

Nursing Guide for Second-Line Tuberculosis Medications



Tuberculosis and Hansen's Disease Unit Drug Resistant TB Monitoring Program

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Introduction

The purpose of this guide is to provide TB nurse case managers with:

- An overview of second-line TB medications;
- Fact sheets and resources to support patient education;
- Nursing cheat sheets on medication-related recommendations;
 and
- Recommended references.

Clinicians prescribe second-line medications to treat certain types of tuberculosis (TB), including drug-resistant TB (DR-TB). Clinicians may recommend second-line TB medications for patients with drug-susceptible TB disease who are intolerant to first-line medications. Although these medications have known side effects, they are necessary and at times the only option to treat TB.

Nurses should understand each drug and the associated monitoring, which can minimize potential adverse reactions. In addition, an element of patient-centered care is educating patients and families on their treatment plans to promote medication adherence.

Overview of Second-Line TB Medications

This section outlines potential side effects and toxicities associated with each drug and summarizes recommended assessments.

Aminoglycosides/Injectable Agents

• Amikacin (AK), 1g/4mL vial:



Side Effects and Symptoms of Medication Toxicity

- General Rash or swelling of the face, shortness of breath (SOB), decreased urination, renal toxicity, electrolyte imbalance, muscle twitching or weakness, pain at injection site
- **Ototoxicity** Hearing loss, tinnitus
- **Vestibular Disturbance** Dizziness, loss of balance

- Baseline, Monthly:
 - ▶ Medication Assessments
 - ♦ Toxicity Assessment
 - ♦ Audiometry Testing
 - Vestibular Testing
 - Laboratory
 - Complete Blood Count (CBC), Comprehensive Metabolic Panel (CMP), and Magnesium
- Other:
 - ► Adjust dose, interval for renal insufficiency, or both
 - ► Rule out pregnancy prior to administering
 - ▶ Can cause permanent hearing loss, early intervention is crucial

Bedaquiline (BDQ)

• 100mg tablet:



Side Effects and Symptoms of Medication Toxicity

- **General** Hepatotoxicity, headaches, arthralgias, rash
- Cardiac Corrected QT interval (QTc) prolongation; chest pain, SOB, fainting or near fainting, sudden fatigue, change in heart rhythm, tachycardia, syncope

- Baseline:
 - ▶ Medication Assessments
 - ♦ Toxicity Assessment
 - ♦ Cardiac monitoring or Electrocardiogram (ECG)
 - ► Laboratory
 - CBC, CMP, Thyroid-Stimulating Hormone (TSH) and Magnesium
- At two weeks:
 - ► ECG
- Monthly:
 - ► Toxicity Assessment
 - ► Cardiac Monitoring or ECG
 - ► CBC, CMP and Magnesium
- Every three months:
 - ► TSH
- Other:
 - ▶ Monitor for signs and symptoms of prolonged QTc interval
 - Swallow tablet whole, take with food
 - Avoid alcohol

Clofazimine (CFZ)

100mg tablet:



Side Effects and Symptoms of Medication Toxicity

- General Bloody or black stools or diarrhea, jaundice, retinopathy, photosensitivity, acne, rare instance-depression or thoughts of hurting self
- **Skin Discoloration** Clofazimine is a dye and may cause skin discoloration and ichthyosis, xerosis; hyperpigmentation resolves 1–2 years after discontinuation
- **GI Intolerance** Severe abdominal symptoms, bleeding, and bowel obstruction
- Cardiac Can cause prolongation of QTc

- Baseline, monthly:
 - ▶ Medication Assessments
 - ♦ Toxicity Assessment
 - ♦ Mental Health Assessment
 - ► Laboratory
 - ♦ CBC, CMP
- Every three months:
 - ► Follow-up Assessment (with prescribing physician)
 - ► Clofazimine Monitoring Form
- Other:
 - ► Prescriber must enroll in the Institutional Review Board (IRB) program to prescribe CFZ
 - ▶ Recommend sunscreen
 - ▶ Rule out pregnancy prior to administration

Cycloserine (CS)

• 250mg capsule:



Side Effects and Symptoms of Medication Toxicity

- **General** Rash, hives, headaches, seizures, insomnia
- Depression and Suicidal Ideation Mental status or mood changes, aggression, depression, disorientation, hallucinations, inability to concentrate, lethargy, nightmares, slurred speech, suicidal thoughts, psychosis

- Baseline, monthly:
 - ▶ Medication Assessments
 - ♦ Toxicity Assessment
 - ♦ Mental Health Assessment
 - ► Laboratory
 - ♦ CBC, CMP
- Other:
 - Adjust with renal failure
 - ▶ **Use Vitamin B6** when giving Cycloserine
 - ▶ Avoid alcohol

Ethionamide (ETA)

• 250mg tablet:



Side Effects and Symptoms of Medication Toxicity

- General Change in vision, headaches, photosensitivity, neuropathy, gastrointestinal (GI) upset, hepatotoxicity, dizziness, hypoglycemia, peripheral neuropathy, hypersensitivity, hypotension, mental disturbance
- **Hypothyroidism** Unusual bruising or bleeding, increased tiredness, hair loss, skin changes, trouble concentrating, irritable, depression, irregular menses, metallic taste, salivation, gynecomastia, impotence

- Baseline, Monthly:
 - ► Toxicity Assessment
 - Laboratory
 - ♦ CBC, CMP and TSH
- Every three months:
 - ► TSH
- Other:
 - ▶ Take with food

Fluoroquinolones (FQN) — Levofloxacin and Moxifloxacin

Levofloxacin (LFX)

• 250mg tablets (varies depending on manufacturer):





• 500mg tablet:



• 750mg tablet:



• 25mg/mL oral solution:



Moxifloxacin (MFX)

• 400mg tablet:



Side Effects and Symptoms of Medication Toxicity

- General GI upset, hepatotoxicity, hypersensitivity, dizziness, headaches, changes in heart rhythm, hypo- and hyper-glycemia, photosensitivity, arthralgias, insomnia, agitation, psychosis, paranoia, depression, peripheral neuropathy, thrush, seizures
- **Tendonitis** Monitor for pain or rupture to tendons
- Cardiac Can cause prolongation of QTc

- Baseline, Monthly:
 - ► Toxicity Assessment
 - ♦ Ask about tendon pain
 - ► Laboratory
 - ♦ CBC, CMP
- Other:
 - ▶ Do not take with milk-based products, antacids, mineral supplements (iron or magnesium) within two hours of medication
 - ► Avoid caffeinated foods and beverages
 - ► Recommend sunscreen

High Dose Isoniazid (INH)

(Adults 15mg/kg)

100mg tablet:



• 300mg tablet:



Side Effects and Symptoms of Medication Toxicity

- General Anemia, agranulocytosis, vasculitis, decreased platelets, fever, chills, rash
- **Hepatotoxicity** GI upset, nausea or vomiting (N/V), clay color stools, dark urine, yellow eyes, jaundice
- **Peripheral Neuropathy** May cause numbness or tingling in extremities
- **Optic Neuropathy** Pain, blurred vision, trouble seeing to the side, loss of color vision, flashing lights

- Baseline, monthly:
 - ▶ Medication Assessments
 - ♦ Toxicity Assessment
 - ♦ Peripheral Neuropathy Monitoring
 - ► Laboratory
 - ♦ Liver Function Tests (LFTs)
- Other:
 - ► Add Vitamin B6 to regimen
 - ► Take one hour before or two hours after antacids
 - ► May interact with other drugs and foods; avoid foods and drinks that contain tyramine; monitor for serotonin syndrome

Linezolid (LZD)

600mg tablet:



• 100mg/5mL oral suspension:



Side Effects and Symptoms of Medication Toxicity

- **General** Neuropathy, GI upset, change in vision, headaches, severe diarrhea, rash, black hairy tongue
- Hematological Lactic acidosis (muscle cramps, body aches, rapid breathing, nausea, and stomach pain), bone marrow suppression, anemia, thrombocytopenia, neutropenia (signs of infection, fatigue, nausea, diarrhea, painful mouth ulcers, loss of appetite), pancytopenia (confusion, SOB, rapid pulse, fever, chills, dizziness, unusual bleeding or bruising, petechiae, purpura, bruising, change in urinary frequency, black or tarry stools, unusual tiredness or weakness, signs and symptoms of infection, such as pale skin, lips, or nail beds)
- **Peripheral Neuropathy** Numbness or tingling in extremities; may be permanent; usually occurs after 12–20 weeks of treatment
- **Optic Neuropathy** Pain, blurred vision, trouble seeing to the side, loss of color vision, flashing lights; may be irreversible; usually occurs after 12—20 weeks of treatment

Recommended Assessments and Monitoring

Baseline, monthly:

- Medication Assessments
 - ♦ Toxicity Assessment
 - ♦ Peripheral Neuropathy Monitoring
 - ♦ Visual Acuity
 - ♦ Ishihara Plates
- ► Laboratory
 - ♦ CBC, CMP
- ➤ Some guidelines recommend weekly measurements of CBC during the initial phase. DSHS recommends consultation with a DSHS-recognized TB medical consultant.

Other:

- ► Add Vitamin B6 to regimen
- ► Monitor blood pressure
- ► Encourage good oral hygiene
- ► May interact with other drugs and foods; avoid foods and drinks that contain tyramine; monitor for <u>serotonin syndrome</u>

Para-Aminosalicylic Acid (PAS)

4g packet:



Side Effects and Symptoms of Medication Toxicity

- **General** GI upset, diarrhea, hepatotoxicity, rash, severe itching or hives, hypokalemia
- **Hypothyroidism** Unusual bruising or bleeding, increased tiredness, hair loss, skin changes, trouble concentrating, irritable, depression, irregular menses, metallic taste, salivation, gynecomastia, impotence

- Baseline:
 - ► Monthly Toxicity Assessment
 - ► Laboratory
 - ♦ CBC, CMP and TSH
- Monthly:
 - ▶ Toxicity Assessment
 - ► CBC and CMP
- Every three months:
 - ► TSH
- Other:
 - ► Sprinkle over applesauce or yogurt or mix with acidic juice
 - ▶ Do not chew granules
 - ► Refrigerate
 - Avoid alcohol

Pretomanid (Pa)

Used as part of the Bedaquiline, Pretomanid, Linezolid (BPaL) or BPaL plus Moxifloxacin (BPaLM) regimen

200mg tablet:



Side Effects and Symptoms of Medication Toxicity

- General Peripheral neuropathy, acne, anemia, nausea, vomiting, headache, indigestion, decreased appetite, rash, itching, abdominal pain, stabbing or burning pain in the chest when breathing, coughing or laughing, lower respiratory tract infection, liver problems, back pain, cough with or without blood, visual impairment, low blood sugar, abnormal loss of weight, diarrhea
- Male Fertility The potential effects on male fertility is unknown.
- Counsel patient on BDQ, LZD, Pa, and MFX side effects and toxicity symptoms

- Baseline, monthly:
 - Medication Assessments
 - ♦ Toxicity Assessment
 - ► Follow assessments and laboratory monitoring as per BDQ and LZD; if BPaL is prescribed with a FQN such as moxifloxacin, ensure FQN monitoring occurs
- Other:
 - ► Take with food
 - Swallow tablet whole
 - ▶ Avoid alcohol or medications that affect the liver
 - ► Counsel males of reproductive age regarding unknown reproductive toxicities
 - ► Avoid in nursing or pregnant women and children <14

Fact Sheets and Medication Resources

Fact sheets and supplemental resources support patient education. Some are patient-friendly while others are aimed at healthcare professionals for clinical understanding.

The following chart includes resources from the U.S. Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the Curry International TB Center, and Heartland National TB Center.

For additional resources, contact a local pharmacist or the <u>Texas Department</u> of <u>State Health Services (DSHS) Pharmacy Branch</u>.

Medication	Source
Amikacin	Heritage Pharmaceuticals — <u>Prescribing Information — Amikacin</u> (PDF)
	Curry International TB Center — <u>Drug-Resistant</u> <u>Tuberculosis: A Survival Guide for Clinicians — Amikacin</u> (PDF)
	Heartland National TB Center — <u>Administration of Amikacin Injection</u> (PDF)
	CDC — Provisional CDC Guidance for the Use of Pretomanid as part of a Regimen [Bedaquiline, Pretomanid, and Linezolid (BPaL)] to Treat Drug-Resistant Tuberculosis Disease
Bedaquiline	Curry International TB Center — <u>Drug-Resistant</u> <u>Tuberculosis: A Survival Guide for Clinicians —</u> <u>Bedaquiline</u> (PDF)
	Janssen Package Insert — <u>Medication Guide — Sirturo</u> (<u>Bedaquiline</u>) (PDF)

Clofazimine	FDA — <u>Prescribing Information — Clofazimine</u> (PDF) Curry International TB Center — <u>Drug-Resistant</u> <u>Tuberculosis: A Survival Guide for Clinicians —</u> <u>Clofazimine</u> (PDF)	
Cycloserine	Curry International TB Center — <u>Drug-Resistant</u> <u>Tuberculosis: A Survival Guide for Clinicians —</u> <u>Cycloserine</u> (PDF)	
Ethionamide	FDA — <u>Prescribing Information — Ethionamide</u> (PDF) Curry International TB Center — <u>Drug-Resistant Tuberculosis: A Survival Guide for Clinicians — Ethionamide</u> (PDF)	
Isoniazid	FDA — <u>Prescribing Information — Isoniazid</u> (PDF) Curry International Tuberculosis Center — <u>Drug-Resistant Tuberculosis: A Survival Guide for Clinicians — Isoniazid</u> (PDF)	
Levofloxacin	FDA — <u>Prescribing Information — Levofloxacin</u> (PDF) Curry International TB Center — <u>Drug-Resistant Tuberculosis: A Survival Guide for Clinicians — Levofloxacin</u> (PDF)	
Linezolid	FDA — <u>Prescribing Information – Linezolid</u> (PDF) Curry International TB Center — <u>Drug-Resistant</u> <u>Tuberculosis: A Survival Guide for Clinicians — Linezolid</u> (PDF)	
Moxifloxacin	FDA — <u>Prescribing Information – Avelox</u> (PDF) Curry International TB Center — <u>Drug-Resistant Tuberculosis: A Survival Guide for Clinicians — Moxifloxacin</u> (PDF)	

Para-amino Salicylic Acid	FDA — <u>PASER Granules</u> Curry International TB Center — <u>Drug-Resistant</u> <u>Tuberculosis: A Survival Guide for Clinicians — Para-Aminosalicylate</u> (PDF)
Pretomanid	TB Alliance — <u>Prescribing Information — Pretomanid</u> (PDF) and <u>Pretomanid and the BPAL Regimen</u> Curry International TB Center — <u>Drug-Resistant Tuberculosis: A Survival Guide for Clinicians — Pretomanid</u> (PDF)
Varies: second-line TB medication resources	Heartland National TB Center — <u>Characteristics of Commonly-Used Second-line Drugs for Drug Resistant TB</u> (PNG); <u>Tuberculosis Adverse Drug Events</u> (PDF); <u>Tuberculosis Medication Drug and Food Interactions</u> (PDF)

Nursing Cheat Sheets

Cheat sheets are stand-alone references. Nurses may cut and save the cheat sheets to place on the back of a badge or in a folder for quick reference.

Quick Reference Laboratory Cheat Sheet, excluding CBC and CMP

Lab	Medication
Magnesium	AK, BDQ
Pregnancy Test	AK, CFZ
TSH	BDQ, ETA, PAS

Quick Reference Toxicity Assessment Cheat Sheet for Individual Medications

Medication	Recommended Toxicity Monitoring
Amikacin (AK)	Audiometry and Vestibular Testing
Bedaquiline (BDQ)	ECG
Clofazimine (CFZ)	Mental Health Assessment
Cycloserine (CS)	Mental Health Assessment
Fluoroquinolones: Moxifloxacin	Monitor Tendon Pain
(MFX) and Levofloxacin (LFX)	
High Dose Isoniazid (INH)	Peripheral Neuropathy Monitoring
Linezolid (LZD)	Peripheral Neuropathy Monitoring
	Visual Acuity and Ishihara Plates
Pretomanid, used with	ECG
Bedaquiline and Linezolid (BPaL)	Peripheral Neuropathy Monitoring
	Visual Acuity and Ishihara Plates



References

American Thoracic Society (2019). <u>Treatment of Drug-Resistant</u> Tuberculosis, An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline.

• Erratum: Treatment of Drug-Resistant Tuberculosis. An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline | American Journal of Respiratory and Critical Care Medicine (atsjournals.org)

American Thoracic Society (ATS), U.S. Centers for Disease Control and Prevention (CDC), European Respiratory Society (ERS), and Infectious Diseases Society of America (IDPS) (2019). Am J Respir Crit Care Med 15; 200 (10) Treatment of Drug-Resistant Tuberculosis: An Official ATS/CDC/ERS/IDPS Clinical Practice Guideline.

Curry International Tuberculosis Center (2022). Drug-Resistant Tuberculosis: A Survival Guide for Clinicians 3rd Edition/2022 Updates.

Center for Disease Control (2024). <u>Provisional CDC Guidance for the Use of Pretomanid as part of a Regimen [Bedaquiline, Pretomanid, and Linezolid (BPaL)] to Treat Drug-Resistant Tuberculosis Disease.</u>

Heartland National TB Center. <u>The Spectrum of Tuberculosis from Infection</u> to Disease-TB at a Glance: <u>3rd Edition</u>. Heartland National TB Center and <u>Mayo Clinic</u>, <u>2020</u>.