

Adverse effects of MDR-TB/ART co-treatment[†]

Signs or symptoms	Response
Abdominal pain	May be caused by several drugs. Take drugs with food (except for DDI or IDV). Treat symptomatically (see <i>Palliative Care</i>).
Nausea, vomiting (see 7.4 of <i>Chronic Care for MDR-TB</i>)	May be caused by many drugs. If due to ARV, will often improve in a few weeks. If due to ethionamide or PAS, it may be chronic. Check for other causes of vomiting (see <i>Acute Care</i>). If mild, advise to take drugs with porridge and treat symptomatically. If serious, rehydrate with ORS or IV line.
Diarrhoea (see 7.5 of <i>Chronic Care for MDR-TB</i>)	If due to ART, will improve in a few weeks. If due to PAS, may be chronic. If dehydrated, re-hydrate with ORS or IV line (see <i>Acute Care</i>). Look and treat for other possible causes of diarrhoea.
Fatigue	Consider anemia, especially if on AZT. Check hemoglobin. Fatigue commonly lasts 4 to 6 weeks especially when starting AZT. If severe or longer than this, call for advice or refer. Consider hypothyroidism due to ethionamide and PAS and check TSH.
Depression, anxiety, nightmares, psychosis (see 7.7 of <i>Chronic Care for MDR-TB</i>)	This may be due to EFZ or cycloserine/terizidone. If due to EFZ, will usually last less than 3 weeks. Mild depression can be managed with amitryptiline at night (see <i>Acute Care</i>). Call for advice or refer if severe depression or suicidal or psychosis. Serious symptoms may resolve with decreased dose of cycloserine/terizidone.
Itching of skin, skin rash	If mild, give antihistamine and monitor closely. If has recently started NVP and not responding to antihistamine, consider changing NVP for EFZ. If generalized, peeling, mucosal involvement, or other symptoms (fever, jaundice, etc.) stop all drugs (including CTX) and challenge later when rash has resolved. Call for advice.

[†] From Section 7.9 of *Chronic Care for MDR-TB*



Jaundice (yellow skin or eyes)	Check liver function tests (AST, ALT, bilirubin) and stop all drugs. May be due to EFZ, NVP, pyrazinamide or ethionamide or other drugs. Call for advice on how to restart drugs.
Pallor: anaemia	If possible measure hemoglobin and exclude OI. Refer/consult (and stop AZT/substitute d4T) if severe pallor or symptoms of anemia or very low hemoglobin (<8 g/dL; <7 g/dL in pregnant woman).
Neuropathy (burning sensation in feet)	May be due to ddl, d4T, cycloserine/terizidone, isoniazid, injectable or other drugs. Switch stavudine for zidovudine. If no improvement, start amitryptiline or carbamazepine (see <i>Acute Care</i>) and call for advice.
Muscle cramps, muscle spasms	May have electrolyte-wasting due to capreomycin. Check potassium immediately; replace low potassium with bananas or potassium supplements.
Headache	Give paracetamol. Assess for meningitis (See <i>Acute Care</i>). If on AZT or EFZ, reassure that this is common and usually self-limited. If chronic, may be due to cycloserine.
Renal insufficiency (swelling, decreased urine, hypertension)	Check creatinine. Stop injectable and call for advice.
Hypothyroidism (fatigue, slowing)	Due to ethionamide and PAS. Do not stop any medications. Give thyroxine 50-100 mcg/day and recheck. The thyroid will go back to normal once MDR-TB treatment is over.
Joint pains	Give non-steroidal anti-inflammatory (ibuprofen).
Fever	Check for common causes of fever (see <i>Acute Care</i>). This could be a side effect, an opportunistic infection or other new infection or immune reconstitution syndrome. Call for advice or refer.
Blue/black nails	Reassure. It is normal with AZT.
Gradual hearing loss (confirm that this is not due to ear wax)	May be due to injectable. Refer or consult.
Dizziness, lack of balance	May be due to injectable. Refer or consult.
Changes in fat distribution	Due to d4T or ddl. Discuss carefully with your patient—can she/he accept it?

Anti-TB drug dosing[†]

Adults and adolescents

Drug	Weight class			
	Average daily dosage	<50 KG	51–65 KG	>65 KG (max dose)
Isoniazid (H) (100, 300 mg)	4–6 mg/kg daily	300 mg	300 mg	300 mg
Rifampicin (R) (150, 300 mg)	10–20 mg/kg daily	600 mg	600 mg	600 mg
Ethambutol (E) (400 mg)	25 mg/kg daily	1200 mg	1400 mg	1600 mg
Pyrazinamide (Z) (500 mg)	30–40 mg/kg daily	1500 mg	1750 mg	2000 mg
Streptomycin (S) (1 g vial)	15–20 mg/kg daily	750 mg	1000 mg	1000 mg
Kanamycin (Km) (1 g vial)	15–20 mg/kg daily	750 mg	1000 mg	1000 mg
Capreomycin (Cm) (1 g vial)	15–20 mg/kg daily	750 mg	1000 mg	1000 mg
Ofloxacin (Ofx) (200 mg)	Usual adult dose is 800 mg	800 mg	800 mg	800-1000 mg
Ciprofloxacin (Cfx) (500 mg)	20-30 mg/kg daily	1500 mg	1500 mg	1500 mg
Moxifloxacin (Mfx) (400 mg)	Usual adult dose is 400 mg	400 mg	400 mg	400 mg
Ethionamide (Eto) (250 mg)	15–20 mg/kg daily	500 mg	750 mg	750–1000 mg
Cycloserine (Cs) (250 mg)	15–20 mg/kg daily	500 mg	750 mg	750–1000 mg
Terizidone (Trd) (250 mg)	15–20 mg/kg daily	500 mg	750 mg	750–1000 mg
PASER (4 g sachets)	150 mg/kg daily	8 g	8 g	8 g

[†] From Section 5.6 of *Chronic Care for MDR-TB*



Children

Medication (common presentation)	DOSE	MAXIMUM DAILY DOSE
Isoniazid (H)	4–6 mg/kg daily or 8–12 mg 3 x wk	300 mg
Rifampicin (R)	10–20 mg/kg daily	600 mg
Ethambutol (E)	25 mg/kg daily	1200 mg
Pyrazinamide (Z)	30–40 mg/kg daily	1500 mg
Streptomycin (S)	20–40 mg/kg daily	1000 mg
Kanamycin (Km)	15–30 mg/kg daily	1000 mg
Capreomycin (Cm)	15–30 mg/kg daily	1000 mg
Ciprofloxacin (Cfx)	20–40 mg/kg daily	1500 mg
Ofloxacin (Ofx)	15-20 mg/kg daily	800 mg
Moxifloxacin (Mfx)	7.5–10 mg/kg daily	400 mg
Ethionamide (Eto)	15–20 mg/kg daily	1000 mg
Cycloserine (Cs)	10–20 mg/kg daily	1000 mg
Terizidone (Trd)	10–20 mg/kg daily	1000 mg
P-aminosalicylic acid (PAS)	150 mg/kg daily	8 g (PASER)

- ❖ For quinolones (ofloxacin, ciprofloxacin, etc.), the daily dose should be given in a single dose once a day.
- ❖ For ethionamide, cycloserine, and PAS, the daily dose is divided into morning and evening doses for better tolerance. When starting treatment, ethionamide and cycloserine may be started at a lower dose and increased until the target dose is reached. For example:
 - 250 mg in the morning for several days
 - 250 mg in the morning and 250 mg in the evening for several days
 - 250 mg in the morning and 500 mg in the evening (target dose)
- ❖ All patients should receive pyridoxine. The recommended daily dose is 50 mg for every 250 mg of cycloserine/terizidone:
 - 50 mg daily if receiving cycloserine 250 mg daily
 - 100 mg daily if receiving cycloserine 500 mg daily
 - 150 mg daily if receiving cycloserine 750 mg daily, etc.



Standardized Category 4 regimen instructions (for 60 kg patient)*

 <p>Pyrazinamide: 3½ tablets (1750 mg) Kanamycin: 1 injection (1000 mg) Ofloxacin: 4 tablets (800 mg) Ethionamide: 1 tablet (250 mg) Cycloserine: 1 capsule (250 mg) PAS: 1 sachet (4 g)[†]</p>	 <p>Ethionamide: 2 tablets (500 mg) Cycloserine: 2 capsules (500 mg) PAS: 1 sachet (4 g)[†] Pyridoxine: 6 tablets (150 mg)</p>
<p><i>May need to stagger MDR-TB and ARV drugs at beginning of treatment</i></p>	
<p>If on ART co-treatment: AZT-3TC: 1 tablet Cotrimoxazole: 1 tablet (960 mg)</p>	<p>If on ART co-treatment: AZT-3TC: 1 tablet EFZ: 1 tablet</p>

[†] PASER formulation of PAS must be taken with an acidic liquid. See insert for details.

If you have any of the following, report to the health worker AT THE NEXT VISIT:












































- Nausea or vomiting
- Diarrhoea
- Tingling, numb or painful feet or legs or hands.

SEEK CARE URGENTLY if:

- Skin rash
- Severe abdominal pain
- Yellow eyes
- Strange visions or thoughts
- Fatigue AND shortness of breath

* From Section 5.9 of *Chronic Care for MDR-TB*

How to start ART co-treatment in an MDR-TB patient (for 60 kg patient)*

	Injectable Phase		Continuation Phase	
MDR-TB				
HIV	ART			
	Cotrimoxazole			
	TB initial phase- until tolerated	Until end of TB initial phase	During continuation phase	After TB treatment completed
	Z:  Km:  Ofx:  Eto:  Cs:  PAS: 	Z:  Km:  Ofx:  Eto:  Cs:  PAS: 	Z:  Ofx:  Eto:  Cs:  PAS: 	
		AZT-3TC:  CTX: 	AZT-3TC:  CTX: 	AZT-3TC:  CTX: 
	Eto:  Cs:  PAS:  Pyridoxine: 	Eto:  Cs:  PAS:  Pyridoxine: 	Eto:  Cs:  PAS:  Pyridoxine: 	
		AZT-3TC:  EFZ: 	AZT-3TC:  EFZ: 	AZT-3TC:  EFZ: 

* From Section 6.2 of *Chronic Care for MDR-TB*



Adherence support[†]



First visit (diagnosis):

- ❖ Prepare the patient (see 2.4, *Adherence Preparation*).
- ❖ Provide list of possible treatment supporters (village health worker, health facility or other community member), and decide on a treatment supporter.
- ❖ Give food package and transportation money to patient.

In between first and second visit:

- ❖ Contact health centre; arrange for injections to be given daily for at least 6 months.

Second visit (first day of treatment):

- ❖ Treatment supporter comes for the first time with the patient.
- ❖ If treatment supporter has not been trained in MDR-TB, provide standard training for DOTS-Plus treatment supporters.
- ❖ Assess understanding of doses (use *Dosing Job Aid*).
- ❖ Give Category 4 drugs (one month supply box) to patient.
- ❖ Give one month supply box of injectable and related supplies to treatment supporter (to take to health centre).
- ❖ Give *Category 4 Treatment Card*, exercise book, and pen to the treatment supporter.
- ❖ Give sputum bottles for next month.
- ❖ Give food package and transportation money to patient.
- ❖ Give transportation money to treatment supporter.

Follow-up visits (monthly):

- ❖ Treatment supporter must accompany patient to all follow-up visits.
- ❖ Assess patient and treatment supporter understanding of doses (use *Dosing Job Aid*). Check that the patient's morning and evening regimen is correct in the treatment supporter's exercise book. Check for side effects.
- ❖ Update the facility-held *Category 4 Treatment Card*.
- ❖ Verify that the patient is being supervised correctly by the treatment supporter.
- ❖ Give sputum bottles for next month.
- ❖ Give food package and transportation money to patient.
- ❖ Give transportation money and incentive to treatment supporter if he/she has fulfilled his/her monthly responsibilities.

[†] From Section 2.3 of *Chronic Care for MDR-TB*

Adherence preparation[†]

ASSESS

- ❖ Understanding of TB drug resistance, and how he/she was infected with a drug-resistant strain.
- ❖ Understanding of MDR-TB therapy.
- ❖ Has the patient demonstrated ability to keep appointments, and to adhere to other medications?
- ❖ Does the patient know his/her HIV serostatus?

ADVISE

- ❖ Drug-resistant TB:
 - Is created when TB patients do not take anti-TB drugs regularly.
 - Can be transmitted to family and friends.
 - Can be easily transmitted to people living with HIV.
- ❖ Offer HIV testing if patient does not know serostatus.
- ❖ MDR-TB treatment lasts for at least 2 years.
- ❖ Second-line anti-TB drugs are weaker than first-line anti-TB drugs. Every single dose must be taken at the correct time of the day. If not, there is a good chance treatment may fail.
- ❖ There is no other treatment for MDR-TB.
- ❖ Second-line anti-TB drugs have many side effects, but these can be managed. The clinical team must communicate closely with the DOTS-Plus treatment supporter about side effects.
- ❖ The patient is most infectious during the first few months when he/she is still smear positive. Windows and doors should be left open in the home to increase ventilation.

AGREE

- ❖ Is the patient willing to undergo at least 2 years of treatment with second-line anti-TB drugs?
- ❖ Is the patient willing to receive directly observed therapy?
- ❖ Who will observe the therapy? Community health worker at home or health worker at a nearby facility?
- ❖ Does the patient understand that the programme will stop treatment if he/she does not take doses regularly?
- ❖ Is the patient willing to come monthly to the MDR-TB clinic for follow-up (usually at a district hospital)?

ASSIST

- ❖ Discuss how taking medications can be integrated into work and home routines.
- ❖ Give food packages if needed.
- ❖ Give support for transportation. If patient lives in a remote area, discuss options such as moving closer to the clinic for a period of time.
- ❖ Refer to MDR-TB therapeutic support group.

ARRANGE

- ❖ For injections to be given at health centre nearest to patient's home.
- ❖ Educate treatment supporter about MDR-TB and how to observe MDR-TB therapy.

[†] From Section 2.4 of *Chronic Care for MDR-TB*

