Pocket Guide

TB (DS & DR) and Latent TB Screening, Diagnosis and Management

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The primary users of this pocket guide are health service providers (physicians, nurses, medical technologists, midwives, and community volunteers) who are providing TB and MDR TB care services.

Contents of the pocket guide were adapted from the prefinal text of NTP MOP, 6th edition.

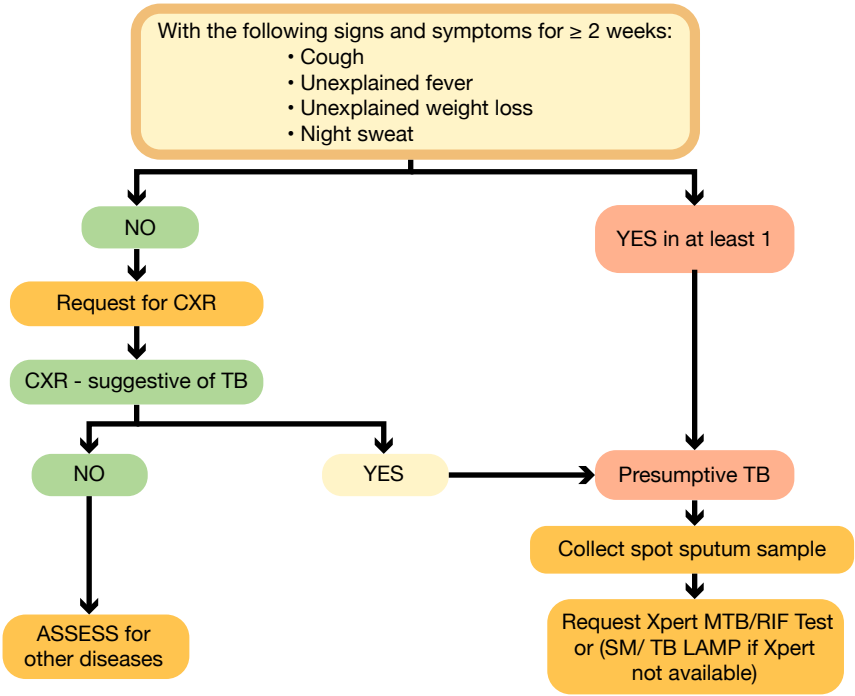
CONTENTS

ABBREVIATIONS, ACRONYMS and SYMBOLS

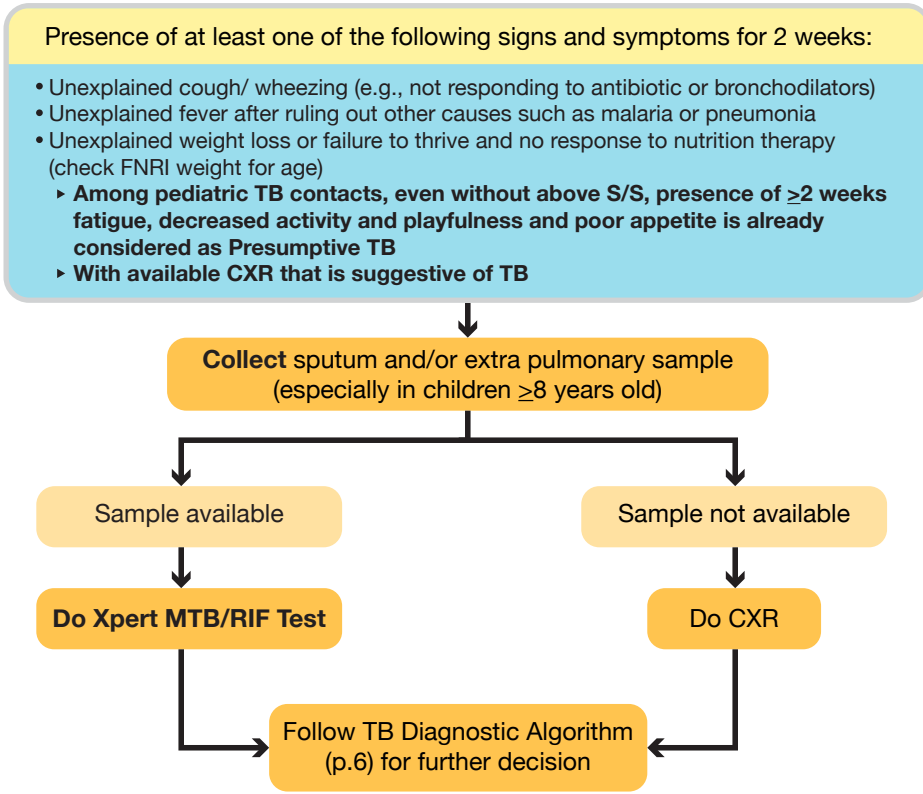
ADR	Adverse Drug Reaction
AE	Adverse Event
AIDS	Acquired Immune Deficiency Syndrome
ALT	Alanine aminotransferase
Am	Amikacin
Amx/Clv	Amoxicillin/Clavulanate
ART	Antiretroviral treatment/therapy
ARV	Antiretroviral
AST	Aspartate aminotransferase
Bdq	Bedaquiline
BID	Twice daily
CBC	Complete Blood Count
Cfz	Clofazimine
Cm	Capreomycin
CP	Continuation Phase
CrCl	Creatinine Clearance
Cs	Cycloserine
CSF	Cerebrospinal Fluid
CXR	Chest X-ray
Dlm	Delamanid
DOT	Directly Observed Treatment
DR-TB	Drug-Resistant Tuberculosis
DST	Drug Susceptibility Testing
DS-TB	Drug-Susceptible Tuberculosis
E	Ethambutol
ECG	Electrocardiogram
EP	Extrapulmonary
FL-LPA	First Line LPA
FQ	Fluoroquinolones
GI	Gastrointestinal
Gx	GeneXpert
H	Isoniazid
Hct	Hematocrit
HdH	High dose Isoniazid
Hgb	Hemoglobin
HIV	Human Immunodeficiency Virus
Imp	Imipenem
IM	Intramuscular
IP	Intensive Phase
IPC	Infection Prevention and Control
IV	Intravenous
Km	Kanamycin
Lfx	Levofloxacin
LLN	Lower Limit of Normal
LPA	Line Probe Assay
LTBI	Latent TB Infection
Lzd	Linezolid
MDR-TB	Multidrug Resistant TB
Mfx	Moxifloxacin
MGIT	Mycobacterial growth indicator tube
Mpm	Meropenem
NTRL	National TB Reference Laboratory
OD	Once a day
PAS	Para-aminosalisylic Acid
p.o.	by mouth
PRN	as needed
PTB	Pulmonary Tuberculosis
Pto	Prothionamide
Q	Every
R	Rifampicin
S	Streptomycin
S/S	Signs and Symptoms
SLI	Secondline Injectables
SLD	Second line drug
SL-LPA	Second Line-Line Probe Assay
SM	Smear Microscopy
SSTR	Standard Short Treatment Regimen
TB	Tuberculosis
TB-LAMP	Loop-mediated isothermal amplification
TBC	TB Culture
TB MAC	TB Medical Advisory Commitee
TID	Three times a day
TNF	Tumor Necrosis Factor
TSH	Thyroid Stimulating Hormone
ULN	Upper Limits of Normal
WBC	White blood cells
WHO	World Health Organization
Z	Pyrazinamide

Screening and Diagnosis of TB Disease

A. Systematic Screening for Active Pulmonary TB in Adults ≥15 years old with Unknown HIV Infection Status in Health Facilities

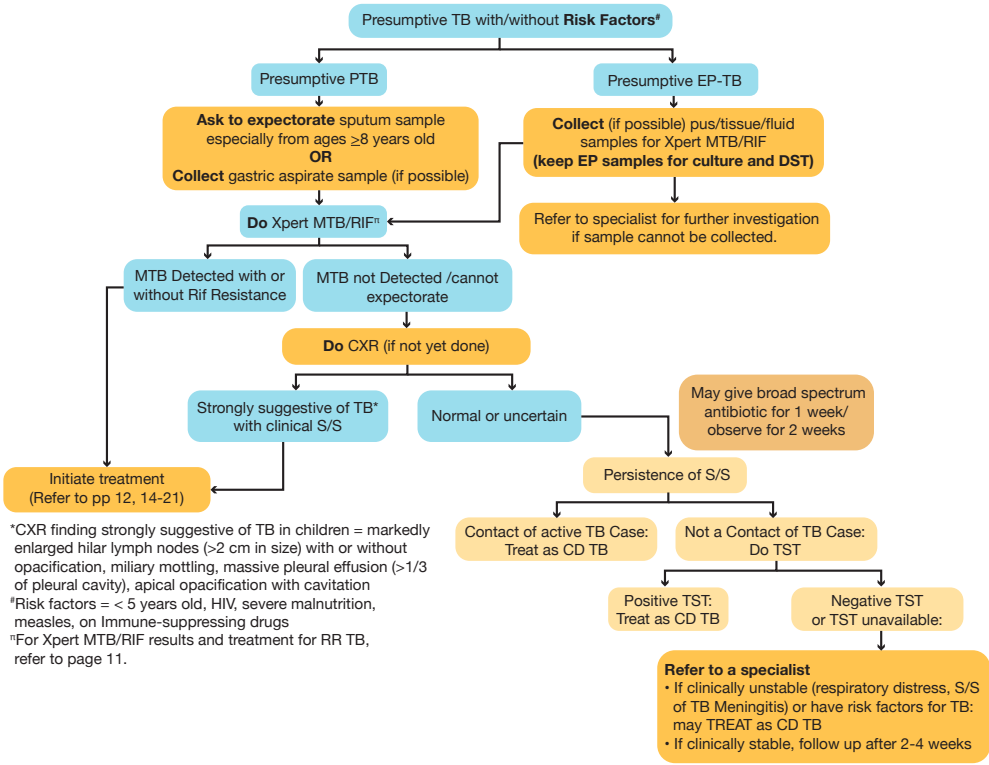


B. Screening for Active Pulmonary TB among Children <15 years old



FNRI - Food and Nutrition Research Institute

C. TB Diagnostic Algorithm for Children <15 Years Old

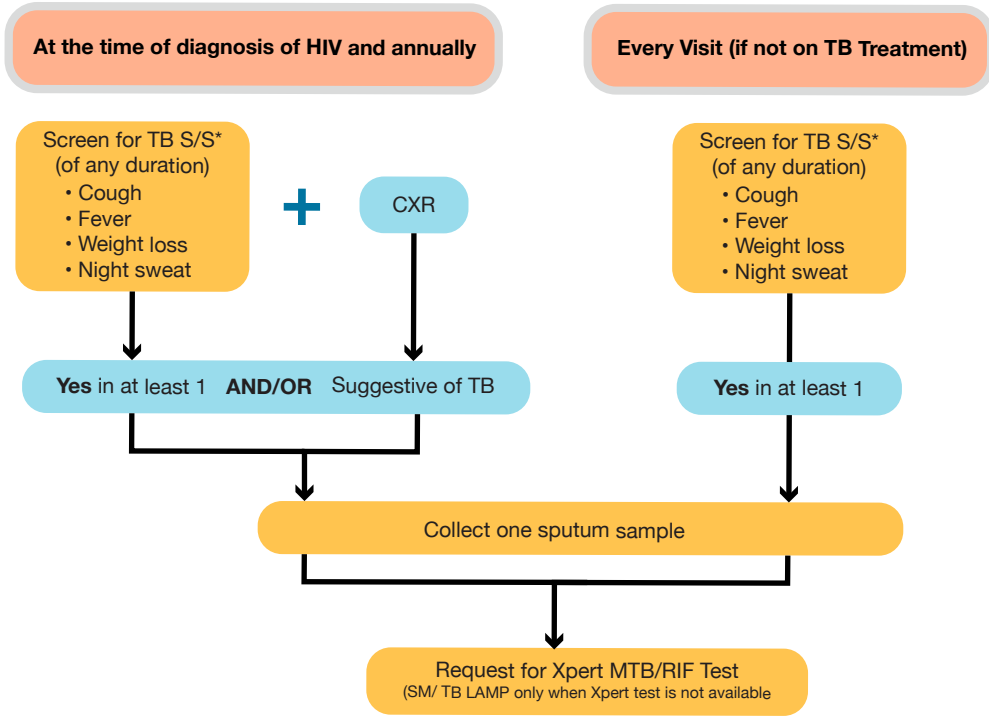


*CXR finding strongly suggestive of TB in children = markedly enlarged hilar lymph nodes (>2 cm in size) with or without opacification, miliary mottling, massive pleural effusion (>1/3 of pleural cavity), apical opacification with cavitation

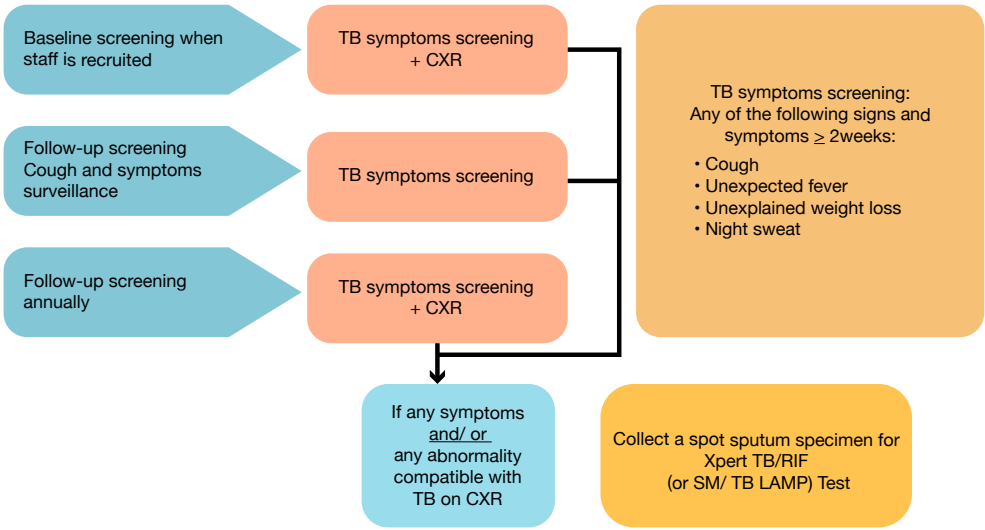
#Risk factors = < 5 years old, HIV, severe malnutrition, measles, on Immune-suppressing drugs

πFor Xpert MTB/RIF results and treatment for RR TB, refer to page 11.

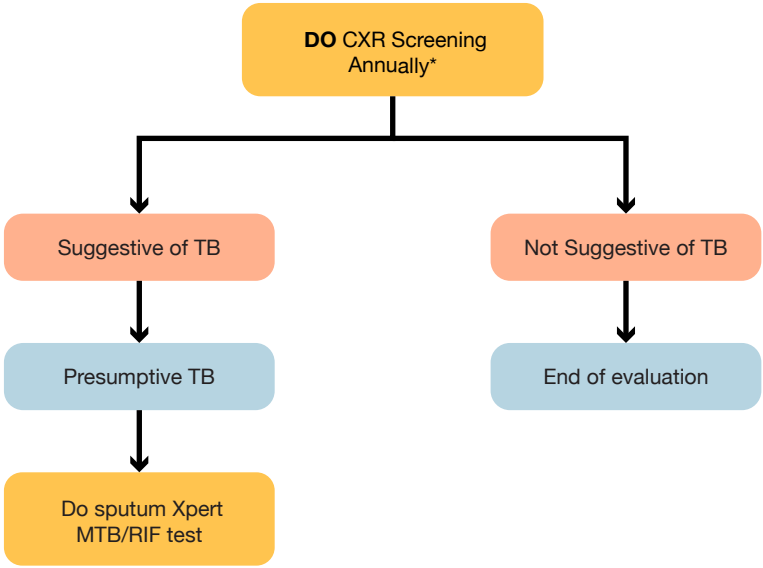
D. Systematic Screening for the Diagnosis of Active Pulmonary TB Disease among PLHIV



E. Screening Among Healthcare Workers



F. Screening of Active Pulmonary TB in Targeted Community/ Workplace and Congregate Setting



*if a person has ≥ 2 weeks cough. immediately collect sputum for Xpert MTB/RIF Testing (No need to do CXR)

Sundan ang mga sumusunod na hakbang sa pagkuha ng maayos na sampol ng plema para sa eksaminasyon para sa TB

1. 
Pumunta sa pinakamalapit na sputum collection area.

2. 
Magmumog ng tubig at siguraduhin na walang tirang pagkain o iba pang laman ang bibig.

3. 
Huminga nang malalim ng tatlong (3) beses at siguraduhing malakas ang pagbuga ng hangin palabas sa baga

4. 
Idahak ang plema mula sa iyong baga

5. 
Buksan ang takip ng boteng lagayan ng plema, ilapit sa iyong mga labi at maingat na idura ang iyong plema sa loob ng lalagyan.

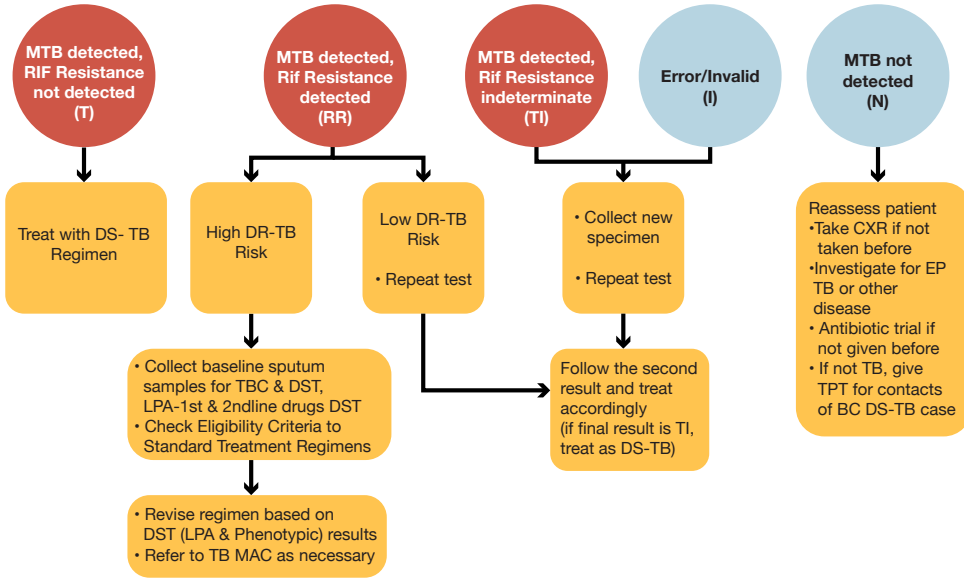
6. 
Siguraduhing may isang (1) kutsarita ang nakolekta mong plema. Isarang mabuti ang lalagyan.

7. 
Dalhin ang sampol ng iyong plema sa tagapangasiwa ng iyong kalusugan.

8. 
Siguraduhing maghugas ng iyong mga kamay.

TB DIAGNOSTIC TEST INTERPRETATION

Interpretation of Xpert MTB/RIF Results and Treatment Decisions



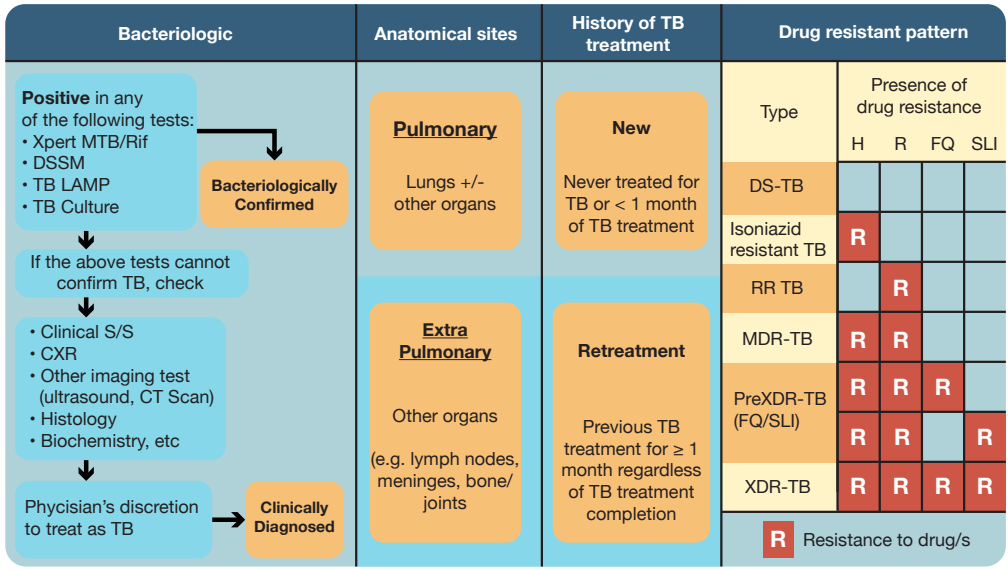
TBC & DST = TB culture and phenotypic DST

Interpretation of LPA Result and Treatment Decision

	Mutation*	Meaning and resistance caused	Treatment regimen
First-line LPA result	InhA	Low level H resistance and confers resistance to Pto	Treat with the regimen for H-resistant TB
	KatG	High level H resistance and confer resistance to high dose H	
	RpoB	Rifampicin resistance with and without H resistance	Treat with MDR-TB regimen
Second-line LPA result (all RR-TB cases)	GyrA, GyrB	FQ resistance (Ofx, Lfx, Mfx)	Treatment with FQ Resistant MDR-TB Regimen If GyrA and D94A mutation is absent, high dose Mfx may still be effective
	rrs	High level injectable (Am, Km, Cm) resistance	Treat with MDR-TB regimen If *eis* mutation is present, Am may still be effective
	eis	low level resistance to Km, susceptibility or low level to Am & Cm	

• This is not provided in the official result but can be requested by TB MAC members from the LPA Laboratory to assist physicians in designing individualized regimens for DR-TB.

TB Case Classification/Definition



TB Treatment and Management

Treatment Regimen	Eligible TB Patients
Regimen 1 2HRZE/4HR	• PTB or EPTB (except CNS, bones, joints) whether new or retreatment, with final Xpert result: – MTB, Rif sensitive – MTB, Rif indeterminate • New PTB or New EPTB (except CNS, bones, joints), with positive DSSM/TB LAMP or clinically diagnosed, and: – Xpert not done – Xpert result is MTB not detected
Regimen 2 2HRZE/10HR	• EPTB of CNS, bones, joints whether new or retreatment, with final Xpert result: – MTB, Rif sensitive – MTB, Rif indeterminate • New EPTB of CNS, bones, joints, with positive DSSM/TB LAMP or clinically diagnosed, and: – Xpert not done – Xpert result is MTB not detected

Schedule of Sputum follow-up examinations (DSSM)* for Pulmonary TB on DS-TB Regimen

Type of PTB	Ff-up 1	Ff-up 2	Ff-up 3
New, CDTB	End of Intensive Phase** (2nd month)	ONLY IF positive at end of Intensive Phase	
		End of 5th month	End of Treatment (6th month)
New, BCTB Retreatment	End of Intensive Phase (2nd month)	End of 5th month	End of Treatment (6th month)

*Xpert MTB/Rif test is not used for follow-up examination to monitor treatment because current-generation PCR-based tests are unable to determine Mycobacterium tuberculosis viability and may test positive even with nonviable or dead bacilli
**for New CDTB, only one (1) follow-up examination is needed if result of this follow-up is negative.

Once the NTP laboratory network has capacity for rapid molecular tests for first line drug-susceptibility (e.g., LPA), a request for FL-LPA should be done for non-converters of DSTB regimens (Regimen 1 and 2) who are still Rifampicin susceptible on Xpert MTB/RIF.

Dosing for Drug Sensitive TB Treatment for Adults and Children

Table 1. Standard Regimens for DS-TB: Dosing for Adults

Weight Band (Kg)	Intensive Phase (2 months HRZE)	Continuation Phase (for NEW) (4 months HR)
	Number of Tablets per day	
25-37	2	2
38-54	3	3
55-70	4	4
>70	5	5

Table 2. Standard Regimens for DS-TB: Dosing for Children using FDC*

Weight band (Kg)	Number of tablets	
	Intensive phase: RHZ 75/50/150*	Continuation phase: RH 75/50
4-7	1	1
8-11	2	2
12-15	3	3
16-24	4	4
25+	Adult dosages recommended	

*compute for Ethambutol based on Table 3, in page 16

Table 3. Standard Regimen for DS-TB:
Dosing for Children using Single Dose Formulations

Body Weight (kgs.)	Isoniazid (200mg/5ml)	Rifampicin (200mg/5ml	Pyrazinamide (250mg/5ml)	Ethambutol (100 or 400 mg/tab)
	10mg/kg	15mg/kg	30mg/kg	20mg/kg
	ml	ml	ml	tablet
3	0.75	1.00	1.75	50mg
4	1.00	1.50	2.50	100mg
5	1.25	2.00	3.00	
6	1.50	2.25	3.50	
7	1.75	2.50	4.25	
8	2.00	3.00	4.75	200mg
9	2.25	3.50	5.50	
10	2.50	3.75	6.00	
11	2.75	4.00	6.50	
12	3.00	4.50	7.25	
13	3.25	5.00	7.75	300mg
14	3.50	5.25	8.50	
15	3.75	5.50	9.00	
16	4.00	6.00	9.50	
17	4.25	6.50	10.25	
18	4.50	6.75	10.75	
19	4.75	7.00	11.50	400mg
20	5.00	7.50	12.00	
21	5.25	8.00	12.50	
22	5.50	8.25	13.25	
23	5.75	8.50	13.75	
24	6.00	9.00	14.50	

Second Line Anti-TB Drugs Grouping

Drug Group	Drugs
Group A: **Include all three medicines (unless they cannot be used)**	Levofloxacin (Lfx) or Moxifloxacin (Mfx) Bedaquiline (BDQ) Linezolid (Lzd)
Group B: **Add one or both medicines (unless cannot be used)**	Clofazimine (Cfz) Cycloserine (Cs)
Group C: **Add to complete the regimen when medicines from Groups A and B cannot be used**	Ethambutol (E) Delamanid (Dlm) Pyrazinamide (Z) Imipenem-Cilastatin (Imp/Cln) or Meropenem (Mpm) Amikacin (Am) or Streptomycin (S) Prothionamide (Pto) P-aminosalicylic acid (PAS)

Type of MDR/RR-TB treatment regimens

Regimen Name	Type of DRTB	Regimen	Remarks
Regimen 3: Standard Short all Oral Regimen (SSOR)	MDR/RR-TB eligible to SLOR	4-6 months: Lfx-Bdq(6)-Cfz-Pto-E-Z-HdH 5 months: Lfx-Cfz-Z-E	Bdq is given for 6 months
Regimen 4: Standard Long all Oral Regimen for FQ Susceptible (SLOR FQ-S)	MDR/RR-TB eligible to SLOR (no FQ resistance)	6 Months: Lfx-Bdq-Lzd-Cfz 12-14 months Lfx-Lzd-Cfz	Request for "Off Label" use from TB MAC for extended use of Bdq (beyond 6 months)
Regimen 5: Standard Long all Oral Regimen for FQ Resistance (SLOR FQ-R)	MDR/RR-TB eligible to SLOR (with FQ resistance)	6 Months: Lzd-Bdq-Dlm-Cfz-Cs 12-14 months: Lzd-Cfz-Cs	Request for "Off Label" and extended use of Bdq and/ or Dlm from TB MAC
Individual Treatment Regimen (ITR)	Retreatment MDR/RRTB cases (not eligible to SSOR nor SLOR)	Design a regimen with at least 4-5 likely effective drugs	Present the case to TB MAC and follow the recommended regimen

Note: *For SSOR and SLOR FQ-S shifted to SLOR FQ-R due to confirmed resistance to FQ, check presence of resistance to SLI. If without SLI resistance, use the same registration number. If with SLI resistance (confirmed XDR-TB), outcome is "Excluded", Classify patient as BC XDR-TB and assign a new registration number.*

Eligibility Criteria for Different MDR/RR-TB Regimens for ADULT, NON-PREGNANT, and NOT a CONTACT of PATIENT who FAILED on MDR-TB TREATMENT

1 Check exclusion criteria for Standard Short All Oral Regimen (SSOR), (if YES to any of the following, DO NOT GIVE SSOR)

1. Disseminated/ extensive TB or severe/intractable extrapulmonary (EP) TB (e.g., TB Meningitis, Bone/Joint TB)
2. Confirmed resistance to fluoroquinolone (Moxifloxacin/Levofloxacin)
3. Exposure to Moxifloxacin/Levofloxacin, Bedaquiline, Clofazimine, Prothionamide for >1 month
4. Risk of toxicity or intolerance to any drugs in SSOR as manifested by:
    - History of heart disease (heart failure, myocardial infarction, cardiac conduction abnormality, arrythmia)
    - QTcF >500 ms
    - History of chronic active hepatitis (AST/ALT >5 times elevated)
    - History of chronic renal insufficiency (Creatinine Clearance <20 ml/min)

If eligible, give SSOR. if not, check eligibility to SLOR FQ-S.

2 Check eligiblity criteria for Standard Long All Oral Regimen (SLOR) for fluoroquinolone susceptible (FQ-S), (if YES to any of the following, DO NOT GIVE SLOR FQ-S)

1. Confirmed resistance to fluoroquinolone (Moxifloxacin/Levofloxacin)
2. Exposure to Moxifloxacin/Levofloxacin, Bedaquiline, Clofazimine, Linezolid for >1 month
3. Risk of toxicity or intolerance to any drugs in SLOR as manifested by:
    - History of heart disease (heart failure, myocardial infarction, cardiac conduction abnormality, arrythmia)
    - QTcF >500 ms
    - History of chronic active hepatitis (AST/ALT >5 times elevated)
    - History of chronic renal insufficiency (Creatinine Clearance <20 ml/min)
    - Severe anemia (Hgb <8 g/dL)

If eligible, give SLOR FQ-S. If not, check eligibility to SLOR FQ-R.

3 Check eligiblity criteria for Standard Long All Oral Regimen (SLOR) for fluoroquinolone Resistant (FQ-R), (if YES to any of the following, DO NOT GIVE SLOR FQ-R)

1. Exposure to Bedaquiline, Clofazimine, Linezolid, Cycloserine, and Delamanid for >1 month
2. Risk of toxicity or intolerance to any drugs in SLOR as manifested by:
    - History of heart disease (heart failure, myocardial infarction, cardiac conduction abnormality, arrythmia)
    - QTcF >500 ms
    - History of chronic active hepatitis (AST/ALT >5 times elevated)
    - History of chronic renal insufficiency (Creatinine Clearance <20 ml/min)
    - Severe anemia (Hgb <8 g/dL)

If eligible, give SLOR FQ-R. If not, consult R-TB MAC for ITR.

Decision Guide on Appropriate Treatment Regimen Based on LPA Results

Initial Regimen	Baseline LPA Result			Clinical and Programmatic Action
	FQ Resistance Detected	High Dose H (HdH) Resistance Detected	Pto Resistance Detected	
SSOR	-	-	-	Continue SSOR
	-	+	-	Continue SSOR
	-	-	+	Continue SSOR
	-	+	+	Shift to SLOR FQ-S Continue dose count if within 1 month from treatment initiation
	+	+/-	+/-	Shift to SLOR FQ-R Restart dose count
SLOR FQ-S	-	+/-	+/-	Continue SLOR FQ-S
	+	+/-	+/-	Shift to SLOR FQ-R Restart dose count
SLOR FQ-R	+/-	+/-	+/-	Continue SLOR FQ-R
ITR	+/-	+/-	+/-	Review initial regimen andrevise if needed in consultation with R-TB MAC

Legend: (-) Resistance NOT Detected; (+) Resistance Detected

MDR/RR TB Regimen for children

DRTB Treatment regimens for children

Age	Regimen 6 FQ susceptible MDR TB	Regimen 7 FQ resistant MDR TB
<3 years	(6a) Lfx-Lzd-Cfz-Cs (PAS/Pto)	(7a) Lzd-Cfz-Cs-PAS (Pto/Dlm)
3-6 Years	(6b) Lfx-Lzd-Cfz-Cs (Dlm/PAS)	(7b) Lzd-Cfz-Cs-Dlm (PAS/Pto)
>6 years	(6c) Bdq-Lfx-Lzd-Cfz (Cs/Dlm)	(7c) Bdq-Lzd-Cfz-Cs (Dlm/PAS)

Treatment Duration:

- 9-12 months for non-severe disease depending on physician's assessment on patient's clinical progress
- 15-18 months for severe or extensive disease

Determine the severity of the disease.
Severity of TB in children is usually defined by the presence of any of the following:

- positive TB bacteriology (smear, Xpert MTB/RIF, culture)
- cavities or bilateral disease on chest radiography or smear-positivity
- extrapulmonary forms of disease other than lymphadenopathy (peripheral nodes or isolated mediastinal mass without compression)
- presence of co-morbid condition or disease such as severe malnutrition or advanced immunosuppression.

Dosing of Medicine Used in Second-line MDR-TB Regimens by Weight Band in Patients <15 Years Old

Group	Medicine	Weight-based daily dose	Formulation	Weight bands for patients older than 14 years old							Usual Upper Daily Dose	Remarks
				5-6 kg	7-9 kg	10-15 kg	16-23 kg	24-30 kg	31-34 kg	>34 kg		
A	Fluoroquinolones Levofloxacin	15-20 mg/kg	100 mg dt	1	1.5	2 or 3	3 or 4	(≥14 y)	(≥14 y)	(≥14 y)	1.5 g	
			250 mg tab	0.5	0.5	1-1.5	1.5-2	2	3	(≥14 y)	1.5 g	
	Moxifloxacin	10–15 mg/kg	400 mg tab	0.8	1.5	2	3	4	(≥14 y)	(≥14 y)	400 mg	Use 10 mg/kg in <6 months
			400 mg tab[c]	2ml	3ml	5ml	0.5 or 0.75	1	(≥14 y)	(≥14y)	400mg	
	Bedaquiline		100 mg tab				2 tabs OD for 2 weeks; then 1 tab OD M/W/F for 22 weeks		4 tabs OD for 2 weeks; then2 tabs OD M/W/F for 22 weeks		-	Only in patients >5 years old (lower dosefrom 15-29 kg; higher dose from >29 kg
	Linezolid	15 mg/kg OD in < 16 kg	20 mg/ml susp	4ml	6ml	8ml	11ml	14ml	15ml	20ml	600mg	
		10-12mg/kg OD in >15 kg	600 mg tab[c]	0.25	0.25	0.25	0.25	0.5	0.5	0.75		
B	Clofazimine	2-5 mg/kg	50 mg cap	1 alt days	1 alt days	1 alt days	1	2	2	(≥14 y)	100mg	Give on alternate days if dose in mg/kg/day is too high
			100 mg cap	M/W/F	M/W/F	1 alt days	1 alt days	1	(≥14 y)	(≥14 y)	100mg	
	Cycloserine	15-20 mg/kg	125 mg mini cap	1	1	2	3	4	(≥14 y)	(≥14 y)		
			250 mg cap[c]	4 to 5 ml[c]	5 to 6 ml[c]	7 to 10 ml[c]	2	2	2	(≥14 y)	1 g	
C	Ethambutol	15-25 mg/kg	100 mg dt	1	2	3	4	-	-	(≥14 y)		
			400 mg tab[c]	3 ml[c]	4 ml[c]	6 ml[c]	1	1 or 1.5	2	(≥14 y)		
	Delamanid		50 mg tab	-	-	-	-	1 bid	1 bid	2 bid	200 mg	Only in patients >2 years old (25 mg BID in 3-5 yrs, 50 mg BID in 6-11 yrs; 100mg BID in 12-17 yrs)
	Pyrazinamide	30 40 mg/kg	150 mg tab	1	2	3	4 or 5	-	-	(≥14 y)		
			500 mg tab	0.5	0.5	0.75 or 1	1.5	2	2.5	(≥14 y)		
	Imipinem - Cilastatin		0.5 g + 0.5 g vial									Not used in patients <15 years Use Meropenem
	Meropenem	20-40mg/kg IV q 8 hrs	1g vial (20ml)	2.5 ml	4 ml	6 ml	8-9 ml	11 ml	≥14 y	≥14 y		To be used with clavulanic acid
	Amikacin	15-20 mg/kg	500 mg/2ml vial	0.4 ml	0.6 ml	0.8-1.0 ml	1.2-1.5 ml	2.0 ml	≥14 y	≥14 y	1 g	
	Streptomycin	20-40 mg/kg	1 gm vial	Calculate according to the dilution used					≥14 y	≥14 y	1 g	
	Prothionamide	15-20 mg/kg	250 mg tab	1	1	2	3	4	4	≥14 y	1 g	

C	p-aminosalicylic acid	200-300. mg/kg in 2 divided doses	PAS acid (4g) sachet	0.5-0.75 g bid	0.75-1 g bid	1-2 g bid	2-3 g bid	3-3.5 g bid	(>14 y)	(>14 y)	-	Full dose can be given once daily if tolerated
			PAS sodium salt (4g) sachet	0.5-0.75 g bid	0.75-1 g bid	1-2 g bid	2-3 g bid	3-3.5 g bid	(>14 y)	(>14 y)		
			PAS sodium salt 60% (9.2g) sachet	1.5 g bid	2-3 g bid	3-4 g bid	4 or 6 g bid	6 or 8 g bid	8-12 g bid	8-12 g bid	-	
Others	Isoniazid	15-20 mg/kg (high.dose)	50mg/5 ml soln	8-10 ml	15 ml	20 ml	-	-	-	-		300 mg isoniazid tablet can be used in patients >20 kg Pyridoxine is always given with high-dose isoniazid in children (12.5 mg od in <5 y olds and 25 mg od in >4 y olds)
			100 mg tab	1	1.5	2	3	4	4	(>14 y)		
	Clavulanic acid	-	250 mg amoxicillin/ 62.5 mg clavulanic acid/5 ml suspension	2 ml bdh	3 ml bdh	5 ml bdh	8 ml bdh	10 ml bdh	(>14 y)	(>14 y)		Only be used with carbapenems

(>14 y) = follow the separate dose for patients older than14 years of age, alt = alternate, bid = two times a day, tab = tablet, g = grams, im = intramuscular, iv = intravenous, kg = kilogram, ml = milligram, M/W/F = Monday, Wednesday, Friday, OD = once a day, soln = solution, tab = tablet

[c] Dissolving in 10 ml distilled water may facilitate administration in patients in lower weight bands & avoids fractioning of solid formulation although biolavailability is uncertain (use of dispersible tablet is perferred if available)

Dosing of Medicine Used In Second-line MDR-TB Regimens by Weight Band in Patients ≥15 Years Old

Group	Medicine	Weight-based daily dose	Formulation	Weight bands for patients older than 14 years old					Usual Upper Daily Dose	Comments
				30-35 kg	36-45 kg	46-55kg	56-70kg	>70kg		
A	Fluoroquinolones Levofloxacin		250 mg tab 500 mg tab 750 mg tab	3 1.5 1	3 1.5 1	4 2 1.5	4 2 1.5	4 2 1.5	1.5	
	Moxifloxacin	Standard dose High dose	400 mg tab 400 mg tab	1 1 or 1.5	1 1 or 1.5	1 1.5 or 2	1 2	1 2	400 mg 800 mg	As used in the standardized shorter MDR-TB Regimen
	Bedaquiline		100 mg tab	4 tabs OD for 2 weeks; then 2 tabs OD M/W/F for 22 weeks					400 mg	
	Linezolid		600 mg tab	(<15y)	(<15y)	1	1	1	1.2 g	
B	Clofazimine		50 mg cap 100 mg cap	2 1	2 1	2 1	2 1	2 1	100 mg 100 mg	
	Cycloserine or Terizidone	10-15 mg/kg	250 mg cap	2	2	3	3	3	1 g	
C	Ethambutol	15-25 mg/kg	400 mg tab	2	2	3	3	3		
	Delamanid		50 mg tab	2 bid	2 bid	2 bid	2 bid	2 bid	200 mg	
	Pyrazinamide	20-30 mg/kg	400 mg tab 500 mg tab	3 2	4 3	4 3	4 3	5 4		
	Imipinem - Cilastatin		0.5 g + 0.5g vial	2 vials (1g + 1g) bid						To be used with clavulanic acid
	Meropenem		1g vial (20ml)	1 vials 3x/day or 2 vials bid						To be used with clavulanic acid
	Amikacin	15-20 mg/kg	500 mg/2ml vial	2.5 ml	3 ml	3 to 4 ml	4 ml	4 ml	1 g	
	Streptomycin	12-18 mg/kg	1 gm vial	Calculate according to the dilution used					1 g	
	Ethionamide or Prothionamide	15-20mg/kg	250 mg tab	2	2	3	3	4	1 g	Once daily dose advised but can start with 2 divided doses until tolerance improves
	p-aminosalicylic acid	8-12 g/day in 2 to 3 divided doses	PAS Na Salt (4gm) sachet PAS Acid (4gm) sachet	1 bid 1 bid	1 bid 1 bid	1 bid 1 bid	1 bid 1 bid	1 to 1.5 bid 1 to 1.5 bid	12 g	
Others	Isoniazid	Standard dose: 4-6 mg/kg High dose: 10-15 mg/kg	300 mg tab 300 mg tab	2/3 1.5	1 1.5	1 2	1 2	1 2		100 mg isoniazid tablet can facilitate the administration of certain dosages Pyridoxine is given with isoniazid in patients at risk (such as dose with HIV and malnutrition)
	Clavulanic acid		125 mg tab	1 bid	1 bid	1 bid	1 bid	1 bid		To be used only with carbapenems (such as imipenem and meropenem)

Dose Adjustment of Anti-TB Drugs in Patients with Renal Insufficiency

	Recommended dose and frequency for patients who have creatinine clearance <30 ml/min and those having renal dialysis (unless otherwise indicated dose after dialysis)
Isoniazid	No adjustment necessary
Rifampicin	No adjustment necessary
Ethambutol	15-25 mg/kg per dose 3 times per week (not daily dose)
Pyrazinamide	25-35 mg/kg per dose 3 times per week (not daily dose)
Rifabutin	Normal dose can be used, if possible monitor drug concentration level to avoid toxicity
Rifapentine	No adjustment necessary
Levofloxacin	750-1000 mg per day 3 times per week (not daily)
Moxifloxacin	No adjustment necessary
Etionamide/Prothionamide	No adjustment necessary
Cycloserine	250 mg once daily or (500 mg per day 3 time per week – not daily)
PAS	4 G/dose, twice daily maximum dose
Bedaquiline	No adjustment necessary in mild to moderate renal impairment, no established dosage in severe renal impairment, use with caution
Delamanid	No adjustment necessary in mild to moderate renal impairment, no established dosage in severe renal impairment, use with caution
Clofazamine	No adjustment necessary
Linezolid	No adjustment necessary
Amoxicillin/ Clavulanate Acid	Creatinine Clearance 10-30 ml/min, 1000 mg twice daily for Amoxicillin component Creatinine clearance <10 ml/min, 1000 mg once daily for Amoxicillin component
High Dose Isoniazid	Recommended dosage not available
Streptomycin	12-15 mg/kg per dose two-three times per week (not daily)
Amikacin	12-15 mg/kg per dose two-three times per week (not daily)
Imipinem/Cilastatin	Creatinine Clearance <20-40 ml/min: 500 mg every 8 hours daily Creatinine Clearance <20 ml/min: 500 mg every 12 hours daily
Meropenem	Creatinine Clearance <20-40 ml/min: 750 mg every 12 hours daily Creatinine Clearance <20 ml/min: 500 mg every 12 hours daily

PREPARATION AND ADMINISTRATION OF IMIPENEM

Prepare a 100ml vial of 0.9 NaCl solution and aspirate 10ml of the solution to dilute each of the imipenem 500mg vial. Shake the combined solutions of Imipenem and 0.9 NaCl well and return them to the 100ml vial of NaCl. Shake well again.

Imipenem is **administered twice daily (q 12 hrs) and infusion can be given for 40 to 60 minutes**, depending on preferred rate of infusion. There is always the risk of phlebitis, obstruction or inflammation at the injection site. Advise the patient on proper care of the injection site.

Prior to the infusion of the imipenem/cilastatin solution, give **1 tab of Co Amoxicav 875mg /125mg tab 30 minutes before the procedure.** For the **second infusion**, instruct the patient to take **1 tab of Co Amoxicav 875mg /125mg tab 30 minutes before the procedure.** Imipenem/cilastatin would only work with the addition of the beta-lactam formulation in AmxClv. **Always use AmxClv with Imipenem.**

The **use of Imp is expected to last until the end of treatment.**

Implantable venous access system port-a-cath will be used for long term IV Imipenem Administration.

RR/MDR-TB Treatment Monitoring

1. Schedule of baseline and follow-up clinical, laboratory and bacteriologic examination for patients on standard short treatment regimen (SSOR/ SSTR)

		Intensive Phase: 4 months, may be extended'up to 6 months				Continuation Phase: 5 months					Post-Treatment Follow-up	
Test/Examination	Baseline	M1	M2	M3	M4	M5	M6	M7	M8	M9	P6	P12
Clinical Evaluation by the PMDT Physician including weight for all and height for children	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Mycobacteriological Tests												
Smear Microscopy	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
TB Culture(TBC)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Drug Susceptibility Testing (DST)	✓	If culture remains positive at month 4 of treatment, in case of culture reversion or culture positive during post-treatment follow-up										
First-line and Second-line Line Probe Assay (LPA)	✓											
Diagnostic Tests												
Chest X-ray (CXR)	✓						✓				✓	✓
Electrocardiogram (ECG)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		
Visual Acuity and Color Vision	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		
Brief Peripheral Neuropathy Screening (BPNS)	✓	✓	✓	✓	✓							
Mental health screening	✓	Monthly if regimen contains Cycloserine (Patient Health Questionnaire-9 or short screening tool may be used)										
Audiometry	✓	Monthly while on injectable (SSTR)										
Blood Chemistry/Hematology/Immunological Tests												
Alanine and Aspartate Transaminase (ALT/AST) *	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		
Complete Blood Count (CBC)	✓	Monthly if regimen contains Linezolid										
Urea Nitrogen, Creatinine, Fasting Blood Sugar (FBS), Potassium (K),	✓											
Thyroid Stimulating Hormone (TSH)	✓						✓					
HIV Rapid Antibody Test	✓											
Pregnancy Test	✓											

*If ALT and AST are higher than upper limit of normal value, consider doing total bilirubin test.

2. Schedule of baseline and follow-up Clinical, Laboratory and Bacteriologic Examinations for Patients on 18-20 months treatment regimens

		Intensive Phase: 6 months						Continuation Phase: 12-14 months														Post-Treatment Follow-up	
Test/ Examination	BL	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15	M16	M17	M18	M19	M20	6m	12m
Clinical Evaluation	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Mycobacteriology Tests																							
Smear Microscopy	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
TB Culture(TBC)	✓	✓	✓	✓	✓	✓	✓		✓		✓		✓		✓		✓		✓		✓	✓	✓
DST	✓	If culture remains positive at month 4 of treatment, in case of culture reversion or culture positive during post-treatment follow-up																					
LPA	✓																						
Diagnostic Tests																							
CXR	✓						✓						✓						✓			✓	✓
ECG	✓	Monthly if regimen contains Bedaquiline, Delamanid, Clofazimine and/or Moxifloxacin																					
Visual Acuity and Color Vision	✓	Monthly if regimen contains Linezolid and/or Ethambutol																					
BPNS	✓	Monthly if regimen contains Linezolid, Cycloserine and/or High Dose Isoniazid																					
Audiometry	Baseline and Monthly if regimen contains Amikacin or Streptomycin																						
Mental health screening	Baseline and Monthly if regimen contains Cycloserine (Patient Health Questionnaire-9 or short screening tool may be used)																						
Blood Chemistry/Hematology/Immunological Tests																							
ALT/AST*	✓	Monthly if regimen contains Bedaquiline and/or Pyrazinamide																					
CBC	✓	Monthly if regimen contains Linezolid																					
FBS,	✓																						
Urea Nitrogen, Creatinine, K	✓	Monthly if regimen contains Amikacin or Streptomycin																					
	BL	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15	M16	M17	M18	M19	M20	6m	12m
TSH	✓	Every 6 months if regimenProthionamide or Para-aminosalicylic Acid (PAS) Every 3 months if regimen contains both Protionamide and Para-aminosalicylic Acid (PAS																					
Albumin	Baseline if regimen contains Delamanid																						
HIV Rapid Antibody Test	✓																						
Pregnancy Test	✓																						

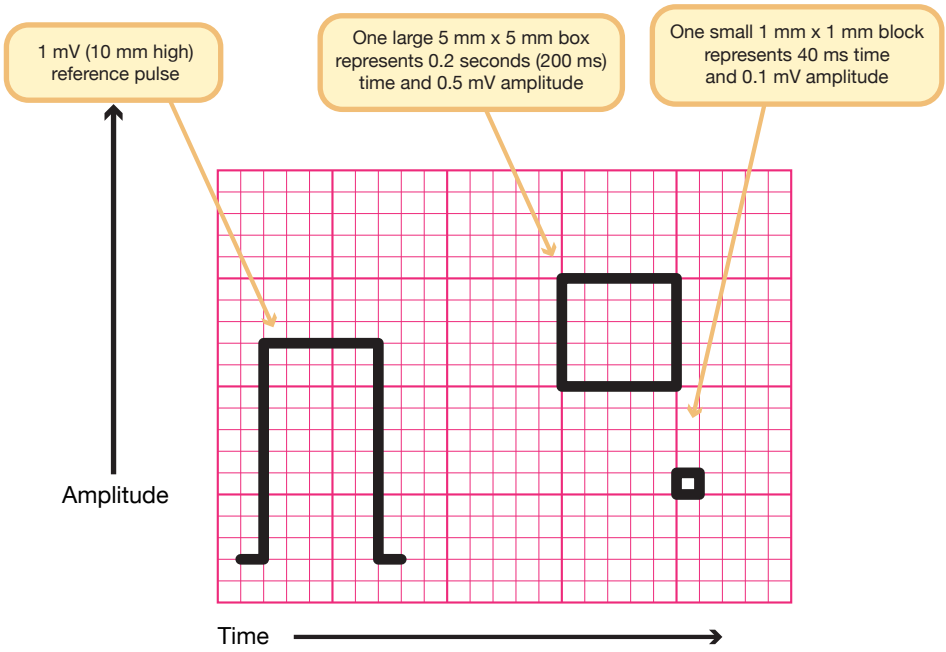
* If ALT and AST are higher than upper limit of normal value, consider doing total bilirubin test. If regimen contain Bdq+Dlm and/ or Mfx+Cfz, more frequent ECG monitoring, every other week for initial 3 months is recommended.

Management of Adverse Event: Ancillary Diagnostic Tests

1. Electrocardiography

a. ECG Machine Calibration

The ECG machine should be calibrated to ensure that the following voltage and speeds apply:



b. Normal Heart Rhythm & QTc

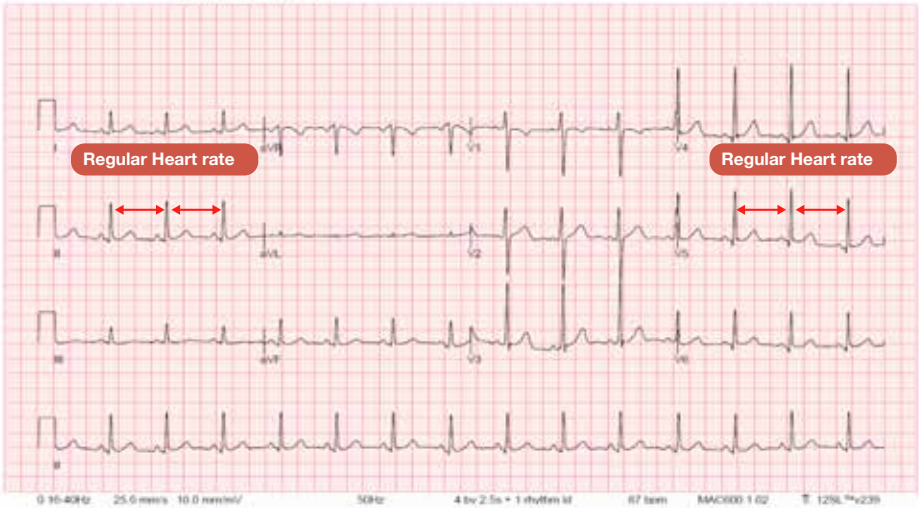
ID: X-97

10-Oct-2016 15:21:21

25 Years
Female

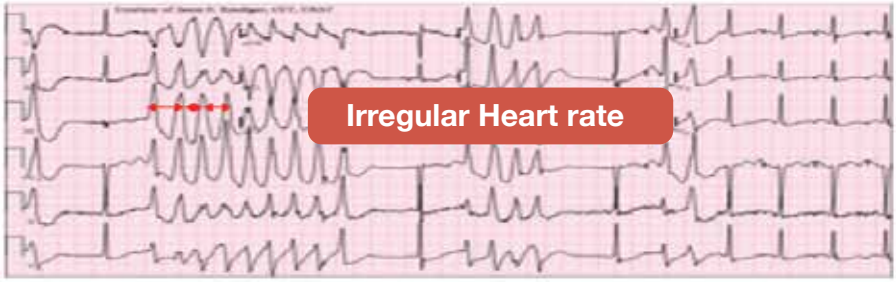
Vent. rate		87 bpm
PR Interval		116 ms
QRS duration		90 ms
QTc	=	445 mc
P duration		90 ms
RR interval		689 ms
P-R-T axes		62 55 43

Normal sinus rhythm (sinus rate 60-100/min)
Normal ECG

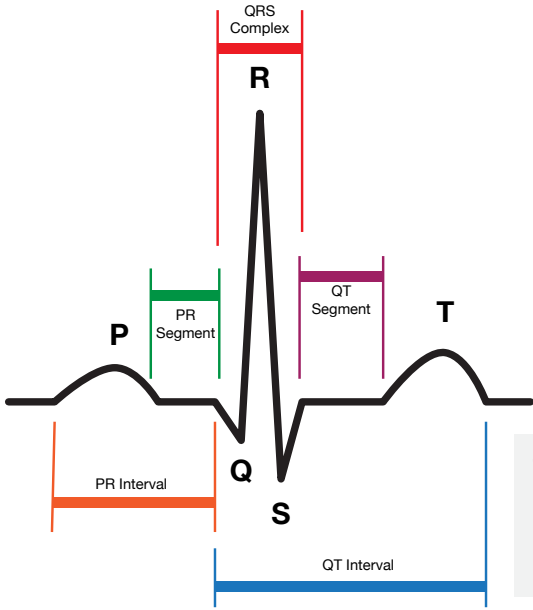


Cardiac dysrhythmia/arrythmia:.

- Hospitalize patient
- Withhold BDQ and all other QT prolonging drugs.



c. Calculation of QTc by using Fredericia Formula



- QTc = Q T/ 3√ RR
- QTc = the corrected QT interval
- QT = the time between the start of the QRS complex and the end of the T wave
- Auto-reporting from the machine may not be programmed with Fredericia formula.
- Read at lead II or V5
- QT: no of small squares x 40 (e.g 9x40=360ms)
- HR: 1500/no of small squares b/t RR (e.g., 1500/17= 88)

Can use calculator app that can be downloaded as per below link:

https://www.thecalculator.co/health/QTc-Calculator-385.html
http://www.qxmd.com/apps/calculate-by-qxmd

QT in milliseconds (ms) and RR interval in seconds (s).

d. Automated QTc value and manual calculation

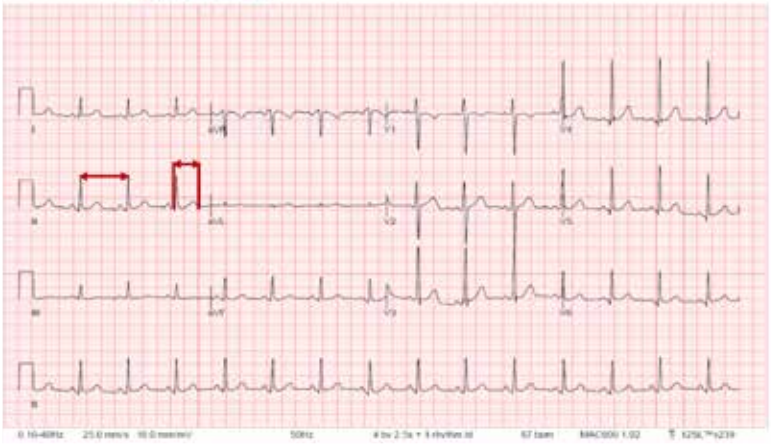
ID: X-97

25 Years
Female

Vent. rate	87 bpm
PR Interval	116 ms
QRS duration	90 ms
QT/QTc	370/445 ms
P duration	90 ms
RR interval	689 ms
P-R-T axes	62 55 43

10-Oct-2016 15:21:21
Normal sinus rhythm (sinus rate 60-100/min)
Normal ECG

AUTOMATED REPORT



Step 1:
RR = 17 squares
= 17 x 0.04 = 0.68 sec

HR = 1500/17 = 88

Step 2:
QT = 9 squares x 40
= 360 ms

Step 3:
QTc= 360/3√0.68
= 360/0.88 = 409 ms

If the two values are <50 ms difference, the machine is more likely to be programmed with Fredericia formula.

Use of Nomogram to get QTcF (QT 420, HR 70, QTcF read as 442)

Heart Rate (beats per minute)		45	50	55	60	65	70	75	80	85	90	95	100	105	110	115	120	125	130	135	140	145	150
R-R interval(sec)		1.33	1.20	1.09	1.00	0.92	0.86	0.80	0.75	0.71	0.67	0.63	0.60	0.57	0.55	0.52	0.50	0.48	0.46	0.44	0.43	0.41	0.40
QT Interval (msec)	300	273	282	291	300	308	316	323	330	337	343	350	356	362	367	373	378	383	388	393	398	403	407
	310	282	292	301	310	318	326	334	341	348	355	361	368	374	379	385	391	396	401	406	411	416	421
	320	291	301	311	320	329	337	345	352	359	366	373	379	386	392	397	403	409	414	419	424	429	434
	330	300	311	321	330	339	347	355	363	371	378	385	391	398	404	410	416	421	427	432	438	443	448
	340	309	320	330	340	349	358	366	374	382	389	396	403	410	416	422	428	434	440	446	451	456	461
	350	318	329	340	350	359	368	377	385	393	401	408	415	422	428	435	441	447	453	459	464	470	475
	360	327	339	350	360	370	379	388	396	404	412	420	427	434	441	447	454	460	466	472	477	483	489
	370	336	348	360	370	380	390	399	407	416	424	431	439	446	453	460	466	473	479	485	491	497	502
	380	345	358	370	380	390	400	409	418	427	435	443	451	458	465	472	479	485	492	498	504	510	516
	390	354	367	379	390	401	411	420	429	438	446	455	462	470	477	484	491	498	505	511	517	523	529
	400	363	376	389	400	411	421	431	440	449	458	466	474	482	490	497	504	511	518	524	531	537	543
	410	373	386	399	410	421	432	442	451	460	469	478	486	494	502	509	517	524	531	537	544	550	556
	420	382	395	408	420	431	442	452	462	472	481	490	498	506	514	522	529	536	543	550	557	564	570
	430	391	405	418	430	442	453	463	473	483	492	501	510	518	526	534	542	549	556	563	570	577	584
	440	400	414	427	440	452	463	474	484	494	504	513	522	530	539	547	554	562	569	577	584	590	597
	450	409	423	437	450	462	474	485	495	505	515	524	534	542	551	559	567	575	582	590	597	604	611
	460	418	433	447	460	472	484	496	506	517	527	536	545	554	563	571	580	588	595	603	610	617	624
	470	427	442	457	470	483	495	506	517	528	538	548	557	566	575	584	592	600	608	616	623	631	638
	480	436	452	466	480	493	505	517	528	539	549	559	569	578	587	596	605	613	621	629	637	644	651
	490	445	461	476	490	503	516	528	539	550	561	571	581	590	600	609	617	626	634	642	650	658	665
	500	454	471	486	500	514	526	539	550	562	572	583	593	603	612	621	630	639	647	655	663	671	679
	510	463	480	495	510	524	537	549	561	573	584	594	605	615	624	634	643	651	660	668	676	684	692
	520	472	489	505	520	534	547	560	572	584	595	606	617	627	636	646	655	664	673	681	690	698	706
	530	482	499	515	530	544	558	571	583	595	607	618	628	639	649	658	668	677	686	694	703	711	719
	540	491	508	525	540	555	568	582	594	606	618	629	640	651	661	671	680	690	699	708	716	725	733
	550	500	518	534	550	565	579	592	605	618	630	641	652	663	673	683	693	702	712	721	729	738	746
	560	509	527	544	560	575	590	603	616	629	641	653	664	675	685	696	706	715	725	734	743	751	760
	570	518	536	554	570	585	600	614	627	640	652	664	676	687	698	708	718	728	738	747	756	765	774
	580	527	546	563	580	596	611	625	638	651	664	676	688	699	710	720	731	741	751	760	769	778	787
	590	536	555	573	590	606	621	636	649	663	675	688	700	711	722	733	743	754	763	773	783	792	801
	600	545	565	583	600	616	632	646	660	674	687	699	711	723	724	745	756	766	776	786	796	805	814

2. How to calculate Creatinine Clearance:

Calculation of Creatinine Clearance
(Estimated Glomerular Filtration Rate)

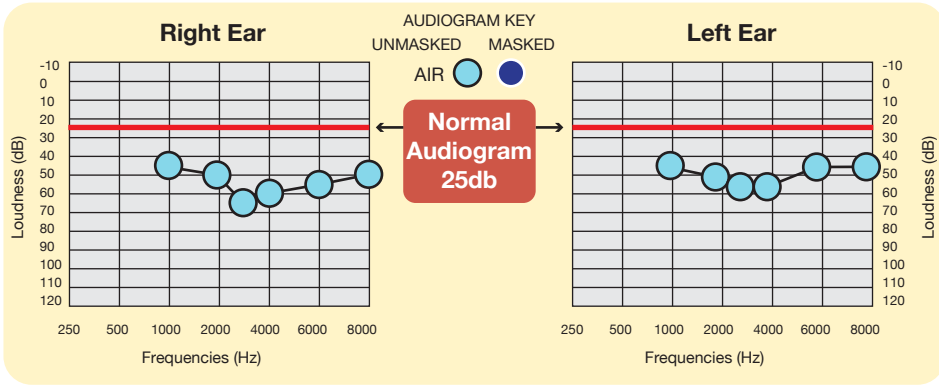
$$\text{weight (kg)} \times (140 - \text{age}) \quad X \quad \frac{\text{Constant}}{\text{Serum Creatinine (umol/L)}}$$

Constant: for Male = 1.23, for Female = 1.04

If Serum Creatinine value is given in mg/dl, it can be converted to umol/l by multiplying by 88.4.

Normal Value: Male = 60-110 umol/L; Female: 45-90umol/L

3. Audiometry Reading and Interpretation



Right Ear Interpretation

Hearing loss was detected. Please consult an audiologist. Threshhold (Hz:dB):
1K:45, 2K:50, 3K:65, 4K:60, 6K:55, 8K:50

Results from the test indicate that hearing loss was present at these frequencies:
1K, 2K, 3K, 4K, 6K, 8K

Left Ear Interpretation

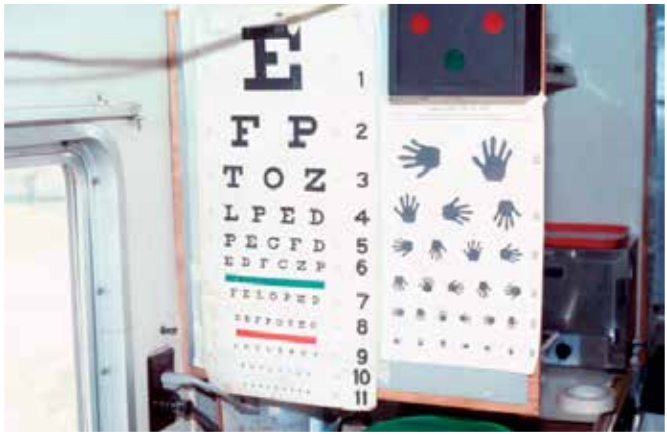
Hearing loss was detected. Please consult an audiologist. Threshhold (Hz:dB):
1K:45, 2K:50, 3K:55, 4K:55, 6K:45, 8K:45

Results from the test: indicate that hearing loss was present at these frequencies:
1K, 2K, 3K, 4K, 6K, 8K

4. How to perform Snellen's Test

Equipment

- Multi-letter Snellen chart
- E or C Snellen chart or a chart with illustrations for patients who cannot read or speak
- Plain occluder (not essential)
- Pinhole occluder
- Torch or flashlight
- Patient's documentation



A multi-letter Snellen chart (left) and a chart with illustrations

Procedure

- Ensure good natural light or illumination on the chart
- Explain the procedure to the patient
- Wash and dry the occluder and pinhole. If no plain occluder is available, ask the patient to wash his/her hands as they will use a hand to cover one eye at a time
- Test each eye separately – the 'bad' eye first
- Position the patient, sitting or standing, at a distance of 6 metres from the chart
- Ask the patient to wear any current distance spectacles, to cover one eye with his/her hand (or with a plain occluder), and to start reading from the top of the chart
- The smallest line he/she can read (the VA) will be expressed as a fraction, e.g. 6/18 or 6/24 (usually written on the chart). The upper number refers to the distance the chart is from the patient (6 metres) and the lower number is the distance in metres at which a person with no impairment should be able to see the chart
- In the patient's documentation, record the VA for each eye, stating whether it is with or without correction (spectacles), for example:

Right VA = 6/18 with correction **Left VA = 6/24 with correction**

- If the patient cannot read the largest (top) letter at 6 metres, move him/her closer, one metre at a time, until the top letter can be seen – the VA will then be recorded as 5/60 or 4/60, etc.
- If the top letter cannot be read at 1 metre (1/60), hold up your fingers at varying distances of less than 1 metre and check whether the patient can count them. This is recorded as counting fingers (CF). Record as: VA = CF
- If the patient cannot count fingers, wave your hand and check if he/she can see this. This is recorded as hand movements (HM). Record as: VA = HM
- If the patient cannot see hand movements, shine a flashlight toward his/her eye from four directions of a quadrant. Record this in the documentation, in the relevant quadrant, as perception of light (PL or √), or no perception of light (NPL or X). Record as:

Right VA =	NPL	NPL	**Left VA =**	PL	NPL
	NPL	NPL		PL	NPL
Right VA =	X	X	**Left VA =**	√	NPL
	X	X		√	NPL

- If 6/6 (normal vision) is not achieved, test one eye at a time with a pinhole occluder (plus any current spectacles) and repeat the above procedure at 6 metres only. The use of the pinhole enables assessment of central vision
- If the vision improves, it indicates the visual impairment is due to a refractive error, which is correctable with spectacles or a new prescription
- Repeat the whole procedure for the second eye
- Summarise the VA of both eyes in the documentation, for example:

Right VA = 6/24 with specs, 6/6 with pinhole **Left VA = NPL**

If using the E or C chart:

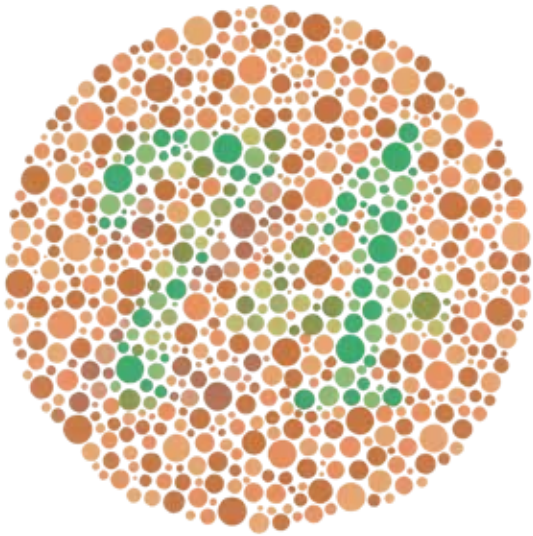
- Point to each letter on each line and ask the patient to point in the direction toward which the open end of the letter is facing
- Follow the same procedure and recording methods as above.

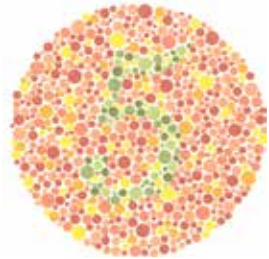
Source: https://www.ncbi.nlm.nih/gov/PMC2040251/

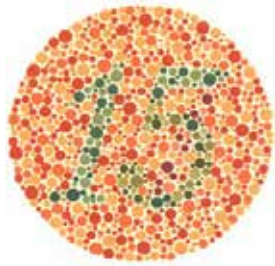
5. For Ishihara Colour Vision Test, please refer to:

1. https://www.colour-blindness.com/colour-blindness-tests/ishihara- colour-test-plates/

2. or get the hard copy of Ishihara Colour Vision Test Book







Adverse Events Management Algorithm

Monitoring and Management of Adverse Events Related to Linezolid

Clinical:

- Ask for peripheral neuropathy signs and symptoms (S/S) at every visit and assess severity by using Brief Peripheral Neuropathy Score (BPNS) - see below if there is any complaint of S/S.
- Ask any change in vision.
- Do color vison test and visual acuity test every visit.
- Examine signs and symptoms of anemia.
  - Pale lips,/sclera,/palms, easily fatigability, weakness, palpitations.

Lab:

- Do complete blood cell counts monthly and if clinically indicated.

Education to patients and family:

- Educate on the above clinical signs and symptoms.
- Advise patients and family to proactively report any experience of the adverse events.

Brief Peripheral Neuropathy Screening Tool (BPNS)

Assess Symptoms and Ask Patient to Score Severity Level	Left	Right
a. Pain, aching, or burning in feet, legs		
b. "Pins and needles" in feet, legs		
c. Numbness (lack of feeling) in feet, legs		
Total Score		

Normal	Mild ---------- Severe									
00	1	2	3	4	5	6	7	8	9	10

Use the single highest severity score above to obtain a total subjective sensory neuropathy score for severity grading.

Severity Grading of Total Score:

Grade 0 = 00	Grade 1 = 01-03	Grde 2 = 04-06	Grde 3 = 07-10

Steps of management

Peripheral neuropathy

Grade 1 severity: decrease Lzd dosage to 300 mg

Grade ≥ 2 severity: stop Lzd, never re-introduce

Visual acuity:

Refer to ophthalmologist to check optic neuritis in case of abnormal color vision test or change in visual acuity

Optic neuritis of any grade (color blindness and/or visual acuity deterioration in the affected eye): Stop Lzd immediately and never re-introduce Lzd

Myelosuppression: (See pages 60 and 69)

Grade 1 severity: decrease Lzd dosage to 300 mg (Hb<9.5 g/dl, Neutrophil<1000/mm3 , Platelet <75,000/ mm3)

Grad ≥ 2 severity: stop Lzd (Hb <8 g/dl, Neutrophil<750/mm3, Platelet <50,000/ mm3), restart at 300 mg dosage when toxicity level decrease to Grade 1

Management of Depression

(Possible causative anti-TB Drugs: Cs, Lfx, Mfx, H, Pto)

Administer Patient Health Questionnaire-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself - or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
9. Moving or speaking so slowly that other people could have noticed. Or the opposite - being fidgety or restless that you have been moving a lot more than usual	0	1	2	3
10. Thoughts that you would be better off dead, or of hurting yourself in some way (Suicidal ideation or attempt)	0	1	2	3

For office coding 0 + _____ + _____ + _____

= Total Score: _____

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

☐ Not difficult at all ☐ Somewhat difficult ☐ Very difficult ☐ Extremely difficult

PHQ9 - Pateint Health Quality 9
Developed by Drs. Robert L. Spitzer, Janet B. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc. No permission required to reproduce, translate, display or distribute.

Severity Grading Scale

PHQ-9 Score	Depression Severity	Proposed Treatment Action
0-4	None-minimal	None
5-9	Mild	Watchful waiting; repeat PHQ-9 at follow up
10-14	Moderate	Treatment plan, consider counseling, follow up and pharmacotherapy
15-19	Moderately Severe	Active treatment with pharmacotherapy and/or psychotherapy
20-27	Severe	Immediate initiation of psychotherapy and, if severe impairment or poor response to therapy, expedited referral to a mental health specialist for psychotherapy and/or collaborative management

⚠ WARNING!

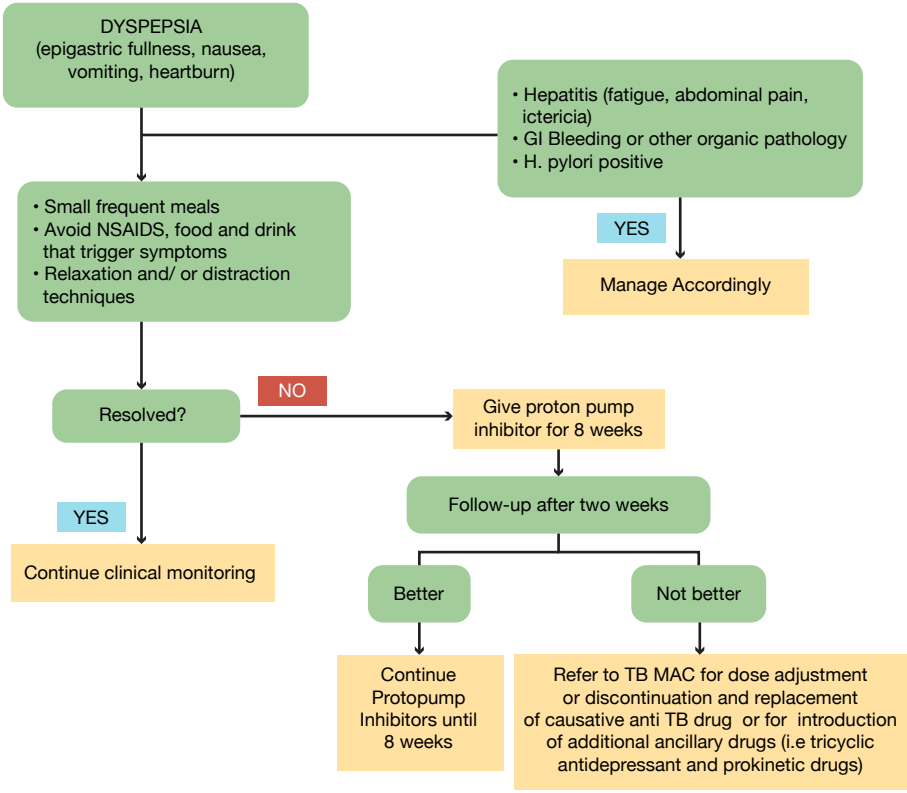
Patients with suicidal ideation must be assessed immediately for possible hospitalization.

(Exclude hypothyroidism & manage accordingly)

Consult with TB MAC for possible dose adjustment, discontinuation or replacement of causative anti TB drug.

Management of Dyspepsia

Possible Causative anti-TB Drugs: **PAS, Pto, Cfz,** FQs, H, E, Z

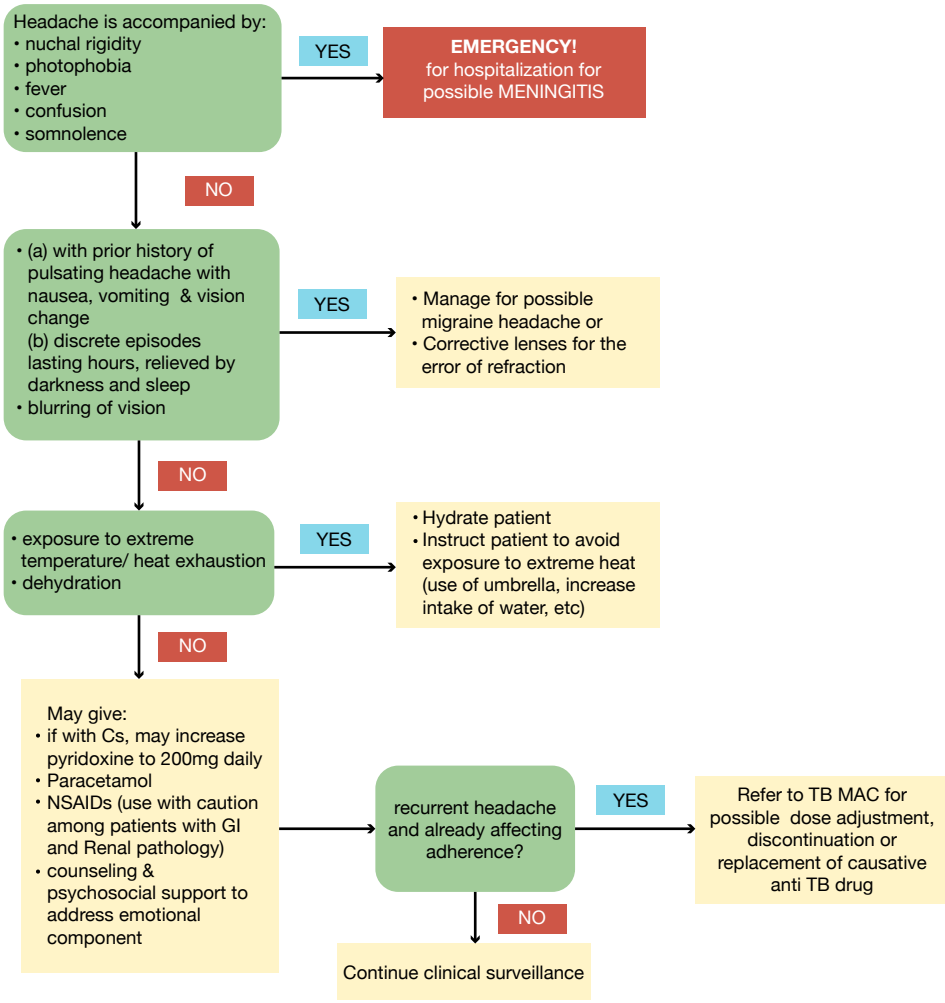


- Food and drinks that may cause & aggravate dyspepsia:
  Alcohol, caffeine, soda and acidic drinks
  Spicy and high fat food
- Proton pump inhibitor
  Lanzoprazole 30 mg/tab 30mins before breakfast
  Pantoprazole 20-40 mg/tab with or without food (normal release), 1hr before meal (controlled-release)
  Omeprazole 20-40 mg/tab 30 mins before breakfast
- Tricyclic anti-depressant
  Amitriptyline HCl 50-75 mg at bed time
- Prokinetic Drug
  Domperidone 10 mg po q8 (use with caution in patients with cardiac pathology)

Management of Headache

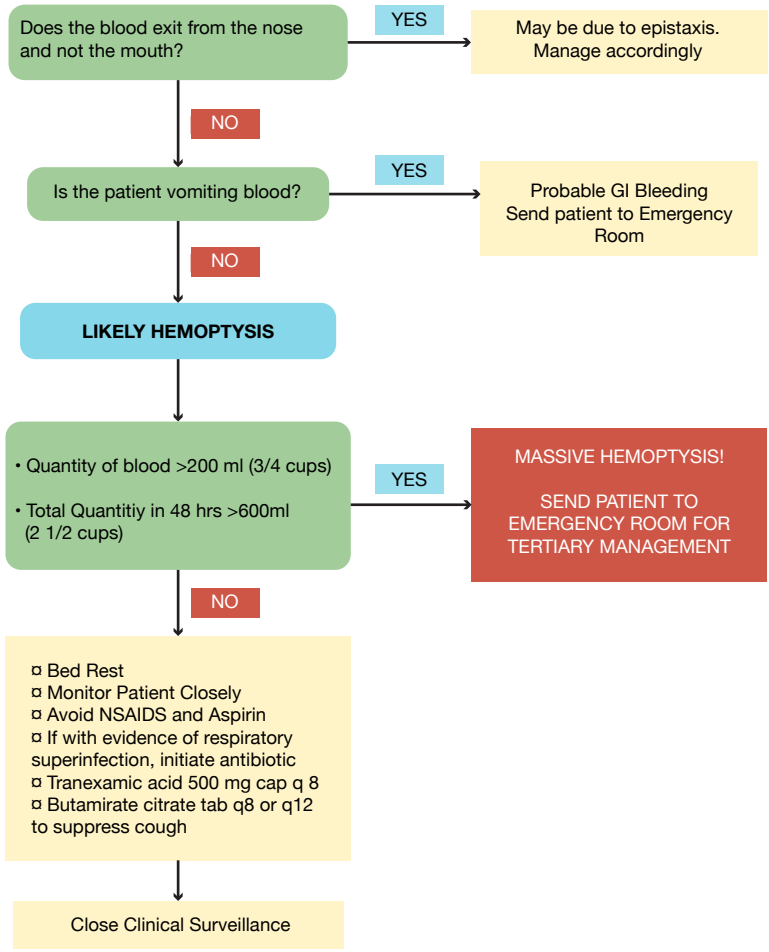
(Possible causative anti-TB Drugs: **Cs,** Bdq, Lfx)

Although headache is one of the side effects of anti-TB treatment, it is important to rule out other causes such as meningitis, migraine and cluster headaches.



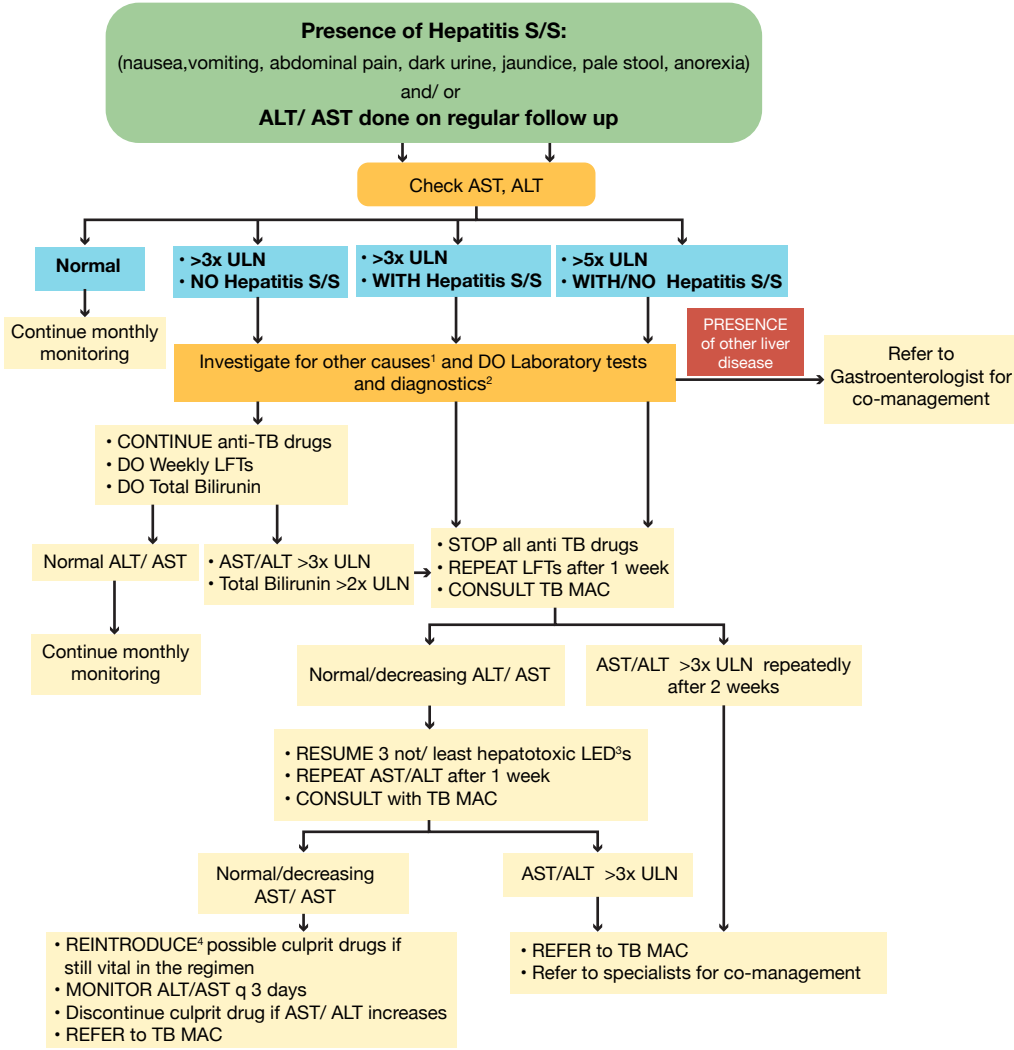
Management of Hemoptysis

Hemoptysis is expectoration of blood originating from the lower airways. It is important to quantify the blood loss and the period of time over which the loss occurred. Blood pressure, heart rate and respiratory rate, as well as blood type should be obtained and documented.



Management of Hepatotoxicity

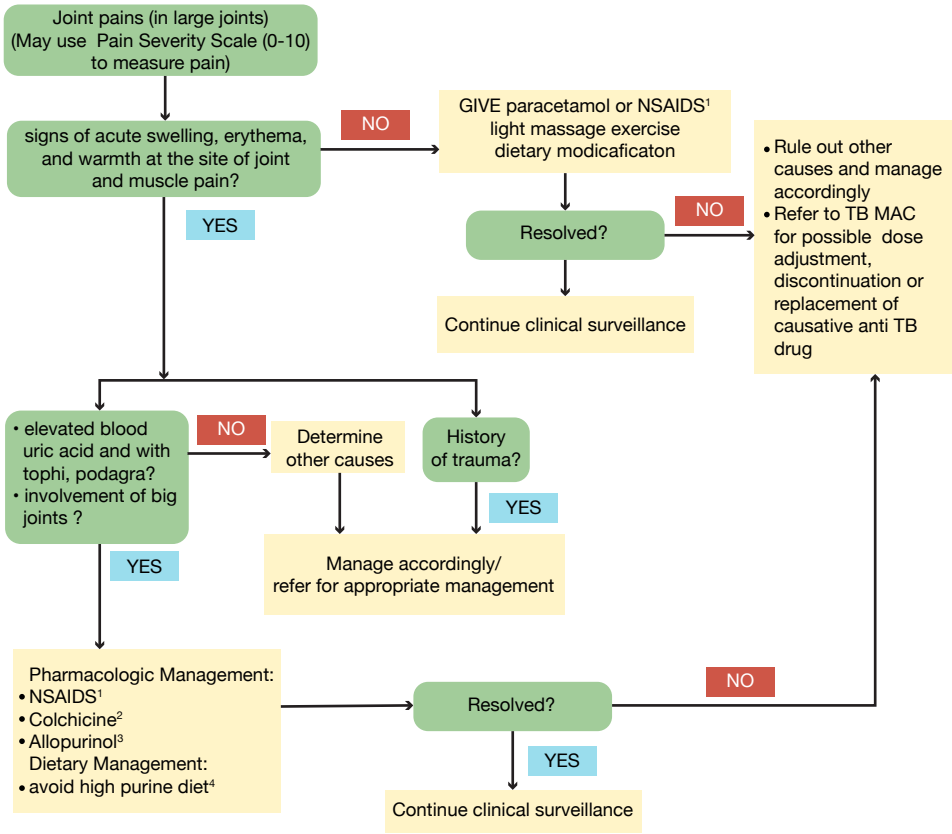
Possible Causative anti-TB Drugs: **Z, H, R, Pto**/ Eto, PAS, Bdq, Cfz, Dlm



[1]Alcoholic and Non Alcoholic liver disease, viral hepatitis
[2]Serology tests for Hep A, Hep B (HbsAg, antiHBC) and Hep C, Hepatobiliary ultrasound, etc.
[3]LED - Likely Effective Drugs
[4]Most hepatotoxic (H,Z,R) drugs will be reintroduced using incremental dose starting with the least culprit drug for 3 days. Repeat AST/ALT q3 days prior to adding another drug.

Management of Joint Pains

(Possible causative anti-TB Drugs: Z, Lfx/Mfx, Pto, Bdq)



[1]Non Steroidal Anti-inflammatory Drugs (NSAIDS), (has to be given with caution in patients with GI, renal and cardiac pathology)

- Mefenamic Acid 500 mg/cap, 1 cap every 8 hrs as needed for pain after meals
- Indomethacin 25 mg tab, 1 -2 tabs every 12 hrs with meals as needed for pain
- Celecoxib 100-200 mg cap every 12 hrs as needed for pain

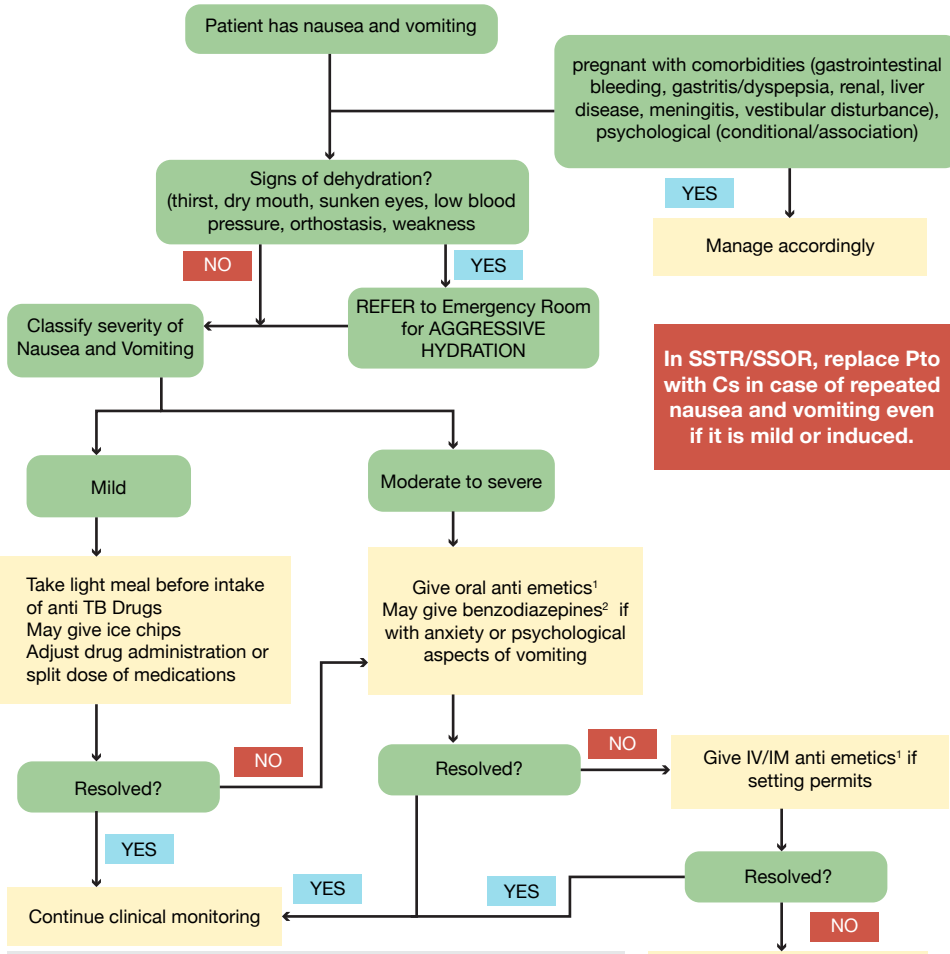
[2]Colchicine - has to be given within 36 hrs of onset of acute attacks initially at 1.2 mg followed by 0.6 mg after an hour (given for acute attacks may also cause GI symptoms such as diarrhea)

[3]Allopurinol - 100 mg/day and may be increased to 200 mg/day after a week to lower blood uric acid levels, hence, reducing symptoms (watch out for Steven Johnson's disease) Not to be used during acute attacks

[4]Food High in Purine
sardines,innards,mussels, anchovies, trouts and salmon,bacon, alcoholic drinks, etc

Management of Nausea and Vomiting

Possible causative anti-TB Drugs: **Pto, PAS,** Cfz, H, Bdq, Dlm, E, Z

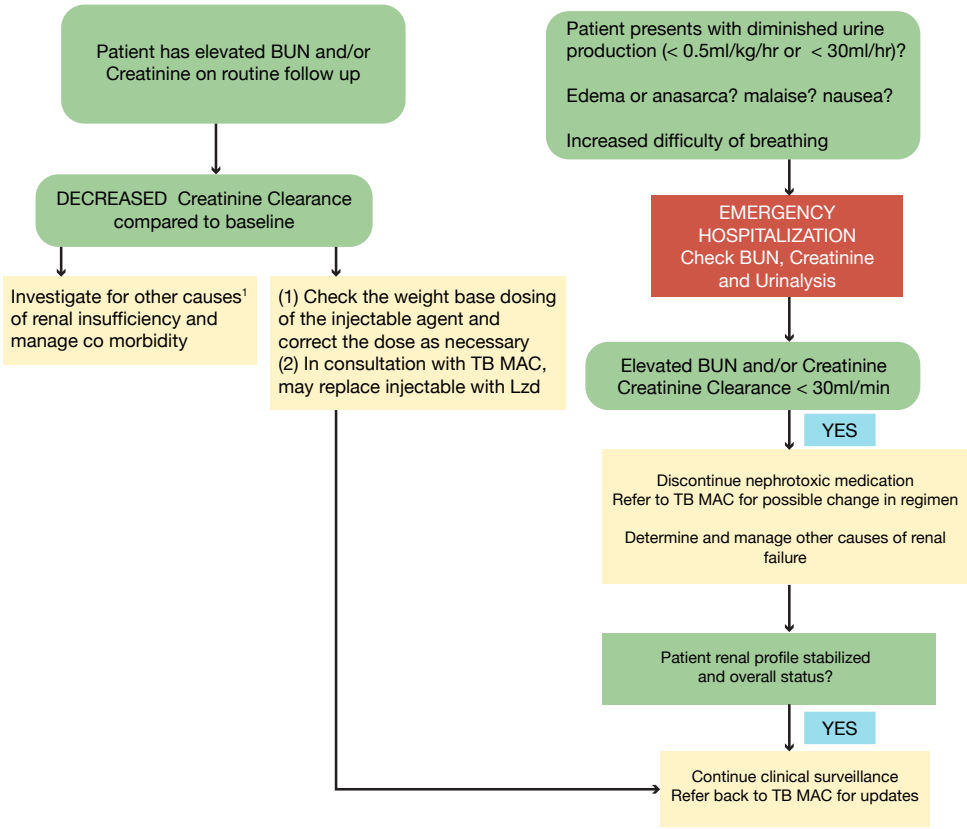


[1]Anti-emetics:
(1) Metoclopromide 10 mg, 30 mins before intake of anti TB meds, q 8 hrs thereafter
(2) Ondansetron 8 mg, 30 mins before intake of anti TB meds, q 8 hrs thereafter (not to be given in patients on Bdq and Dlm)
(3) Combination of Metoclopromide and Ondansetron. Watch out for Concomitant Cardiac Pathology prior to use.
Both anti- emetics may be given as oral, IV or IM

[2]Benzodiazepines
(1) Diazepam 5 mg/tab OD

Management of Nephrotoxicity

Possible Causative anti-TB Drugs: **S, Km, Am, Cm**



[1]Other causes of renal insufficiency
(1) diabetes
(2) dehydration
(3) congestive heart failure
(4) urinary obstruction
(5) urinary tract infection
(6) prostatic hypertrophy

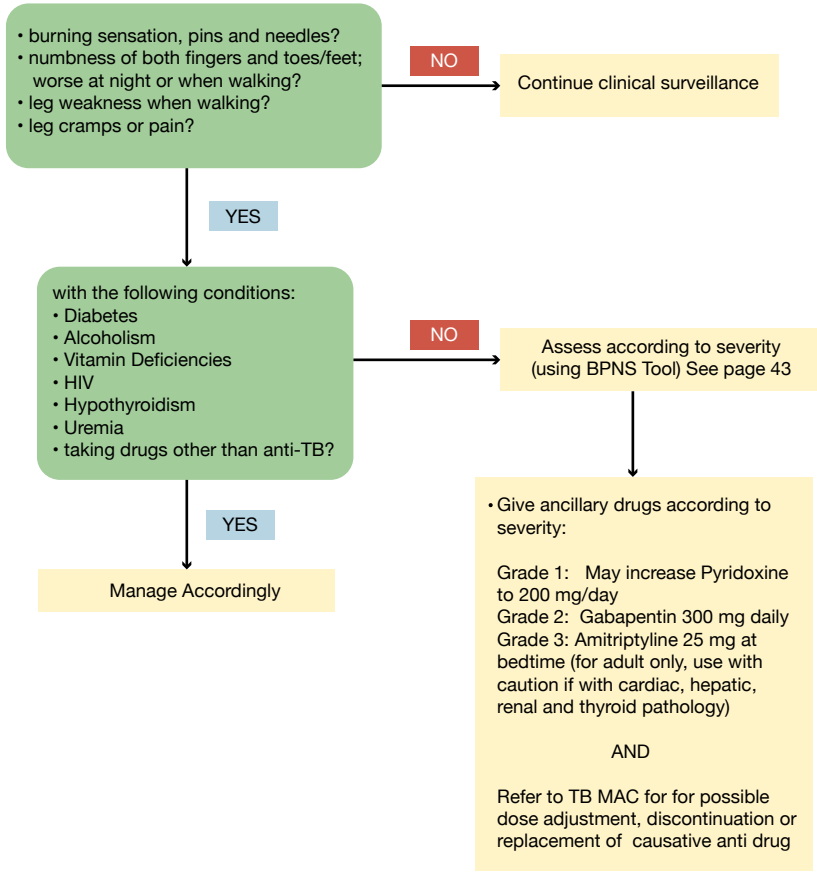
Calculation of Creatinine Clearance (Estimated Glomerular Filtration Rate)

$$\text{weight (kg)} \times (140 - \text{age}) \quad \times \quad \frac{\text{Constant}}{\text{Serum Creatinine (umol/L)}}$$

Constant: for Male = 1.23, for Female = 1.04
If Serum Creatinine value is given in mg/dl, it can be converted to umol/l by multiplying by 88.4.

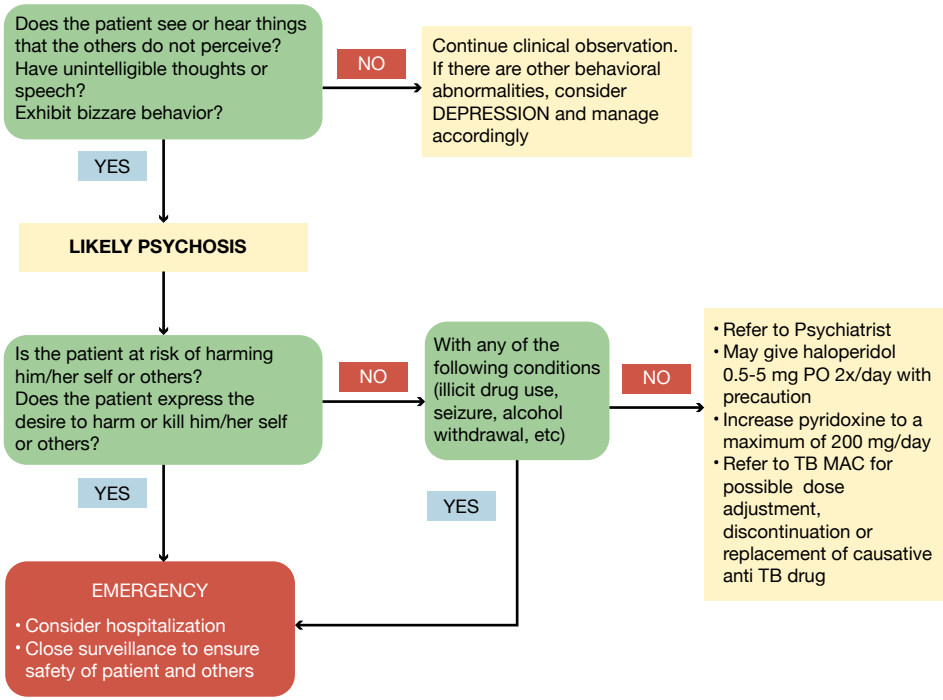
Management of Peripheral Neuropathy

(Possible causative anti-TB Drugs: **Lzd, H, Cs,** S, Am, Km,Cm, Lfx, Mfx)



Management of Psychosis

(Possible causative anti-TB Drugs: **Cs,** Lfx, Mfx, H, Pto)



Management of Prolonged QTc

	Grade 1 (Mild)	Grade 2 (Moderate)	Grade 3 (Severe)
Prolonged QTc (ECG)	QTc 450 - 480 ms	QTc 481 - 500 ms	QTc ≥501 ms on at least two separate ECGs
Action to be taken	Check ECG weekly until QTc becomes normal or stable. Rule out other possible cause of QTc prolongation (e.g., hypokalemia, other concomitant drug) and correct it. Continue anti-TB treatment.		Discuss the case with TB MAC immediately. Follow the advice from the MAC. Do ECG every 2-3 days. Stop all anti-TB medication and refer immediately to hospital.

Indication to Consult with Physician or TB MAC

- Repeated or induced vomiting, abdominal pain/gastritis
- Severe joint pain not responding to NSAID
- Hearing loss
- Change of vision
- Tinitus/vertigo/dizziness
- Tingling, burning sensation on feet/hands not responding to 1 week with high dose of pyridoxine
- Depression
- Psychosis
- AST/ALT: >3 ULN
- CrCl: <50 ml/min (or) > 2 times of ULN
- K+: <3.5 mmol/L
- QTc >500ms or 60ms increase from baseline

Indication for Referral to Hospital

- **Seizure**
- **Arrythmia (fast/slow and irregular heart beat)**
- **Severe renal toxicity (Oliguria or Creatinine Clearance <30 ml/min).**
- **Severe hepatotoxicity (Jaundice, AST/ALT: >5 times of ULN, Total Billirubin >3 times of ULN)**
- **Severe electrolyte imbalance (K+ <2.5 mmol/l, Mg+ <1.4 mmol/l)**
- **Severe anemia (Hb<8g/dl)**
- **Acute psychotic crisis**
- **Severe depression**
- **Any other clinical condition that warrants further evaluation and management**

In the referral note, INDICATE patient's anti-TB drugs and other ancillary drugs

ACTIVE DRUG SAFETY MONITORING and Management (aDSM)

An active and systematic clinical and laboratory assessment of patients while on treatment. It applies to patients on treatment with (a) new and repurposed anti-TB drugs, (b) novel MDR-TB regimens, and (c) regimens for extensively drug resistant TB (XDR-TB).

Serious Adverse Events (SAE) refers to any untoward medical occurrence that at any dose:

- Results in death
- Is life threatening
- Requires inpatient hospitalization or results in prolongation of existing hospitalization
- Results in persistent disability/incapacity
- Is a congenital anomaly/birth defect
- SAE that do not immediately result in one of the above outcomes, but which require an intervention to prevent a serious outcome are included

Adverse Events of Special Interests (AESI)

AESI refers to adverse event documented to have occurred during clinical trials and for which the monitoring programme is specifically sensitized to report regardless of its seriousness, severity or causal relationship to the TB treatment.
These are the following:

- Acute kidney injury
- Hepatitis
- Hypokalemia
- Hypothyroidism
- Myelosuppression (Anemia, Leukopenia, Thrombocytopenia: any or all of these)
- Optic Nerve Disorder
- Ototoxicity (hearing impairment, hearing loss)
- Pancreatitis
- Peripheral Neuropathy
- Prolonged QT interval (using Fridericia Formula)
- Psychiatric Disorders and CNS toxicity

Severity Grading of Adverse Event (AE)

Adverse event	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
	Mild	Moderate	Severe	Life threatening	Death
	Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated	Minimal, local or non-invasive intervention indicated; limiting age-appropriate instrumental activities of daily living (ADL)*	Medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting selfcare ADL**	Urgent intervention indicated	

(All AEs from grade 3 to 5 are to be reported electronically/manually to FDA/PD. Some grade 3 and all grade 4 are to be managed at hospital level. For the purpose of managing AEs at peripheral health facilities level, only 3 levels of grading for AEs are illustrated below.)

Adverse Event	Grade 1 (Mild)	Grade 2 (Moderate)	Grade 3 (Severe)
Rash, Allergy, Anaphylaxis			
Allergic reaction	Transient flushing or rash, drug fever <38 degrees C (<100.4 degrees F); intervention not indicated	Intervention or infusion interruption indicated; responds promptly to symptomatic treatment (e.g., antihistamines, NSAIDS, narcotics); prophylactic medications indicated for <=24 hrs	Prolonged (e.g., not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae (e.g., renal impairment, pulmonary infiltrates)
Anaphylaxis			Symptomatic bronchospasm, with or without urticaria; parenteral intervention indicated; allergy-related edema/angioedema; hypotension

GASTROINTESTINAL			
	Grade 1 (MILD)	**Grade 2 (MODERATE)**	**Grade 3 (SEVERE)**
Abdominal Pain	Mild pain	Moderate pain; limiting instrumental ADL	Severe pain; limiting selfcare ADL
ALT (SGPT)	>ULN - 3.0 x ULN	>3.0 - 5.0 x ULN	>5.0 - 20.0 x ULN
AST (SGOT)	>ULN - 3.0 x ULN	>3.0 - 5.0 x ULN	>5.0 - 20.0 x ULN
Bilirubin (Total)	>ULN - 1.5 x ULN	>1.5 - 3.0 x ULN	>3.0 - 10.0 x ULN
Diarrhea	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4 - 6 stools per day over baseline; moderate increase in ostomy output compared to baseline	Increase of ≥7 stools per day over baseline; incontinence; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting selfcare ADL
Gastritis	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; altered GI function; medical intervention indicated	Severely altered eating or gastric function; TPN or hospitalization indicated
Nausea	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition	Inadequate oral caloric or fluid intake; tube feeding, TPN, or hospitalization indicated
Vomiting	1 - 2 episodes (separated by 5 mins) in 24 hrs	3 - 5 episodes (separated by 5 minutes) in 24 hrs	≥6 episodes (separated by 5 minutes) in 24 hrs; tube feeding, TPN or hospitalization indicated

MUSCULOSKELETAL			
	Grade 1 (MILD)	**Grade 2 (MODERATE)**	**Grade 3 (SEVERE)**
Arthralgia	Mild pain	Moderate pain; limiting instrumental ADL	Severe pain; limiting selfcare ADL
ELECTROLYTE ABNORMALITIES			
Hypokalemia	<LLN - 3.0 mmol/L	<LLN - 3.0 mmol/L; symptomatic; intervention indicated	<3.0 - 2.5 mmol/L; hospitalization indicated
Hypomagnesaemia	<1.4 - 1.2 mmol/L	<1.1 - 0.9 mmol/L	<0.8 - 0.6 mmol/L
RENAL			
Acute Kidney Injury	Creatinine level increase of >0.3 mg/dL; creatinine 1.5 - 2.0 x above baseline	Creatinine 2 - 3 x above Baseline	Creatinine >3 x baseline or >4.0 mg/dL; hospitalization indicated
NEUROLOGICAL			
Depression	Mild depressive symptoms	Moderate depressive symptoms; limiting instrumental ADL	Severe depressive symptoms; limiting self care ADL; hospitalization not indicated
Headache	Mild pain	Moderate pain; limiting instrumental ADL	Severe pain; limiting self -care ADL
Hearing Impaired	Adults (on a 1, 2, 3, 4, 6 and 8 kHz audiogram): Threshold shift of 15 - 25 dB averaged at 2 contiguous test frequencies in at least one ear. Adults (if by clinical monitoring): subjective change in hearing in the absence of documented hearing loss. Pediatric (on a 1, 2, 3, 4, 6 and 8 kHz audiogram): Threshold shift >20 dB at 8 kHz in at least one ear.	Adults (on a 1, 2, 3, 4, 6 and 8 kHz audiogram): Threshold shift of >25 dB averaged at 2 contiguous test frequencies in at least one ear. Adults (if by clinical monitoring)): hearing loss but hearing aid or intervention not indicated; limiting instrumental ADL. Pediatric (on a 1, 2, 3, 4, 6 and 8 kHz audiogram): Threshold shift >20 dB at 4 kHz and above in at least one ear.	Adults (on a 1, 2, 3, 4, 6 and 8 kHz audiogram): Threshold shift of >25 dB averaged at 3 contiguous test frequencies in at least one ear; therapeutic intervention indicated. Adults (if by clinical monitoring): hearing loss with hearing aid or intervention indicated; limiting self care ADL. Pediatric (on a 1, 2, 3, 4, 6 and 8 kHz audiogram): hearing loss sufficient to indicate therapeutic intervention, including hearing aids; threshold shift >20 dB at 3 kHz and above in at least one ear; additional speech-language related services indicated

	Grade 1 (MILD)	Grade 2 (MODERATE)	Grade 3 (SEVERE)
Optic Neuritis	Asymptomatic; clinical or diagnostic observations only	Limiting vision of the affected eye (20/40 or better)	Limiting vision in the affected eye (worse than 20/40 but better than 20/200)
Peripheral Sensory Neuropathy	Asymptomatic; loss of deep tendon reflexes or paresthesia	Moderate symptoms; limiting instrumental ADL	Severe symptoms; limiting self care ADL**
Psychosis	Mild psychotic symptoms	Moderate psychotic symptoms (e.g., disorganized speech; impaired reality testing)	Severe psychotic symptoms (e.g., paranoid; extreme disorganization); hospitalization not indicated
Seizure	Brief partial seizure; no loss of Consciousness	Brief generalized seizure	Multiple seizures despite medical intervention
ENDOCRINE			
Hypothyroidism	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; thyroid replacement indicated; limiting instrumental ADL	Severe symptoms; limiting selfcare ADL; hospitalization Indicated
METABOLIC			
Lactic Acidosis	Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated	Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting selfcare ADL
CARDIOVASCULAR			
Prolonged QTc (ECG)	QTc 450 - 480 ms	QTc 481 - 500 ms	QTc >= 501 ms on at least two separate ECGs
HEMATOLOGICAL			
Anemia	Hemoglobin (Hgb) <LLN - 10.0 g/dL; <LLN - 6.2 mmol/L; <LLN -100 g/L	Hgb <10.0 - 8.0 g/dL; <6.2 - 4.9 mmol/L; <100 - 80g/L	Hgb <8.0 g/dL; <4.9 mmol/L;<80 g/L; transfusion indicated
Platelet Count Decreased	<LLN - 75,000/mm^3; <LLN -75 x 10^3/mL	<75,000 - 50,000/mm^3; <75.0 <75.0 - 50.0 x 10^3/mL	<50,000 - 25,000/mm^3; <50.0 -25.0 x 10^3/mL
Absolute neutrophil count low	1500 - 1000/mm^3	999 - 750/mm^3	749 - 500/mm^3

** ADL - Activities of Daily Living

Checklist to Monitor Clinical Condition and Adverse Events by Treatment Supporter

ENGLISH

Observe and ask the followings signs and symptoms. tick(✓) in Yes or No column. If yes, refer patient/report to heath center.	Yes	No
Fever		
Cough		
Cough with blood		
Shortness of breath		
Yellow coloration of skin and/or eyes		
Pale lips and/or fingers & palms		
Checking for Adverse Events		
Have you had any nausea?		
Have you had vomiting?		
Have you had abdominal pain?		
Have you noticed yellowing of your eyes or your skin?		
Have you had diarrhea?		
Have you had pain or burning in your legs?		
Have you had any change in vision?		
Have you had any hearing loss?		
Have you had any dizziness, vertigo or tinnitus?		
Have you had leg cramping?		
Do you feel weaker than before?		
Do you get easily tired than before?		
Have you had any fainting or light-headedness?		
Do you have any chest pain?		
Do you feel pounding/racing or slowness of heart beat/fluttering in chest?		
Do you have any headache?		
Do you feel sad?		
Have you had loss of sleep or sleep disturbance?		
Do you have thoughts of not worth of living?		
Do you feel anxious or agitated?		
Do you hear voices or see things that may not be there?		
Have you had any convulsion/seizures?		
Do you have any rashes?		
Do you have any pain in the joints?		

FILIPINO

Obserbahan at tanungin kung mayroon ang pasyente ng mga sumusunod na sintomas. Lagyan ng tsek (✓) ang kahon katapat ng meron o wala ayon sa sagot ng pasyente. I-refer ang pasyente sa doctor o sa pinakamalapit na health center kapag mayroon isa sa mga sintomas na nabanggit.	**Yes**	**No**
Lagnat		
Ubo		
Ubo o pag-ubo na may kasamang dugo		
Hirap sa paghinga		
Paninilaw ng balat at mata		
Pamumutla ng labi, palad at mga daliri		
Mayroon ka bang nararamdaman kagaya ng mga sumusunod:		
Pakiramdam na nasusuka?		
Pagsusuka?		
Pananakit ng tyan o sikmura?		
Paninilaw ng mata at balat?		
Pagtatae?		
Pananakit o pamamanhid ng binti?		
Pagbabago sa paningin o panlalabo ng paningin?		
Paghina ng pandinig? Ugong sa loob ng tainga?		
Pagkahilo?		
Pamumulikat?		
Mas mahina ba ang pakiramdam mo ngayon?		
Mas madali ka bang mapagod ngayon?		
Nawawalan ka ba ng malay o nakararamdam ka ba ng panghihilo?		
Paninikip at pagkabog ng dibdib?		
Nakararamdam ka ba ng mabilis o mahinang pagtibok ng puso?		
Pananakit ng ulo?		
Malulungkutin?		
Pagkabalisa o kulang sa tulog?		
Walang ganang mabuhay?		
Pagka-aburido o pagkabalisa?		
May naririnig ka bang boses na di naririnig ng iba?		
Kumbulsyun o pangingisay?		
Pangangati at pamamantal ng balat?		
Pananakit ng kasukasuan?		

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Description of Some Important Drug Side Effects for the TREATMENT SUPPORTER

Drug Side Effect	Signs and Symptoms
Arrthymia (irregular pulse or heart beat)	QTc prolongation (>500 ms) in ECG recording If symptomatic: fainting attack, chest pain, sweating, light-headedness or dizziness, shortness of breath, fluttering in chest, feeling of racing or slowness heart rate
Peripheral Neuropathy	A nerve problem that can cause weakness, tingling sensation and numbness, most often in fingers, toes, arms and legs More severe cases can cause a person to have difficulty walking or using hands More common in patients with diabetes or alcoholism
Psychotic Symptoms	Person sees or hears voices or noises that are not real Person hears voices telling them to hurt themselves or other people Person becomes obsessed about something (for example: religion) or about a person Confusion, aggression, serious difficulty in sleeping

Description of Some Important Drug Side Effects for the TREATMENT SUPPORTER

Drug Side Effect	Signs and Symptoms
Depression	• Difficulty concentrating • Too much sleeping, not able to sleep • Loss of appetite or increase in appetite • Feeling hopeless about life or helpless to change their lives
Hypothyroidism	The thyroid gland is not producing enough thyroid hormone Feeling of tiredness or low energy and weight gain
Hepatitis	When the liver becomes swollen and does not work as well as it should. With symptoms of loss of appetite, nausea, stomach pain, severe vomiting, dark urine, pail stool and yellowish discoloration of skin and sclerae
Kidney failure	The kidneys are unable to produce urine and these wastes remain in the body, nausea, loss of appetite, weakness, confusion, muscle cramp
Electrolyte disturbance	An imbalance of chemicals in the body that can cause the patient to feel weak, have cramps and in serious cases can cause heart problems

Ancillary Drugs used in Managing Adverse Event

ADVERSE EVENT	ANCILLARY DRUG	DOSAGE
Gastrointestinal Drugs		
Nausea, vomiting, upset stomach	Metoclopramide	10 mg/tab/IV/IM 30 minutes before taking anti TB Drugs; can be given 3-4x/day as needed for vomiting Renal Dose: CrCl <40 ml/min: decrease dose by 50% CrCl <10 ml/min: decrease dose by 75%
For Anticipatory Vomiting	Ondansetron (and other serotonin 5-HT3 receptor antagonist)	4-8 mg p.o. 30 minutes before taking anti TB drugs, repeated q 8 hours
	Diazepam	2-10 mg 30-60 minutes prior to taking anti TB Drugs (watch out for dependence and addiction)
Heartburn, acid indigestion, sour stomach, ulcer	H2-blockers Ranitidine Famotidine	300 mg/tab p.o. at bedtime 40 mg/tab p.o. at bedtime
	Proton Pump Inhibitors Omeprazole Lansoprazole *Avoid antacids because they can decrease absorption of fluoroquinolone	20 mg/tab p.o. at bedtime 15 mg/tab p.o. at bedtime
Diarrhea	Loperamide	4 mg initially; 2 mg after each loose stool max of 16 mgs for 24 hrs

Ancillary Drugs used in Managing Adverse Event

Psychiatric Drugs		
Depression	Sertraline	Start 25-50 mg p.o. daily, usual effective dose 50-200 mg/day, maximum dose 200 mg/day
Insomnia	Diphenhydramine, Zoldipem	25-50 mg p.o. at bed time 10 mg/tab p.o. at bed time
Psychosis	Haloperidol	Start 0.5 to 5.0 mg p.o. 2 or 3 times a day. Usual effective dose 2-10 mg/day (note: include biperiden to address extrapyramidal symptoms)
	Quetiapine Fumarate	Immediate Release: Initially at 25 mg p.o. q 12 hr, increased daily in increments of 25-50 mg q 8-12 hr to 300-400 mg/day at intervals of > 2 days
Prophylaxis of neurological complications of cycloserine and isoniazid	Pyridoxine (vitamin B6)	At least 50 mg for every 250 mg of Cycloserine
Peripheral neuropathy	Gabapentin	300mg/tab p.o. q 8hrs
	Pregabalin*	50mg/tab p.o. q 8 hrs

Note: Use ancillary drugs that are included in the latest Philippine National Formulary Essential Medicine List.

*Not in the Essential Medicine List but may be considered as an alternative drug

Ancillary Drugs used in Managing Adverse Event

Seizures	Diazepam (for active seizing)	0.2-0.4 mg/kg up to 5-30 mg IV
	Phenytoin	Intravenous load: 10-20 mg/kg (1,000 mg in typical adult) IV, not faster than 50 mg/min Oral load: 400 mg initially, then 300 mg in two hours and four hours Maintenance 5 mg/kg or 100 mg p.o. three times a day
	Carbamazepine	200-400 mg p.o. two or four times a day
	Valproic acid	Start 15 mg/kg p.o. daily or divided in two daily doses, maximum 60 mg/kg
	Phenobarbital	Intravenous load: 15-20 mg/kg up to 300-800 mg IV at 25-50 mg/min Maintenance: 60 mg p.o. two or three times a day

Ancillary Drugs used in Managing Adverse Event

Vestibular symptoms	Meclizine	25 mg/tab p.o. q 6 hrs
Musculoskeletal pain, arthralgia, headaches	Ibuprofen Mafenamic Acid Paracetamol Celecoxib	200 mg/tab p.o. q 8 hrs PRN in full stomach 500 mg/tab p.o. q 8 hrs PRN in full stomach 500 mg/tab p.o. q 4 hrs PRN 100-200 mg/cap p.o. BID
Cutaneous reactions, itching	Hydrocortisone cream Calamine/zinc oxide ointment*	1-2% apply to affected area 3-4x/day PRN Apply to affected area, 3-4x/day
Systemic hypersensitivity reactions	Antihistamines Diphenhydramine Cetirizine Corticosteroids prednisone dexamethasone	25-50 mg/cap p.o. q 6-8 hrs 10 mg/tab p.o. once a day 1-2 mg/kg/day and decrease dose at 5-10mg daily 4-8 mg/tab q 8hrs

Note: Use ancillary drugs that are included in the latest Philippine National Formulary Essential Medicine List

*Not in the Essential Medicine List but may be considered as an alternative drug

Ancillary Drugs used in Managing Adverse Event

Electrolyte wasting	Potassium Chloride	3.3-3.5: 40 mEq PO daily 2.9-3.2: 60-80 mEq p.o. daily 2.7-2.8: 60 mEq p.o. three times a day 2.4-2.6: 80 mEq p.o. every eight hours < 2.4: 10 mEq/hr IV and 80 mEq p.o. every six to eight hours
	Magnesium gluconate	1.5–1.9: 1,000 mg-1,200 mg 1.0–1.4: 2,000 mg/IV or IM < 1.0: 3,000 mg-6,000 mg/IV or IM
	Calcium replacement therapy	500 mg tab p.o. 3x/day Note: K and Mg replacement must be given 2 hours before or four hours after intake of FQ
Myelosuppression	Iron Supplementation, decrease dose of Lzd	Epoetin alfa prefilled syringes of 10 000 UI or 40 000 IU/ml to be stored in cold chain (2°C to 8°C). Dosing Epoetin alfa: 150 IU/Kg three times a week or 450 IU/Kg once a week SQ or IV (to be used with caution in patients with epilepsy, thrombocytosis, chronic liver failure, hyperkalemia and hypertension)
	Erythropoietin	
	Blood transfusion	

Treatment Outcome Definition for Drug Sensitive Tuberculosis

TREATMENT OUTCOME	DEFINITION
Cured	A patient with bacteriologically-confirmed TB at the beginning of treatment and who was smear- or culture-negative in the last month of treatment and on at least one previous occasion in the continuation phase
Treatment Completed	• BC at start of treatment with smear (-) or culture (-) in the last month of treatment and on at least one occasion in the continuation phase • BC at start of treatment – completed the recommended course of treatment without evidence of failure – without any record of negative smear and culture results in the last month of treatment and on at least one occasion in the continuation phase • CD who completed the recommended course of treatment
Treatment Failed	• Smear or culture positive at 5th month of treatment or later during treatment • Treatment terminated due to evidence of additional acquired resistance (e.g., Rif-Res on Xpert at 2nd month of treatment) • A patient for whom follow-up sputum examination was not done (e.g., child or EPTB) and who does not show clinical improvement anytime during treatment • Severe uncontrolled adverse drug reaction
Died	• Patient died for any reason during TB treatment
Lost to Follow up	• Interrupted treatment for at least 2 consecutive months • A patient diagnosed with active TB but was not started on treatment
Not Evaluated	• A patient for whom no treatment outcome is assigned • This includes patients transferred to another facility for continuation of treatment but the final outcome was not determined

Treatment Outcome Definition for Drug Resistant Tuberculosis treated with Standard Short All Oral Regimen (SSOR)

TREATMENT OUTCOME	DEFINITION
Cured	• BC at start of treatment • Completed the recommended duration of treatment without evidence of failure • At least 3 consecutive negative cultures after the intensive phase (at least 30 days apart)
Treatment Completed	• Completed the recommended duration of treatment • No record of 3 consecutive cultures after intensive phase • No evidence of clinical deterioration
Treatment Failed	• Presence of any of the following: - Treatment terminated or need for permanent regimen change - Lack of evidence of at least two* consecutive negative cultures (and not followed by a positive culture) by the end of an extended intensive phase (6 months) of the shorter regimen - Positive sputum smear (confirmed by two consecutive samples) after > 6 months of treatment - Culture reversion** in the continuation phase after conversion to negative - Evidence of additional acquired resistance to a FQ or a SLI, - Adverse drug reaction resulting to switching to a new regimen
Died	• Patient died for any reason during TB treatment
Lost to Follow up* **	• Interrupted treatment for at least 2 consecutive months
Not Evaluated	• A patient for whom no treatment outcome is assigned. • This includes patients transferred to another facility for continuation of treatment but the final outcome was not determined.

*Perform culture from two specimens every month during the intensive phase or do culture after 4, 6, 8, 12 and 16 weeks of treatment

** Culture reversion (to positive) after an initial conversion; two consecutive cultures taken at least 30 days apart, are found to be positive during continuation phase.

Remark: In all other situations when failure is suspected, the possible causes, patient management strategy and registration of outcome will be discussed by the expert committee

*** If a patient has received the SSTR/SSOR for more than a month and returns for treatment after an interruption of 2 consecutive months or more, he is not restarted on the SSTR/SSOR but on a longer MDR-TB regimen which is individualized based on the medicines most like to be effective. If the interruption is less than 2 months, e.g., medical indication in case of adverse events (AE), or patient's decision, then the SSTR/SSOR can be continued and the missed doses added to the rest of the treatment.

Treatment Outcome Definition for Drug Resistant Tuberculosis treated with Standard Long Oral Regimen (SLOR) and Individualized Treatment Regimen (ITR)

TREATMENT OUTCOME	DEFINITION
Cured	• BC at start of treatment • Completed the recommended duration of treatment without evidence of failure • At least 3 consecutive negative cultures after the intensive phase (at least 30 days apart)
Treatment Completed	• Completed the recommended duration of treatment • No record of 3 consecutive cultures after intensive phase • No evidence of clinical deterioration
Treatment Failed	• Treatment terminated or need for permanent regimen change of at least two anti-TB drugs because of: - Lack of conversion by the end of 8 month from the start of treatment or - Bacteriological reversion after the conversion to negative in the initial 8 month of treatment or - Evidence of additional acquired resistance to fluoroquinolones or other second-line drugs in the regimen - Adverse drug reaction that needed to completely stop MDR/RR-TB treatment
Died	• Patient died for any reason during TB treatment
Lost to Follow up* **	• Interrupted treatment for at least 2 consecutive months
Not Evaluated	• A patient for whom no treatment outcome is assigned • This includes patients transferred to another facility for continuation of treatment but the final outcome was not determined

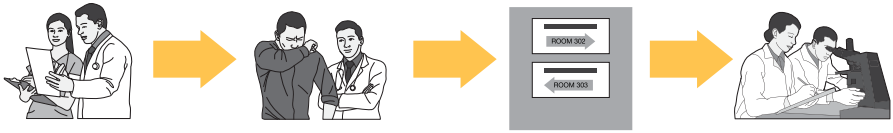
- Culture conversion (to negative); two consecutive cultures taken at least 30 days apart, are found to be negative, the specimen collection date of the 1st culture is taken as culture conversion date
- Culture reversion (to positive) after an initial conversion; two consecutive cultures taken at least 30 days apart, are found to be positive, for the purpose of defining "Treatment Failed", culture reversion is considered only when itoccurs after 8 months of treatment

TB Infection Prevention & Control

Prevention of Transmission of TB in Health Care Settings

STEP	Action	Description
1	**Screen**	• Designate health care worker (Triage) to screen patients with prolonged cough immediately after they arrive at the facility. • Separate patients with symptoms of TB and patients on treatment from other patients
2	**Educate**	• Instruct all patients with cough on cough hygiene (i.e. covering the nose and mouth when coughing or sneezing) • Educate on safe sputum disposal
3	**Separate**	• Keep patients with symptoms of TB and patients on treatment away from other patients and allow them to stay in a well ventilated waiting area • If possible, provide face masks or tissue to cover their mouths and noses while waiting
4	**Investigate for TB or refer to TB Clinic**	• Perform recommended TB diagnostic tests or collect and send specimen to TB diagnostic facility
5	**Monitor and evaluate**	• Monitor and evaluate the TB prevention plan

Prevention of TB Transmission In Healthcare Settings



Screen

- Designate of health care worker (Triage) to screen patients with prolonged cough immediately after they arrive at the facility.
- Separate patients with symptoms of TB and patients on treatment from other patients

Educate

- Instruct all patients with cough on cough hygiene (i.e. covering the nose and mouth when coughing or sneezing
- Educate on safe sputum disposal

Separate

- Segregate patients with TB symptoms and patients on TB treatment from other patients and allow them to stay in a well ventilated waiting area
- If possible, provide face masks or tissue to cover their mouths and noses while waiting

Investigate or refer

Perform recommended TB diagnostic tests or collect and send specimen to TB diagnostic facility

TB Preventive Treatment

Population groups to receive TB preventive treatment after exclusion of active TB disease

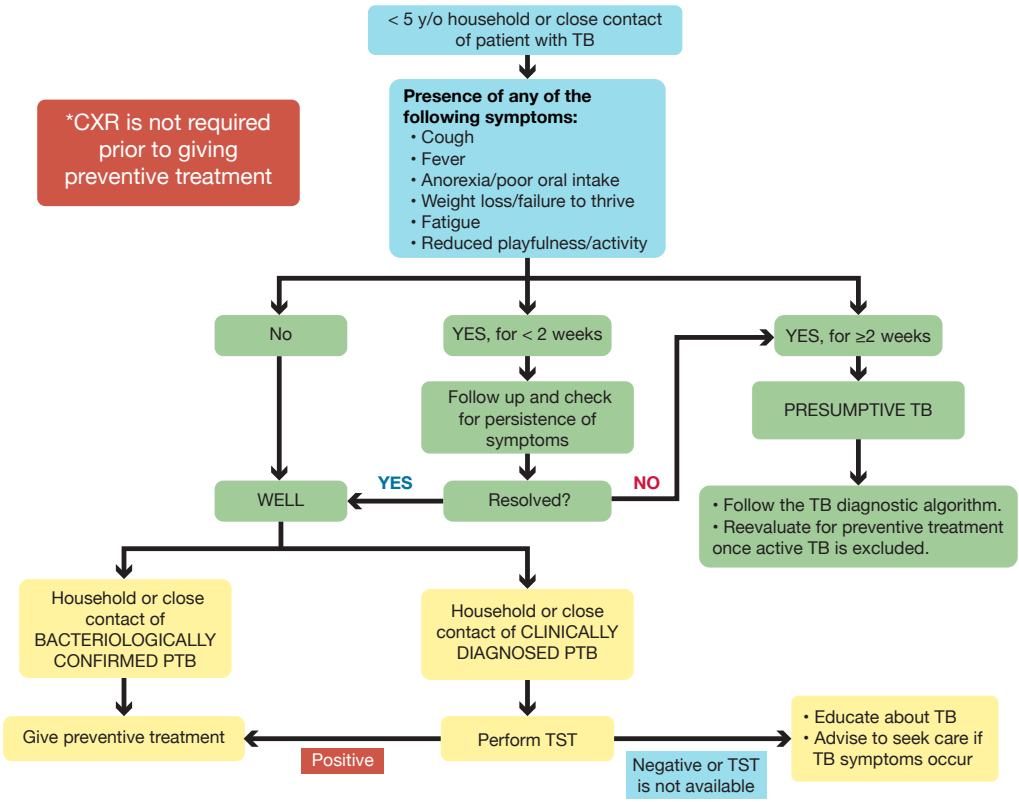
- All household contacts of bacteriologically-confirmed pulmonary TB
- Children less than 5 years old who are household contacts of clinically diagnosed pulmonary TB
- Close contact of bacteriologically-confirmed pulmonary TB (outside the houshold)
- People living with HIV
- Other risk groups
    - Patients receiving dialysis
    - Patients preparing for an organ or hematological transplantation
    - Patients initiating anti-TNF treatment
    - Patients with silicosis

Checking eligibility of different risk groups for TB Preventive Treatment using TST

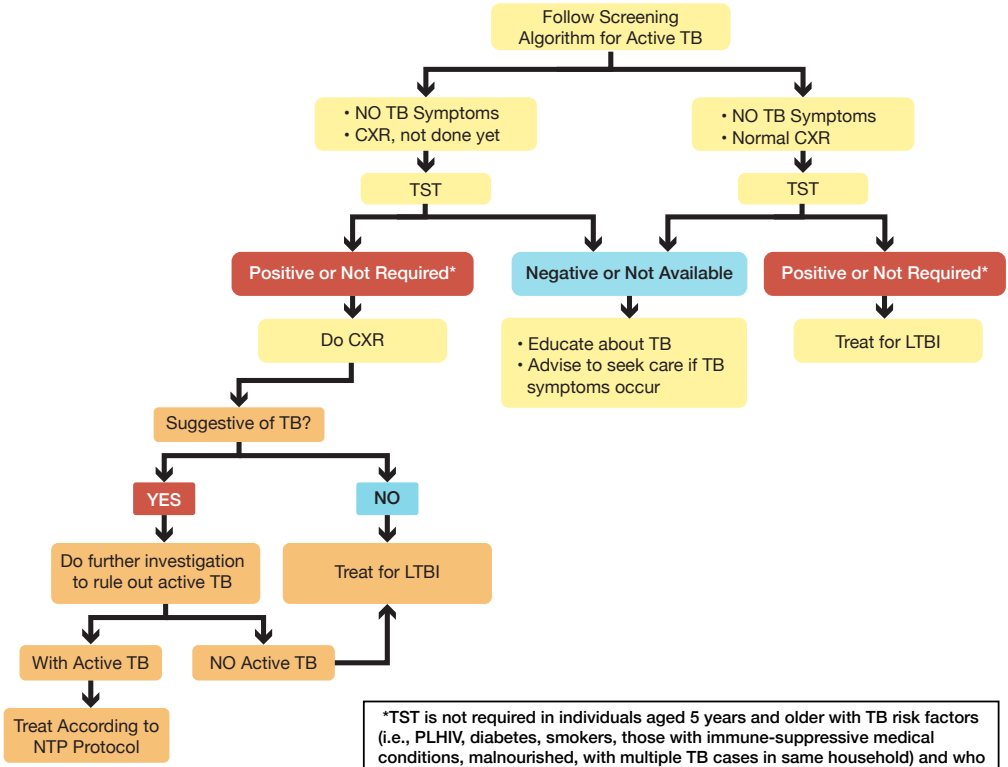
	TST NOT REQUIRED (Eligible for LTBI Tx)	TST REQUIRED (Eligible if positive)	NOT ELIGIBLE*
	<5yo, BC TB index	<5yo, CD TB index	---
HH contacts	≥5yo, BC TB index with TB risk	≥5yo, BC TB index, no TB risk	≥5yo, CD TB index
Close contacts	---	All ages, BC TB index	All ages, CD TB index
PLHIV	Ages ≥1yo		Age <1yo (If not contact of a TB case)
Other Risk Groups	---	• Patient receiving dialysis, • Patients preparing for an organ or hematological transplantation • Patients initiating anti-TNF treatment • Patients with silicosis • Individuals in jails or prisons	---

* TB Risk - PLHIV, diabetes, smokers, those with immune-suppressive medical conditions, malnourished, with multiple people with TB in same household

LTBI algorithm in HIV-negative child contacts<5 years old

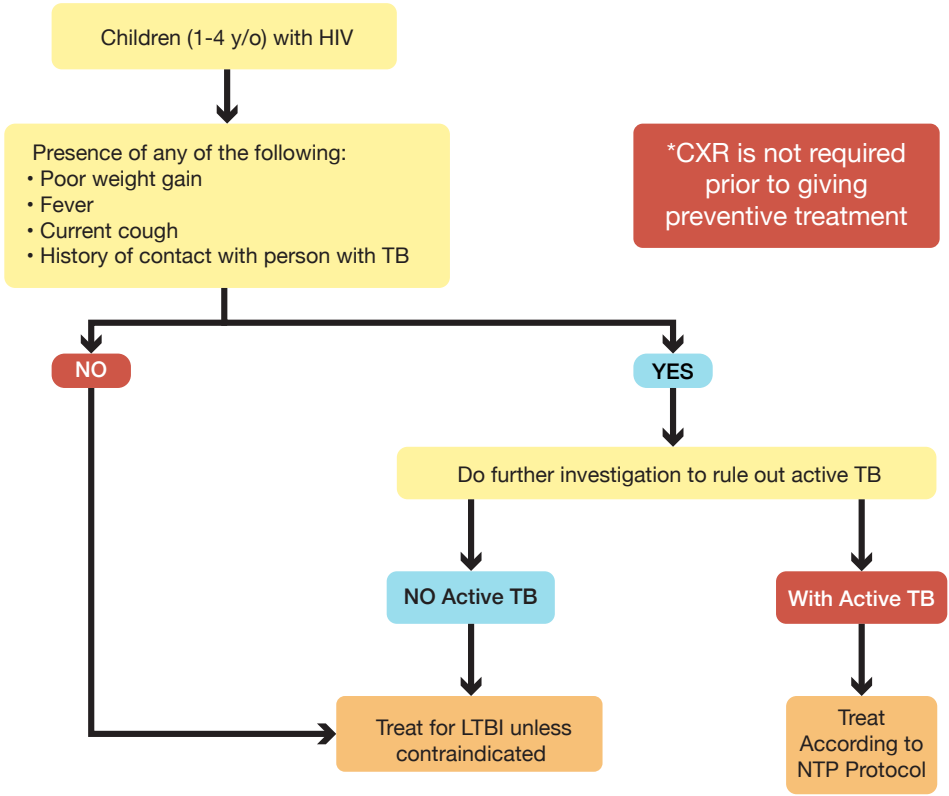


LTBI algorithm in HIV-negative at-risk individuals ≥ 5 years old

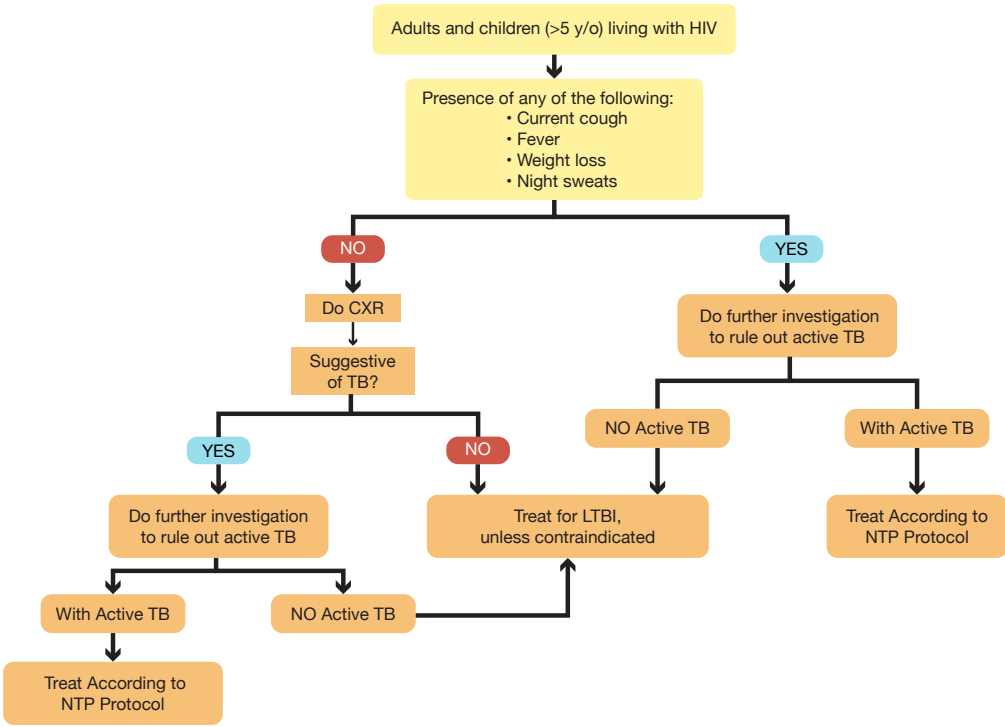


*TST is not required in individuals aged 5 years and older with TB risk factors (i.e., PLHIV, diabetes, smokers, those with immune-suppressive medical conditions, malnourished, with multiple TB cases in same household) and who are household contacts of bacteriologically confirmed pulmonary TB.

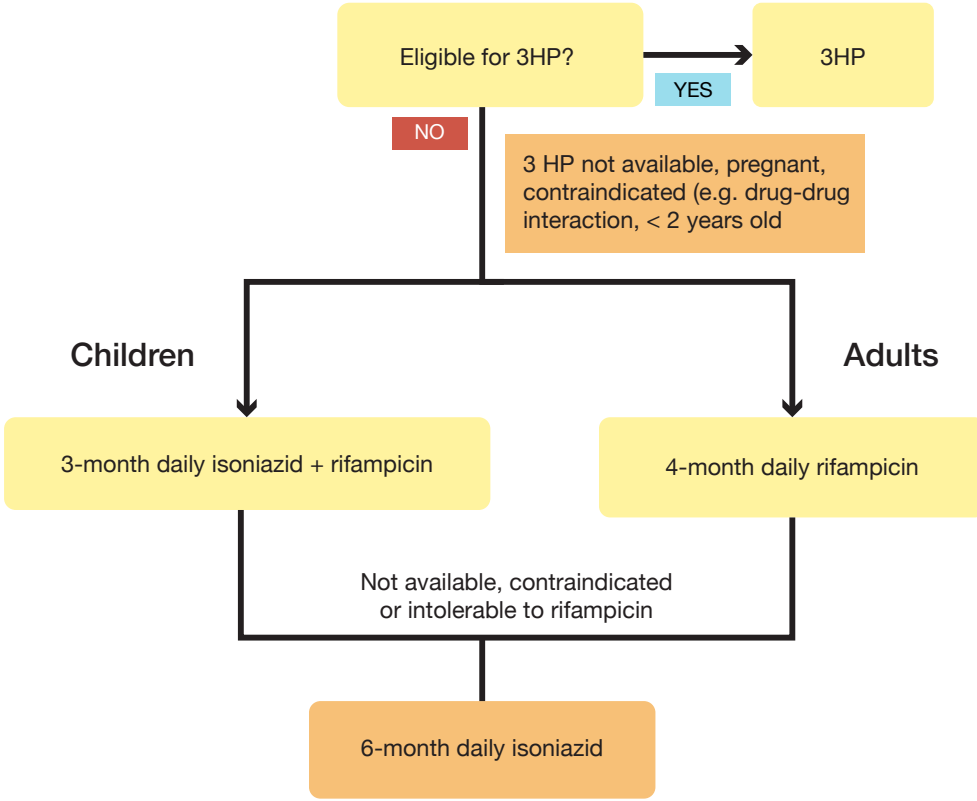
LTBI algorithm in children with HIV aged 1-4 years



LTBI algorithm in adults and children (≥ 5 yo) with HIV



Selection of TB preventive treatment regimens



Dosing for 6H, 4R and 3HR in children

Body Weigth (kg)	Dosage (in ml)	
	isoniazid 200mg/ 5ml (at 10mg/kg)	Rifampicin 200mg/ 5ml (at least 15mg/kg)
2.1-3	0.75	1.0
3.1-4	1.0	1.5
4.1-5	1.25	2.0
5.1-6	1.5	2.25
6.1-7	1.75	2.5
7.1-8	2.0	3.0
8.1-9	2.25	3.5
9.1-10	2.5	3.75
10.1-11	2.75	4.0
11.1-12	3.0	4.5
12.1-13	3.25	5.0
13.1-14	3.5	5.25
14.1-15	3.75	5.5
15.1-16	4.0	6.0
16.1-17	4.25	6.5
17.1-18	4.5	6.75
18.1-19	4.75	7.0
19.1-20	5.0	7.5
20.1-21	5.25	8.0
21.1-22	5.5	8.25
22.1-23	5.75	8.5
23.1-24	6.0	9.0
24.1-25	6.25	9.5
25.1-26	6.5	9.75
26.1-27	6.75	10.0
27.1-28	7.0	10.5
28.1-29	7.25	11.0
29.1-30	7.5	11.25

Dosing for 3-month weekly rifapentine and isoniazid in adults and children ≥ 2 years old

Age	≥2 yo	2-11 yo	≥12yo
Body Weight (in kgs)	Rifapentine 100mg/tab	Isoniazid 200mg/5ml (at 25mg/kg)	Isoniazid 200mg/5ml (at 15mg/kg)
	No. of tablets	in ml	in ml
10-12	1 tabs	7.5ml	--
12.1-14	2	8.75	--
14.1-16	3	10.0	--
16.1-18	3	11.0	--
18.1-20	3	12.0	--
20.1-22	3	13.0	--
22.1-24	3	14.5	--
24.1-25	3	15.0	--
25.1-27	4	17.0	10.0
27.1-30	4	18.5	11.0
30.1-32	4	20.0	12.0
32.1-35	5	21.0	13.0
35.1-37	5	22.5	14.0
37.1-40	5		15.0
40.1-42	5		16.0
42.1-45	5		17.0
45.1-50	5		18.0
50.1-55	6		20.0
55.1-58	6		21.0
>=58.1	6		22.5

Dosing for 6H and 4R in adults

Drug	Dosing in Adults
Isoniazid (H)	5 mg/kg (range: 4-6 mg/kg Not to exceed 400mg daily)
Rifampicin (R)	5 mg/kg (range: 8-12 mg/kg Not to exceed 600mg daily)

Definition of LTBI treatment outcomes

- **Completed** - an individual who has completed the prescribed duration of treatment and remains well or asymptomatic during the entire period.
- **Lost to follow-up** - an idividual who interrupted TB preventive treatment for two (2) consecutive months or more.
- **Died** - an individual who dies for any reason during the course of therapy.
- **Failed** - an individual who developed active TB disease anytime while on TB preventive treatment.
- **Not Evaluated** - an individual who has been transferred to another health facility with proper referral slip for continuation of TB preventive treatment and whose treatment outcome is not known; include here discontinued by physician because patient cannot tolerate (e.g. severe ADR) or refused to continue.

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