Appendix 46 - TUBERCULOSIS

Table 1: Drug Therapy For Susceptible Tuberculosis Or Empiric Selection Tell Culture Sensitivity Results			
Intensive Phase		Continuation Phase	
Drug Combination	Duration	Drug Combination	Duration
A. Standard Regimen			
Isoniazid (INH) + Rifampin (RIF) + Pyrazinamide + Ethambutol (EMB)	2 Months N.B: stop ethambutol if culture sensitive to Isoniazid (INH) and Rifampin (RIF)	Isoniazid (INH) + Rifampin (RIF)	standard: 4 Months extension: additional 3 months (total 7 months) for patients who had cavitation on the initial (or follow-up) chest radiograph and, in addition, are culture positive at the time of completion of the intensive phase of treatment. Or HIV patient not on antiretroviral therapy.
Regimen: 7 days/ week (preferred) or 5 days/week (only under direct observed therapy)			
B. Alternative Regimen Composition used in case of intolerance to first-line drugs or the presence of monoresistance			
Intensive Phase		Continuation Phase	
Drug Combination	Duration	Drug Combination	Duration
if Pyrazinamide can not be used: Isoniazid (INH) + Rifampin (RIF) + Ethambutol (EMB)	2 months	Isoniazid (INH) + Rifampin (RIF)	7 months
if EMB cannot be used: Isoniazid (INH) + Rifampin (RIF) + Quinolones (Levo OR Moxi)	2 months	Isoniazid (INH) + Rifampin (RIF)	7 months
if INH cannot be used: Quinolones (Levo OR Moxi) + Rifampin (RIF) + Pyrazinamide + Ethambutol (EMB)		Quinolones (Levo OR Moxi) + Rifampin (RIF)	7 months
If a rifamycin cannot be used in the initial regimen due to resistance or intolerance: refer to Table 3			
if several agent of standard regimen cannot be used: refer to Table 3			
C. Tuberculous Meningitis			
Intensive Phase		Continuation Phase	
Drug Combination	Duration	Drug Combination	Duration
for adults: Isoniazid (INH) + Rifampin (RIF) + Pyrazinamide + Ethambutol (EMB)	2 Months N.B: stop ethambutol if culture sensitive to Isoniazid (INH) and Rifampin (RIF)	Isoniazid (INH) + Rifampin (RIF)	7- 10 months
for children: Isoniazid (INH) + Rifampin (RIF) + Pyrazinamide + ethionamide or Aminoglycosides	2 Months	Isoniazid (INH) + Rifampin (RIF)	7- 10 months
D. Culture-Negative Pulmonary Tuberculosis in Adults			
Intensive Phase		Continuation Phase	
Drug Combination	Duration	Drug Combination	Duration
Isoniazid (INH) + Rifampin (RIF) + Pyrazinamide + Ethambutol (EMB)	2 Months N.B: stop ethambutol if culture sensitive to Isoniazid (INH) and Rifampin (RIF)	Isoniazid (INH) + Rifampin (RIF)	2 Months
E. Patient with hepatic disease			
Intensive Phase		Continuation Phase	
Drug Combination	Duration	Drug Combination	Duration
if Pyrazinamide cannot be used: Isoniazid (INH) + Rifampin (RIF) + Ethambutol (EMB)	2 months	Isoniazid (INH) + Rifampin (RIF)	7 months
Treatment without INH and PZA: For advanced liver disease patients, Rifampin (RIF) + Ethambutol (EMB) + a fluoroquinolone (levo or Moxi) or injectable, or cycloserine for 12–18 months			
Treatment without INH: Based on outcomes of studies on INH-resistant tuberculosis, a Rifampin (RIF) + Pyrazinamide + Ethambutol (EMB) ± a fluoroquinolone (levo or Moxi) could be considered for a total duration of at least 6 months			
For patients with severe, unstable liver disease: EMB + a fluoroquinolone (levo or Moxi)+ cycloserine + second-line injectable (Streptomycin OR Amikacin/ kanamycin OR Capreomycin) for 18–24 months			
N.B: Measuring serum aminotransferases and total bilirubin concentrations every 1–4 weeks for at least the first 2–3 months of treatment			
F. Patient with Recurrent Tuberculosis			
1) For patients with relapse who were treated for drug-susceptible tuberculosis using DOT, experts recommend retreatment using the standard intensive phase regimen until the results of susceptibility tests are known.			
2) intensive phase regimen of daily INH + RIF + PZA + EMB + fluoroquinolone (levo or Moxi) + an injectable agent (Amikacin, Streptomycin, Kanamycin, Capreomycin, Carbapenems with clavulanic acid) ± second-line drug (Cycloserine			

Table 2: For latent TB		
Regimens	CDC 2020	WHO 2020
3 months isoniazid + rifapentine given once weekly	Preferred	All are alternative to each other and the choice will depend on availability of appropriate formulations and considerations for age, safety, drug–drug interactions and adherence.
3 months of isoniazid + rifampicin given daily	Preferred	
4 months rifampin given daily	Preferred	
9 months isoniazid given daily	Alternative	
6 months isoniazid given daily	Alternative	
1-month regimen of daily rifapentine + isoniazid	Alternative	not mentioned
12 months isoniazid given daily	Alternative	not mentioned

Table 3: Drug Therapy for Multi-drug resistant Tuberculosis (resistant to INH and RIF ± resistance to other AB)	
Intensive Phase	Continuation Phase
Duration: 5 drug regimens FOR 5 and 7 months after culture conversion **Select 5 drugs** from the following (to which the isolate is susceptible or has low likelihood of resistance): • **Strong Evidence** ○ Fluoroquinolones (levo or moxi) ○ Bedaquiline • **Conditional Evidence** ○ Clofazimine ○ Linezolid ○ Cycloserine ○ Ethambutol (only when other more effective drugs cannot be assembled to achieve a total of five drugs in the regimen) ○ Injectable Agents (Amikacin, Streptomycin) ○ Injectable Carbapenems With Clavulanic Acid) ○ Pyrazinamide • **Based on WHO recommendation**: Delamanid • **Conditional evidence against:** (used only if more effective drugs are available to construct a regimen with at least five effective drug) ○ P-Aminosalicylic Acid ○ Ethionamide/ Prothionamide	• **Duration:** total treatment duration range: • **for MDR-TB:** between 15 and 21 months after culture conversion • **For XDR-TB:** • between 15 and 24 months after culture conversion **Select 4 drugs** from the following (remove one from agent selected in intensive phase): • **Strong Evidence** ○ Fluoroquinolones (levo or moxi) ○ Bedaquiline • **Conditional Evidence** ○ Clofazimine ○ Linezolid ○ Cycloserine ○ Ethambutol (only when other more effective drugs cannot be assembled to achieve a total of five drugs in the regimen) ○ Injectable Agents (Amikacin, Streptomycin) ○ Injectable Carbapenems With Clavulanic Acid) ○ Pyrazinamide • **Based on WHO recommendation**: Delamanid • **Conditional evidence against:** (used only if more effective drugs are available to construct a regimen with at least five effective drug) ○ P-Aminosalicylic Acid ○ Ethionamide / Prothionamide
For the treatment of isoniazid-resistant:	
regimen: Rifampin (RIF) + Pyrazinamide + Ethambutol (EMB) + Fluoroquinolones (levo or moxi) Duration: 6-month duration as whole treatment regimen or 6-month duration for Rifampin (RIF) + Ethambutol (EMB) + Fluoroquinolones (levo or moxi) and 4-month duration for Pyrazinamide (in selected situations (i.e., noncavitary and lower burden disease or toxicity from pyrazinamide)	
Treatment of Contacts Exposed to MDR-TB	
Regimen: single agent fluoroquinolone (levo or moxi) ± second drug, on the basis of drug susceptibility of the source-case M. tuberculosis isolate. Duration: 6 to 12 months N.B: pyrazinamide should not be routinely used as the second drug.	

Table 3: Drug Therapy for Multi-drug resistant Tuberculosis (resistant to INH and RIF ± resistance to other AB)	
Intensive Phase	Continuation Phase
Duration: 5 drug regimens FOR 5 and 7 months after culture conversion **Select 5 drugs** from the following (to which the isolate is susceptible or has low likelihood of resistance): • **Strong Evidence** ○ Fluoroquinolones (levo or moxi) ○ Bedaquiline • **Conditional Evidence** ○ Clofazimine ○ Linezolid ○ Cycloserine ○ Ethambutol (only when other more effective drugs cannot be assembled to achieve a total of five drugs in the regimen) ○ Injectable Agents (Amikacin, Streptomycin) ○ Injectable Carbapenems With Clavulanic Acid) ○ Pyrazinamide • **Based on WHO recommendation**: Delamanid • **Conditional evidence against:** (used only if more effective drugs are available to construct a regimen with at least five effective drug) ○ P-Aminosalicylic Acid ○ Ethionamide/ Prothionamide	• **Duration:** total treatment duration range: • **for MDR-TB:** between 15 and 21 months after culture conversion • **For XDR-TB:** • between 15 and 24 months after culture conversion **Select 4 drugs** from the following (remove one from agent selected in intensive phase): • **Strong Evidence** ○ Fluoroquinolones (levo or moxi) ○ Bedaquiline • **Conditional Evidence** ○ Clofazimine ○ Linezolid ○ Cycloserine ○ Ethambutol (only when other more effective drugs cannot be assembled to achieve a total of five drugs in the regimen) ○ Injectable Agents (Amikacin, Streptomycin) ○ Injectable Carbapenems With Clavulanic Acid) ○ Pyrazinamide • **Based on WHO recommendation**: Delamanid • **Conditional evidence against:** (used only if more effective drugs are available to construct a regimen with at least five effective drug) ○ P-Aminosalicylic Acid ○ Ethionamide / Prothionamide
For the treatment of isoniazid-resistant:	
regimen: Rifampin (RIF) + Pyrazinamide + Ethambutol (EMB) + Fluoroquinolones (levo or moxi) Duration: 6-month duration as whole treatment regimen or 6-month duration for Rifampin (RIF) + Ethambutol (EMB) + Fluoroquinolones (levo or moxi) and 4-month duration for Pyrazinamide (in selected situations (i.e., noncavitary and lower burden disease or toxicity from pyrazinamide)	
Treatment of Contacts Exposed to MDR-TB	
Regimen: single agent fluoroquinolone (levo or moxi) ± second drug, on the basis of drug susceptibility of the source-case M. tuberculosis isolate. Duration: 6 to 12 months N.B: pyrazinamide should not be routinely used as the second drug.	