review was conducted to evaluate current international guideline recommendations and supporting evidence for the use of delamanid in the treatment of MDR/RR-TB.

¹ World Health Organization. *Global tuberculosis report 2025*. Geneva: World Health Organization; 2025.

- The World Health Organisation (WHO) consolidated guidelines on tuberculosis, Module 4: Treatment and Care,^{2,3} which were considered to be of high-quality by AGREE-II assessment, and a recently published randomised control trial, the BEAT TB study, were reviewed.
- WHO Consolidated guideline recommendations relevant to delamanid include:
 - Recommendation 1.2. WHO suggests the use of a 6-month treatment regimen composed of bedaquiline, delamanid, linezolid (600 mg), levofloxacin, and clofazimine (BDLLfxC) in MDR/RR-TB patients with or without fluoroquinolone resistance. (*Conditional recommendation, very low certainty of evidence*)
 - This recommendation applies to people with diagnosed pulmonary TB of all ages, including children, adolescents, PLHIV, and pregnant and breastfeeding women.
 - Recommendation 3.1. In MDR or RR-TB patients on longer regimens, all three Group A agents (refer table below), and at least one Group B agent should be included to ensure that treatment starts with at least four TB agents likely to be effective, and that at least three agents are included for the rest of treatment if bedaquiline is stopped. If only one or two Group A agents are used, both Group B agents are to be included. If the regimen cannot be composed with agents from Groups A and B alone, Group C agents (including delamanid) are added to complete it. (*Conditional recommendation, very low certainty of evidence*).
 - Recommendation 3.8. Delamanid may be included in the treatment of MDR/RR-TB patients aged 3 years or more on longer regimens. (*Conditional recommendation, moderate certainty of evidence*). In children with MDR/RR-TB aged below 3 years delamanid may be used as part of longer regimens. (*Conditional recommendation, very low certainty of evidence*)
 - Although the WHO recommendations are conditional and based on very low to moderate certainty evidence, they reflect the limited treatment options available for drug-resistant TB and the need to maximise the number of likely effective medicines in an individualised regimen.
- The BEAT Tuberculosis trial, which enrolled pregnant and breastfeeding women and children ≥ 6 years, showed that the efficacy of the 6- month bedaquiline, linezolid, delamanid, clofazimine and/or levofloxacin regimen was non-inferior to a 9-month or longer regimen to treat RR-TB, including fluoroquinolone-resistant TB. Safety outcomes were also similar.
 - Of the 170 female participants (42.2%), 9 (5.3%) were pregnant at baseline: one was in the first trimester, six were in the second trimester, and two were in the third trimester. One participant became pregnant during the trial. All pregnancies resulted in singleton live births, with one premature delivery. Among the pregnant participants, two serious adverse events occurred which were not related to treatment. One pregnant participant in the trial-strategy group had a recurrence of tuberculosis disease.
 - Thirty participants (7.4%) were 8 to 17 years of age. All participants younger than 18 years of age had a successful outcome at the end of treatment and the end of follow-up. Delamanid was discontinued in one child because of neuropsychiatric adverse reactions.
 - The BEAT Tuberculosis provides evidence for a shorter treatment option of comparable duration to BPAL-L for these vulnerable populations.
- Inclusion of delamanid on the Essential Medicines List aligns with current evidence-based WHO recommendations and will ensure availability of an important treatment option for patients requiring individualised management of drug-resistant tuberculosis.

Key Recommendations

Type of ERC recommendation	We recommend against the option and for the alternative (strong)	We suggest not to use the option or to use the alternative (conditional)	We suggest using the option (conditional)	We recommend the option (strong)		
	☐	☐	X	☐		
High level summary of conclusions	It is recommended that delamanid be included on the EML for people with DR-TB requiring individualised treatment regimens, including in children, adolescents, adults and pregnant or breastfeeding women.					
NEMLC Ratification	Date	Comments/Recommendation				
EML Status	EML	Non-EML – contingent on stated reference price threshold in Rand Value	Non-EML			
	X	☐	☐			
Therapeutic Interchange Considerations (if applicable)*	If YES:	Alternative medicine/s name (INN)	Alternative/s SAHPRA registered?	Formulation/s	Equipotent dose/ Dose range and dosing interval	If NO, tick box
						X
Trigger for review	New evidence for safety or efficacy					

REVIEW TEAM

Review contributors as detailed below:

Name & Affiliation	Declaration of Interests	Defining the PICO	Protocol development	Literature search	Study selection	Data extraction & characteristics of	Quality appraisal	Data analysis	GRADE assessment	Write up and referencing	Clinical Expertise &	Quality assurance
Jessica Taylor	None to declare	n/a	n/a	n/a	X	n/a	n/a	n/a	n/a	X	X	X
Zahiera Adam	None to declare	n/a	n/a	n/a	X	n/a	n/a	n/a	n/a	X		X
Jane Riddin	None to declare	n/a	n/a	n/a	X	n/a	n/a	n/a	n/a	X		X

Background and rationale

Delamanid is a first-in-class bicyclic nitroimidazole that was first approved by the European Medicines Agency in 2014. In 2019, the South African Health Products Regulatory Authority (SAHPRA) registered delamanid for use, in combination with other anti-tuberculosis medicines, for the treatment of adults with pulmonary multidrug-resistant tuberculosis (MDR-TB) when an effective treatment regimen cannot be constructed because of drug resistance or intolerance. Since then, delamanid has been included in various treatment regimens recommended by the South African National Tuberculosis Programme. Delamanid is listed on the Master Health Product List as a non-EML medicine and is available for procurement in the public sector. It has not previously undergone formal evaluation by the National Essential Medicines List Committee (NEMLC) for inclusion in the National Essential Medicines List (EML). Current South African programmatic guidelines for the management of RR-TB recommend delamanid in combination with other anti-TB medicines, as part of individualised treatment regimens for people with RR-TB not eligible for a 6-month BPaL-L² regimen. People not eligible for BPaL-L include pregnant women, children and adolescents < 15 years, and adults with severe extrapulmonary DR-TB. In addition, individualised regimens containing delamanid may be required by some adults with limited treatment options due to drug resistance, such as bedaquiline-resistance, or toxicity.

In 2025/2026, the development of dedicated tuberculosis chapters for the Primary Healthcare, Adult Hospital, as well as update of the Paediatric Hospital Standard Treatment Guidelines (STGs) was undertaken. The objective was to update treatment recommendations and ensure alignment, as far as possible, with national tuberculosis programme guidance. This process necessitated consideration of the inclusion of delamanid in the EML for the management of drug-resistant tuberculosis. Given the widespread programmatic use of delamanid in South Africa since 2019, it was not considered an efficient use of resources to undertake a full de novo evidence review to support inclusion in the EML. Instead, this limited review was conducted to evaluate current international guideline recommendations and the supporting evidence for the use of delamanid in the treatment of drug-resistant tuberculosis.

Methods

1. Data Sources

The World Health Organization (WHO) consolidated guidelines for the treatment of tuberculosis were identified and recommendations relevant to delamanid were extracted. Additionally, the recently published BEAT TB study (Conradie et.al. 2026) was identified.⁴

Results

Description of included studies

1.1. Clinical Practice Guidelines

- World Health Organization: Consolidated Guidelines on Tuberculosis:
 - WHO 2025. Consolidated Guidelines on Tuberculosis: Module 4: Treatment – Drug-resistant tuberculosis treatment.
 - This guideline was appraised as being of high quality using the AGREE II tool (overall quality of this guideline score of 6)

²A 6-month regimen of bedaquiline, linezolid, pretomanid with or without levofloxacin.

Domain	
Scope and purpose	21 (100%)
Stakeholder involvement	17 (77.8%)
Rigour of development	49 (85.4%)
Clarity of presentation	17 (77.8%)
Applicability	23(79.2%)
Editorial Independence	12 (83.3%)

1.2. RCTs

Conradie et.al. 2026⁴

Study ID	Country	Type of study	Primary outcome	Study Duration	Intervention	Comparison	Age Median (IQR)	Sample Size
Conradie, et.al. 2026	South Africa: Durban Gqeberha	Phase 3, open-label, pragmatic, randomised, controlled non-inferiority trial.	The primary efficacy end point was a successful outcome (cure or completion of treatment) at the end of treatment and 76 weeks after randomisation. The primary safety end point was adverse events of grade 3 or higher.	76 weeks	Bedaquiline, linezolid, delamanid, and levofloxacin OR clofazimine OR both for 6 months.	9-month South African standard-of-care treatment for rifampicin-resistant tuberculosis*	35 (28.0 – 43.0) < 18 years: 30 (7.4%)	Intervention: 203 Control: 200 61% susceptible to fluoroquinolones

*At study start and throughout, the South African standard treatment for RR-TB was a 9-month, all-oral regimen consisting of bedaquiline (used for 6 months), linezolid (used for first 2 months), levofloxacin, ethambutol, high-dose isoniazid (for 4 months, extended to 6 months if the patient remains sputum smear positive at the end of 4 months), pyrazinamide and clofazimine, followed by treatment with levofloxacin/moxifloxacin, clofazimine, ethambutol and pyrazinamide (for 5 months). If fluoroquinolone resistance was diagnosed, then an 18-month regimen of bedaquiline, linezolid, clofazimine, terizidone and delamanid was given.

Effectiveness and/or safety

WHO Consolidated guidelines on Tuberculosis: Module 4: Treatment. Guideline Recommendations:

RECOMMENDATION	ADDITIONAL COMMENTS
Recommendation 1.2. WHO suggests the use of a 6-month treatment regimen composed of bedaquiline, delamanid, linezolid (600 mg), levofloxacin, and clofazimine (BDLLfxC) in MDR/RR-TB patients with or without fluoroquinolone resistance. <i>(Conditional recommendation, very low certainty of evidence)</i>	- Drug susceptibility testing (DST) for fluoroquinolones is strongly encouraged in people with MDR/RR-TB. Although it should not delay the initiation of the BDLLfxC, the test results should guide the decision on whether levofloxacin or clofazimine should be retained. - This recommendation applies to the following: - People with MDR/RR-TB or pre-XDR-TB (i.e. MDR/RR-TB and resistance to fluoroquinolones). - Patients with less than 1 month of previous exposure to bedaquiline, linezolid, delamanid or clofazimine. When exposure is greater than 1 month, these patients may still receive the regimen if resistance to

	the specific medicines involved in such exposure has been ruled out. ○ People with diagnosed pulmonary TB of <u>all ages, including children, adolescents, PLHIV, and pregnant and breastfeeding women.</u> ○ People with all forms of extrapulmonary TB except for TB involving the CNS, osteoarticular TB, or disseminated forms of TB with multiorgan involvement. ○ Children and adolescents who do not have bacteriological confirmation of TB or resistance patterns but who do have a high likelihood of MDR/RR-TB (based on clinical signs and symptoms of TB, in combination with a history of contact with a patient with confirmed MDR/RR-TB). ● When resistance to fluoroquinolones is unknown, the regimen should be started as BDLLfxC and then adjusted based on the DST results. In cases of quinolone susceptibility, clofazimine should be dropped and the regimen started or continued as bedaquiline, delamanid, linezolid and levofloxacin (BDLLfx). In cases of resistance to fluoroquinolones, levofloxacin should be dropped and the regimen started or continued as bedaquiline, delamanid, linezolid and clofazimine (BDLC). The rationale for this recommendation is based on the evidence and considerations described in detail in the following two subsections. Data from an RCT (BEAT Tuberculosis trial: NCT04062201) showed that the efficacy and safety of the BDLLfxC regimen was similar to that of the control arm regimen (WHO-recommended 9-month or longer regimens), and offers advantages based on its shorter duration and lower pill burden than the comparators. It was judged that implementing this regimen was probably feasible and acceptable, with equity probably improved, and that implementing this regimen was probably suitable for most population groups, including pregnant and breastfeeding women, children and PLHIV.
Recommendation 3.1. In MDR or RR-TB patients on longer regimens, all three Group A agents (refer table), and at least one Group B agent should be included to ensure that treatment starts with at least four TB agents likely to be effective, and that at least three agents are included for the rest of treatment if bedaquiline is stopped. If only	Group A: fluoroquinolones (levofloxacin and moxifloxacin), bedaquiline and linezolid were considered highly effective and strongly recommended for inclusion in all regimens unless contraindicated. Group B: clofazimine and cycloserine or terizidone were conditionally recommended as agents of second choice. Group C: included all other medicines that can be used when a regimen cannot be composed with Group A or

one or two Group A agents are used, both Group B agents are to be included. If the regimen cannot be composed with agents from Groups A and B alone, Group C agents are added to complete it. <i>(Conditional recommendation, very low certainty of evidence).</i>	Group B agents. The medicines in Group C are ranked by the relative balance of benefit to harm usually expected of each. Anti-TB medicine grouping <table><tr><th>Groups and steps</th><th>Medicine</th><th>Abbreviation</th></tr><tr><td rowspan="4">Group A: Include all three medicines</td><td>Levofloxacin or moxifloxacin</td><td>Lfx Mfx</td></tr><tr><td>Bedaquiline^{b,c}</td><td>Bdq</td></tr><tr><td>Linezolid^d</td><td>Lzd</td></tr><tr><td></td><td></td></tr><tr><td rowspan="2">Group B: Add one or both medicines</td><td>Clofazimine</td><td>Cfz</td></tr><tr><td>Cycloserine or terizidone</td><td>Cs Trd</td></tr><tr><td rowspan="8">Group C: Add to complete the regimen and when medicines from Groups A and B cannot be used</td><td>Ethambutol</td><td>E</td></tr><tr><td>Delamanid^e</td><td>Dlm</td></tr><tr><td>Pyrazinamide^f</td><td>Z</td></tr><tr><td>Imipenem–cilastatin or meropenem^g</td><td>Ip–Cln Mpm</td></tr><tr><td>Amikacin (or streptomycin)^h</td><td>Am (S)</td></tr><tr><td>Ethionamide or prothionamideⁱ</td><td>Eto Pto</td></tr><tr><td>P-aminosalicylic acid^j</td><td>PAS</td></tr><tr><td></td><td></td></tr></table> Group A: fluoroquinolones (levofloxacin and moxifloxacin), bedaquiline and linezolid were considered highly effective and strongly recommended for inclusion in all regimens unless contraindicated. Group B: clofazimine and cycloserine or terizidone were conditionally recommended as agents of second choice. Group C: included all other medicines that can be used when a regimen cannot be composed with Group A or Group B agents. The medicines in Group C are ranked by the relative balance of benefit to harm usually expected of each.	Groups and steps	Medicine	Abbreviation	Group A: Include all three medicines	Levofloxacin or moxifloxacin	Lfx Mfx	Bedaquiline ^{b,c}	Bdq	Linezolid ^d	Lzd			Group B: Add one or both medicines	Clofazimine	Cfz	Cycloserine or terizidone	Cs Trd	Group C: Add to complete the regimen and when medicines from Groups A and B cannot be used	Ethambutol	E	Delamanid ^e	Dlm	Pyrazinamide ^f	Z	Imipenem–cilastatin or meropenem ^g	Ip–Cln Mpm	Amikacin (or streptomycin) ^h	Am (S)	Ethionamide or prothionamide ⁱ	Eto Pto	P-aminosalicylic acid ^j	PAS		
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Recommendation 3.8. Delamanid may be included in the treatment of MDR/RR-TB patients aged 3 years or more on longer regimens. <i>(Conditional recommendation, moderate certainty of evidence)</i> In children with MDR/RR-TB aged below 3 years delamanid may be used as part of longer regimens. <i>(Conditional recommendation, very low certainty of evidence)</i>	To answer the PICO question on the use of delamanid in children aged below 3 years, data were reviewed by the guideline development group 2021 from a Phase 1, open-label, age de-escalation trial designed to assess the pharmacokinetics, safety and tolerability of delamanid administered twice daily for 10 days in children with MDR/RR-TB on treatment with an optimized background regimen (protocol 242–12–232) and from the corresponding open-label extension study (protocol 242–12–233). Data from cohorts 1 (age 12–17 years), 2 (age 6–11 years), 3 (age 3–5 years) and 4 (age 0–2 years) for both protocols were reviewed. Exposures in the 0–2-year age group were lower than those of children aged 3 years and older, necessitating a modelling or simulation approach to dosing. No cardiac safety signals distinct from those reported in adults were observed in children aged 0–2 years. However, consideration of these																																		

	findings should take into account that children had lower drug exposures than adults. Pharmacodynamic simulations suggested that clinically meaningful changes in QT (i.e. prolongation) would be unlikely in children aged below 3 years, even if higher doses were used to reach drug exposures comparable to those achieved in adults. CNS effects (paraesthesia, tremors, anxiety, depression and insomnia) were included in the delamanid label for both adults and children as important potential safety concerns for the drug. In March 2021, the study sponsor released a statement of intent to modify the labelling to include hallucinations as an adverse reaction. This new safety signal has been more prevalent among children than adults, with 15 reports in 14 children aged 2 – 16 years in India, the Philippines, South Africa, Tajikistan and Ukraine. Children experiencing this safety signal included some with extensively resistant forms of TB (MDR/XDR-TB) treated with delamanid under programmatic conditions (12 reports) and children enrolled in a clinical trial studying delamanid for TB prevention (3 reports). Seven of the 15 reports were for children also receiving cycloserine (under programmatic conditions). The guideline development group noted the importance of side-effects involving the CNS in young children, considering their dynamic brain development. In addition to data from the trials, data from a paediatric DR-TB individual participant data were analysed descriptively (24 231 records from all six WHO regions, the majority from India and South Africa). The search was conducted in April 2020. Just under 20 000 of these records were used for a matched analysis of treatment outcomes in children being treated for DR-TB. The paediatric DR-TB IPD included only seven children aged below 3 years treated with delamanid, 14 children aged 3–6 years and 69 children aged 6–12 years. All 21 children aged below 6 years were successfully treated. The number of children was insufficient for a matched analysis.
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Conradie et.al. 2026

The BEAT Tuberculosis trial³, a phase 3 open-label pragmatic randomised controlled non-inferiority trial in South Africa, assessed a 6-month treatment strategy for pulmonary RR-TB. Eligible participants had pulmonary tuberculosis with resistance to rifampicin with or without resistance to isoniazid or fluoroquinolones (or both). Children ≥ 6 years, and pregnant or breastfeeding women were eligible. Participants were randomly assigned to a regimen consisting of bedaquiline, linezolid, delamanid, and levofloxacin or clofazimine or both for 6 months (the trial strategy); or 9-months of South African standard of care at the time (control strategy). In the trial-strategy group, when the results of fluoroquinolone susceptibility testing were available either levofloxacin (if the results showed fluoroquinolone resistance) or clofazimine (if the results showed fluoroquinolone susceptibility) was discontinued. If the susceptibility results were available at the time of randomization, either levofloxacin or clofazimine was not initiated. At study start and throughout, the South African standard treatment for RR-TB was a 9-month, all-oral regimen consisting of bedaquiline (used for 6 months), linezolid (used for first 2 months), levofloxacin, ethambutol, high-dose isoniazid (for 4 months, extended to 6 months if the patient remains sputum smear positive at the end of 4 months), pyrazinamide and clofazimine, followed by treatment with levofloxacin/moxifloxacin, clofazimine, ethambutol and pyrazinamide (for 5 months). If fluoroquinolone resistance was diagnosed in the control strategy arm, then an 18-month regimen of bedaquiline, linezolid, clofazimine, terizidone and delamanid was given. The primary efficacy outcome was successful treatment outcome (cure or completion of treatment) at the end of treatment and at 76 weeks after randomisation. Cure was defined as adequate treatment adherence ($\geq 80\%$ of doses taken) and two negative sputum specimens obtained before the end of treatment, at least 14 days apart. Completion of treatment was defined as adequate adherence without evidence of treatment failure (defined as lack of sputum culture conversion, bacteriologic reversion, or substitution of two or more drugs because of adverse effects) but no record of two or more consecutive negative sputum specimens obtained at least 14 days apart. The primary safety endpoint was an adverse event of grade 3 or higher. The composite efficacy-safety end point was a successful outcome at end of follow-up and no adverse events of grade 3 or higher during treatment. The primary efficacy analysis was performed in the intention-to-treat population. For the primary analysis, the between group difference (risk difference) in the percentage of participants who met criteria for the primary end point (a successful outcome) at the end of treatment and at 76 weeks after randomisation was compared. Non-inferiority was determined if the upper boundary of the 95% confidence interval for the risk difference was less than 10 percentage points. A total sample size of 400 patients would provide 87.3% power to show non-inferiority assuming a proportion cure of 0.60 in the control strategy and 0.65 in the study strategy (an absolute increase of 0.05) or 89.4% assuming a proportion cure of 0.65 in the control strategy and 0.7 in the study strategy. Between August 2019 and October 2022, 403 participants were randomised. The median age was 35 years, and 30 participants (7.4%) were 8 to 17 years of age. A total of 205 participants (50.9%) were PLHIV, with a median CD4 count of 194 cells/mm³.

Outcome – Successful outcome (Cure or completion of treatment):

Successful outcome at the end of treatment and at 76 weeks: 86.1% (174 of 202) in trial-strategy group, and 86% (172 of 200) in control group; adjusted risk difference: -0.2 percent points 95% CI -6.9 to 6.5; $p=0.001$ for non-inferiority.

Treatment effects did not appear to vary by age, sex, HIV status, status of sputum smear at baseline (positive vs. negative), presence of cavities on chest radiography, or fluoroquinolone resistance although the trial was not powered to rule out differences across subgroups. All participants younger than 18 years of age had a successful

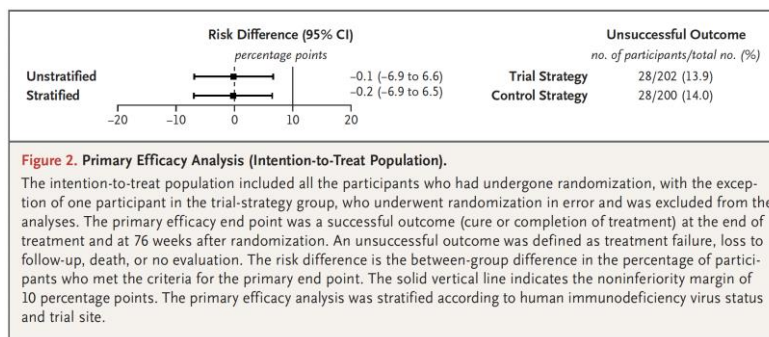
³ Conradie F, Badat T, Poswa A, Rajaram S, Kooverjee S, et.al. A Pragmatic Trial of a 6-month strategy for rifampicin-resistant tuberculosis. NEJM. 2026; 394: 2429-2439.

outcome at the end of treatment and the end of follow-up. One pregnant participant in the trial-strategy group had a recurrence of tuberculosis disease.

Table 2. Primary Efficacy Analysis (Intention-to-Treat Population).*

Variable	Trial Strategy (N = 202)	Control Strategy (N = 200)	Total (N = 402)
	<i>number (percent)</i>		
Primary end point: successful outcome at end of treatment and at end of follow-up	174 (86.1)	172 (86.0)	346 (86.1)
Cure at end of treatment and at end of follow-up	160 (79.2)	162 (81.0)	322 (80.1)
Cure at end of treatment and negative culture at last visit	14 (6.9)	10 (5.0)	24 (6.0)
Unsuccessful outcome at end of treatment	14 (6.9)	22 (11.0)	36 (9.0)
Treatment failure	7 (3.5)	10 (5.0)	17 (4.2)
Lost to follow-up during treatment	2 (1.0)	4 (2.0)	6 (1.5)
Died during treatment	4 (2.0)	7 (3.5)	11 (2.7)
Not evaluated because of withdrawn consent	1 (0.5)	1 (0.5)	2 (0.5)
Unsuccessful outcome at end of follow-up	14 (6.9)	6 (3.0)	20 (5.0)
Recurrence after cure at end of treatment	10 (5.0)	4 (2.0)	14 (3.5)
Died after cure at end of treatment	4 (2.0)	2 (1.0)	6 (1.5)

* The intention-to-treat population included all the participants who had undergone randomization, with the exception of one participant in the trial-strategy group, who underwent randomization in error and was excluded from the analyses. Participants were followed for 76 weeks after randomization. A successful outcome was defined as cure or completion of treatment. An unsuccessful outcome was defined as treatment failure (lack of sputum culture conversion, bacteriologic reversion, or substitution of two or more drugs because of adverse effects), loss to follow-up, death, or no evaluation.



Outcome – Adverse events:

Adverse events (grade 3 or higher) that occurred during treatment: 31.2% (63 of 202) in trial-strategy group and 37% (74 of 200) in control group. Among the pregnant participants, two serious adverse events occurred which were not related to treatment. Delamanid was discontinued in one child because of neuropsychiatric adverse reactions.

Table 3. Safety (Safety Population).^a

Adverse Event	Trial Strategy (N = 202)	Control Strategy (N = 200)	Total (N = 402)	Risk Difference (95% CI) [†]
Grade ≥3 event	69 (34.2)	76 (38.0)	145 (36.1)	3.8 (-5.5 to 13.2)
Grade ≥3 event during treatment	63 (31.2)	74 (37.0)	137 (34.1)	5.8 (-3.4 to 15.1)
Treatment-related grade ≥3 event [‡]	52 (25.7)	56 (28.0)	108 (26.9)	2.3 (-6.4 to 10.9)
Serious adverse event at any time	45 (22.3)	44 (22.0)	89 (22.1)	-0.3 (-8.4 to 7.8)
Serious adverse event during treatment	38 (18.8)	42 (21.0)	80 (19.9)	2.2 (-5.6 to 10.0)
Notable event [§]	36 (17.8)	31 (15.5)	67 (16.7)	-2.3 (-9.6 to 5.0)
Death at any time	10 (5.0)	10 (5.0)	20 (5.0)	0.0 (-4.2 to 4.3)
Death during treatment	6 (3.0)	8 (4.0)	14 (3.5)	1.0 (-2.6 to 4.6)
Death after treatment	4 (2.0)	2 (1.0)	6 (1.5)	-1.0 (-3.3 to 1.4)
Anemia leading to treatment discontinuation	10 (5.0)	8 (4.0)	18 (4.5)	-1.0 (-5.0 to 3.1)
Anemia leading to blood transfusion	20 (9.9)	11 (5.5)	31 (7.7)	-4.4 (-9.6 to 0.8)
Grade ≥3 liver abnormality	4 (2.0)	9 (4.5)	13 (3.2)	2.5 (-0.9 to 6.0)
Peripheral neuropathy leading to treatment discontinuation	10 (5.0)	7 (3.5)	17 (4.2)	-1.5 (-5.4 to 2.5)
Optic neuropathy leading to treatment discontinuation	7 (3.5)	2 (1.0)	9 (2.2)	-2.5 (-5.3 to 0.4)
QTcF ≥480 msec	12 (5.9)	19 (9.5)	31 (7.7)	3.6 (-1.7 to 8.8)
QTcF ≥500 msec	5 (2.5)	7 (3.5)	12 (3.0)	1.0 (-2.3 to 4.4)
Treatment-related serious adverse events [‡]				
Related to linezolid	20 (9.9)	16 (8.0)	36 (9.0)	-1.9 (-7.5 to 3.7)
Related to bedaquiline	4 (2.0)	7 (3.5)	11 (2.7)	1.5 (-1.7 to 4.7)
Related to levofloxacin	3 (1.5)	4 (2.0)	7 (1.7)	0.5 (-2.0 to 3.1)
Related to clofazimine	6 (3.0)	7 (3.5)	13 (3.2)	0.5 (-2.9 to 4.0)
Related to delamanid	2 (1.0)	2 (1.0)	4 (1.0)	0.0 (-1.9 to 2.0)

^a The safety population included all the participants who had undergone randomization and received at least one dose of the assigned treatment. QTcF denotes corrected QT interval calculated with the use of Fridericia's formula.

[†] The risk difference is the difference in percentage points.

[‡] Included are events that were at least possibly related to treatment.

[§] Notable events included grade 3 or 4 cardiotoxic effects, increase in aspartate aminotransferase or alanine aminotransferase level, pregnancy, and peripheral neuropathy.

Outcomes – pregnancy outcomes

Of the 170 female participants (42.2%), 9 (5.3%) were pregnant at baseline: one was in the first trimester, six were in the second trimester, and two were in the third trimester. One participant became pregnant during the trial. All pregnancies resulted in singleton live births, with one premature delivery.

Costs

Delamanid is currently procured as a non-EML medicine for use in the public sector.

Product	Brand As Per Contract	Supplier Name	Price*
Delamanid; 50mg; Tablet; 48 Tablets	DELTIBA	Viatrix Healthcare (Pty) Ltd	R1498.4

MHPL (Jul 2026)

As delamanid is already being used for select MDR/RR-TB regimens in the public sector in accordance with the National RR-TB guideline, we do not anticipate any incremental budget impact through its listing on the EML.

Discussion and Conclusion

Current South African National TB programme guidelines for the management of RR-TB recommend delamanid, in combination with other appropriate anti-TB medicines, as part of individualised or rescue regimens for children, adolescents, adults, and pregnant or breastfeeding women with MDR/RR-TB not eligible for BPAL-L, or when drug resistance or toxicity, necessitate an individualised approach.

The WHO classifies delamanid as a Group C medicine and recommend using it to construct effective longer individualised MDR/RR-TB regimens when Group A and Group B medicines are insufficient due to resistance or toxicity. Although the WHO recommendations are conditional and based on very low to moderate certainty

evidence, they reflect the limited treatment options available for drug-resistant TB and the need to maximise the number of likely effective medicines in an individualised regimen.

The recently published BEAT-Tuberculosis trial provides additional evidence supporting the inclusion of delamanid in a shorter, all-oral regimen for RR-TB. Importantly, the trial enrolled patient groups who are not eligible for the current South African standard-of-care BPAL-L regimen, including pregnant and breastfeeding women and children under 15 years of age, thereby providing evidence for a shorter treatment option of comparable duration to BPAL-L for these vulnerable populations.

Inclusion of delamanid on the Essential Medicines List aligns with current evidence-based WHO recommendations and will ensure availability of an important treatment option for patients requiring individualised management of drug-resistant tuberculosis.

References

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