LIFT-TB Philippines
Leveraging Innovation for Faster Treatment of Tuberculosis
Introducing the BPaL Regimen under Operational Research

In collaboration with the National Tuberculosis Control Program (NTP) – Department of Health (DOH)

Tropical Disease Foundation, Inc.

ADVERSE EVENTS OF SPECIAL INTEREST IN THE BPAL OPERATIONAL RESEARCH
(SEVERITY GRADING SCALES)

1. Peripheral Neuropathy
Clinical management of peripheral neuropathy according to severity grading

Grade Severity	Grade 1 Mild	Grade 2 Moderate	Grade 3 Severe	Grade 4 Life-threatening
Neurosensory alteration	Mild discomfort: no treatment required; and/or BPNS subjective sensory neuropathy score 1-3 on any side	Moderate discomfort: non-narcotic analgesia required; and / or BPNS subjective sensory neuropathy score 4-6 on any side	Severe discomfort: or narcotic analgesia required with symptomatic improvement; and / or BPNS subjective sensory neuropathy score 7-10 on any side	Incapacitating; or not responsive to narcotic analgesia
Action	Stop or reduce dose of Lzd. If symptoms improve, consider restarting Lzd at a lower dose 600 mg or 300 mg.	Stop Lzd, provide symptomatic care. If symptoms improve, consider restarting Lzd at 600 mg or 300 mg. Stop Lzd permanently if symptoms reappear	Stop Linezolid; do not restart. Provide symptomatic relief.	

*BPNS - Brief Peripheral Neuropathy Screen

2. Myelosuppression
Clinical management of myelosuppression according to severity grading

Severity Grade	Grade 1 Mild	Grade 2 Moderate	Grade 3 Severe	Grade 4 Life-threatening
Anaemia	10.5 - 9.5 g/dL	9.4 – 8.0 g/dL	7.9 – 6.5 g/dL	< 6.5 g/dL
Platelets decreased	99,999-75,000/mm^3	74,999-50,000/mm^3	49,999-20,000/mm^3	< 20,000/mm^3
While blood cells decreased	<LLN - 3,000/mm^3	<3,000 - 2,000/mm^3	<2,000 - 1,000/mm^3	< 1,000 /mm^3
Absolute neutrophil count low	1500 - 1000/mm^3	999 - 750/mm^3	749 - 500/mm^3	<500/mm^3
Action	Monitor carefully, do weekly FBC and consider reduction of Lzd dose to 600 mg or 300 mg daily	Monitor carefully, do weekly FBC and consider reduction of Lzd dose to 600 mg or 300 mg daily. In case of Grade 2 neutro-penia, stop Lzd. Restart at lower dose once toxicity has reduced to Grade 1	Stop Lzd immediately. In case of Grade 3 anemia, consider EPO if available. Restart at reduced dose once toxicity has decreased to Grade 1 or consider stopping Lzd permanently	Stop Lzd immediately. Hospitalize patient and consider blood transfusion or EPO. Restart at reduced dose once toxicity has decreased to Grade 1 or consider stopping Lzd permanently

*LLN- lower limit of normal FBC – Full Blood Count EPO - Erythropoietin

ADVERSE EVENTS OF SPECIAL INTEREST IN THE BPAL OPERATIONAL RESEARCH
(SEVERITY GRADING SCALES)

3. Optic Neuritis
Clinical management of optic nerve disorder according to severity grading

Grade Severity	Grade 1 Mild	Grade 2 Moderate	Grade 3 Severe	Grade 4 Life-threatening
Optic nerve disorder	Asymptomatic or mild symptoms; clinical or diagnostic observations only or unable to read 4 or more plates in color vision test	Symptomatic; moderate decrease in visual acuity (20/40 [6/12] or better) or drop of 2 lines on VA (Snellen) chart or unable to read 4 or more plates in color vision test	Limiting vision in the affected eye; visual acuity worse than 20/40 [6/12] but better than 20/200 [6/60]) or drop of more than 2 lines (Snellen chart) or unable to read 4 or more plate (color vision test)	Blindness (20/200 [6/60] or worse) in the affected eye
Action	Stop Lzd immediately if there are any suspicions of optic neuritis and refer to an ophthalmologist	Stop Lzd immediately if there are any suspicions of optic neuritis and refer to an ophthalmologist. Do not restart unless there is an alternative diagnosis	Stop Linezolid immediately if there are any suspicions of optic neuritis and refer to an ophthalmologist. Do not restart if diagnosis is confirmed.	

*VA – Visual Acuity **Feet ***Meters

4. QT Prolongation
Clinical management of prolonged QT interval according to severity grading

Severity Grade	Grade 1 Mild	Grade 2 Moderate	Grade 3 Severe	Grade 4 Life-threatening
Normal values: Male (M): <450 ms Female (F): <470 ms	QTcF 450 – 480 ms	QTcF 481 – 500 ms	QTcF> 500 ms on at least two separate ECGs ≥30 min apart, without signs and symptoms of serious arrhythmia	QTcF >= 501 or >60 ms change from baseline and one of the following: (Torsade de pointes or polymorphic ventricular tachycardia or signs/symptoms of serious arrhythmia)
Action	• Monitor ECG more closely (at least weekly) until QTcF has returned to less than grade 1. • Check electrolytes and replete as necessary, • Check for other potential causes and manage accordingly,		• Hospitalize, check, and replace electrolytes as necessary. • Stop the BPaL regimen and other suspected causative drugs, including non-TB drugs. • Check for other potential causes and manage accordingly • Repeat ECG after ≥24 hours but < 48 hours, until QTcF < 500 ms.	

*QTcF –QT Interval corrected by the Fridericia formula ECG - Electrocardiogram

ADVERSE EVENTS OF SPECIAL INTEREST IN THE BPAL OPERATIONAL RESEARCH
(SEVERITY GRADING SCALES)

5. Hepatoxicity

Clinical management of elevated liver enzymes according to severity grading

Grade Severity	Grade 1 Mild	Grade 2 Moderate	Grade 3 Severe	Grade 4 Life-threatening
ALT /AST	>ULN – 3.0 x ULN	>3.0 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN
Bilirubin	>ULN - 1.5 x ULN	>1.5 - 3.0 x ULN	>3.0 - 10.0 x ULN	>10.0 x ULN
Action	Continue treatment regimen. Patients should be followed until resolution (return to baseline) or stabilization of AST/ALT elevation.		Stop full BPaL regimen, including other non-TB drugs; measure LFTs weekly. Treatment may be reintroduced after toxicity is resolved, (liver enzymes returned to Grade 1).	

* ULN – upper limit of normal LFT – Liver Function Test