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TREATMENT OF TUBERCULOSIS (TB) IN ADULTS WITH HIV INFECTION

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This resource is intended to assist clinicians in managing patients with HIV and latent tuberculosis infection (LTBI), and drug-susceptible pulmonary tuberculosis disease (TB). This guide summarizes the guidelines for the diagnosis and treatment of LTBI and TB and includes clinical signs and symptoms, adult dosing, available dosage forms, drug-drug interactions, side effects, and important patient counseling points.

AETC AIDS Education & Training Center Program Southeast

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Resources

Unless otherwise noted, the information contained in this card has been adapted from the resources listed below.

For additional up-to-date information on the diagnosis and treatment of LTBI and/or TB disease:

- CDC TB homepage https://www.cdc.gov/tb
- CDC LTBI resources https://www.cdc.gov/tb/publications/ltbi/ltbiresources.html
- Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020. https://www.cdc.gov/mmwr/volumes/69/rr/rr6901a1.htm
- Centers for Disease Control and Prevention and the National TB Controllers Association: Testing and Treatment of Latent Tuberculosis Infection in the United States: Clinical Recommendations. http://www.tbcontrollers.org/resources/tb-infection/clinical-recommendations/#.YGSWji2caqA
- Centers for Disease Control and Prevention. Latent Tuberculosis Infection: A Guide for Primary Health Care Providers. https://www.cdc.gov/tb/publications/ltbi/pdf/LTBIbooklet508.pdf
- Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. https://www.thoracic.org/statements/resources/tb-opi/treatment-of-drug-susceptible-tuberculosis.pdf
- Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children. https://www.thoracic.org/statements/resources/tb-opi/diagnosis-of-tuberculosis-in-adults-and-children.PDF
- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/
- Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection/whats-new-guidelines
- Update of Recommendations for Use of Once-Weekly Isoniazid-Rifapentine Regimen to Treat Latent Mycobacterium tuberculosis Infection. https://www.cdc.gov/mmwr/volumes/67/wr/pdfs/mm6725a5-H.pdf

The information contained in this publication is intended for medical professionals, as a quick reference to the national guidelines. This resource does not replace nor represent the comprehensive nature of the published guidelines. Recognizing the rapid changes that occur in this field, clinicians are encouraged to consult with their local experts or research the literature for the most up-to-date information to assist with individual treatment decisions for their patient. If your patient should experience a serious adverse event, please report the event to the FDA (www.fda.gov/Safety/MedWatch/HowToReport/default.htm) to help increase patient safety.

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LATENT TUBERCULOSIS INFECTION

Latent tuberculosis infection (LTBI) is the presence of *Mycobacterium tuberculosis* (M.tb) in the body without signs and symptoms, or radiographic or bacteriologic evidence of tuberculosis (TB) disease.

DIAGNOSIS OF LTBI: TUBERCULIN SKIN TEST (TST) OR INTERFERON GAMMA RELEASE ASSAY (IGRA)

- Pts with HIV have a 3-16% risk per year for developing TB disease if infected with M.tb
- Test pts with HIV for LTBI, with either a TST or IGRA, at time of entry into care, regardless of risk or CD4 count
- If the initial test is negative, consider re-testing with a different test when risk for infection, progression to TB disease, and a poor outcome are increased
- All pts with (+) test for LTBI should be evaluated for TB disease (i.e., chest x-ray [CXR] and clinical evaluation for pulmonary and extrapulmonary symptoms) before starting LTBI therapy
- Tuberculosis Screening, Testing, and Treatment of U.S. Health Care Personnel can be found online at: https://www.cdc.gov/mmwr/volumes/68/wr/mm6819a3.htm

Tuberculin Skin Test

- Information about TST can be found online at: https://www.cdc.gov/tb/publications/factsheets/testing/skintesting.htm.
- Pts who have repeat TSTs (e.g. healthcare workers, staff/residents of congregate settings) should have two-step testing done initially. Pts with (-) initial TST should have 2nd test 1-3 wks later; a (+) 2nd test indicates prior infection (booster effect).

Interpretation of TST Results

- A (+) TST result in pts with HIV is ≥ 5 mm induration
- Possible reasons for false (+) TST result:
  - Infection with nontuberculous mycobacteria
  - Prior Bacillus Calmette-Guérin (BCG) vaccine or cancer treatment (use of IGRA preferred)
  - Improper administration and/or interpretation of results
- Possible reasons for false (-):
  - Immuosuppression due to HIV
  - Recent TB infection (within 8-10 wks after exposure)
  - Extremes of age (young children, elderly)
  - Concurrent bacterial, fungal, or viral infections
  - Overwhelming TB disease
  - Immunosuppression due to medications, malignancy, or other conditions
  - Problem with tuberculin used (e.g., improper storage), poor administration technique (e.g., subcutaneous instead of intradermal), improper reading or result interpretation
  - Recent live virus vaccination (administer TST at same time as vaccine or wait 4-6 wks afterwards). Current Covid-19 vaccines do NOT contain live virus.
- Effect of monkeypox vaccine (live, non-replicating vaccine) on TST is not known. Can consider delaying TST. See https://www.cdc.gov/tb/publications/letters/2022/jynneos-vaccine.html
- Anergy testing is NOT recommended
- SNTC Caliper for reading a TST. Order online: https://sntc.medicine.ufl.edu/home/index#/products/15

Contraindications to a TST

Do not re-test persons with a serious reaction to a prior TST.
TST is NOT contraindicated in:

- Adults or children previously vaccinated with BCG
- Pregnant or breastfeeding women
- Any person previously tested with TST or IGRA

Interferon (IFN) Gamma Release Assays (IGRAs)

- IGRAs are blood tests that detect IFN-gamma release in response to *Mycobacterium tuberculosis* specific antigens.
- IGRA specificity ranges 92%-97%, compared to 56%-95% for TST.
- Samples should be drawn, transported, processed, and interpreted according to each manufacturer's recommendations
  - QuantiFERON - TB Gold Plus (Qiagen) https://www.quantiferon.com/us/products/quantiferon-tb-gold-plus-us/
  - T-SPOT TB Test (Oxford Immunotec Limited) https://www.tspot.com/resources/

NOTE: Blood samples must be processed within 8-16 hours after collection so that the white blood cells remain viable

- Additional information about IGRAs can be found online at: https://www.cdc.gov/tb/publications/factsheets/testing/igra.htm

Recommendations on the Use of IGRA

- IGRA can be used in place of a TST in all situations
- IGRA is preferred in:
  - Persons who received BCG vaccination or cancer therapy
  - Groups with low rates of return for TST results (e.g., homeless persons, drug-users, and those who previously failed to return for TST reading)
- Similar to TST, live virus vaccines may affect IGRA results. Perform IGRA either on the same day as live virus vaccines or 4-6 wks after. Current Covid-19 vaccines do NOT contain live virus.
- Effect of monkeypox vaccine (live, non-replicating vaccine) on IGRA is not known. Can consider delaying IGRA. See https://www.cdc.gov/tb/publications/letters/2022/jynneos-vaccine.html

Recommendations for Repeat TST or IGRA

- If CD4 increases > 200 cells/mm^3 in response to antiretroviral therapy (ART) (immunosuppression may cause false (-) TST/IGRA)
- Pts exposed to a person with pulmonary TB disease; retest again 8-10 wks after TB exposure ended
- Consider re-testing if pt experiences a new risk factor for TB exposure such as:
  - work or residence in a correctional facility or other high risk congregate setting
  - travel to a country where active TB disease is common (most countries in Latin America, the Caribbean, Africa, Asia, Eastern Europe and Russia)
  - uses IV drugs
  - has been homeless or has stayed in a shelter
  - close contact with recent immigrants and other high risk non-US born individuals

Treating LTBI (to prevent TB disease)

Treat pts with HIV for LTBI only after TB disease ruled out:

- No pulmonary or extra-pulmonary symptoms of TB disease
- No physical findings of TB disease AND patient has either:
  - (+) diagnostic test for LTBI or
  - known contact to pulmonary TB even if TST or IGRA are (-)
- Collaborate with local health department to provide directly observed therapy (DOT) to ensure completion of LTBI treatment

NOTE: If pt has hx of inadequately treated TB or CXR suggestive of prior TB (e.g, fibrotic changes), rule out TB disease before considering LTBI therapy. Consult an HIV/TB expert.

Monitoring Patients Treated for LTBI

- Monitor all pts clinically at least monthly, including physical exam, side effect and adherence assessment
- Perform baseline ALT and total bilirubin in all pts: re-check monthly in pts with risk factors for hepatotoxicity (e.g., liver disease, including hepatitis B or C, regular alcohol use, pregnant or < 3 mos post-partum, receiving ART)
- Perform CBC with diff and platelets at baseline if a rifamycin is used and repeat testing if results abnormal or pt has symptoms suggestive of hematologic adverse reaction
- Instruct pt to seek medical attention for fever, jaundice, dizziness, rash, aches, > 1 day of nausea, vomiting, weakness, abdominal pain, loss of appetite
- Discontinue LTBI treatment if ALT ≥ 5x ULN (even if no symptoms) or ALT ≥ 3x ULN with symptoms
- Rash and flu-like symptoms may be sign of serious hypersensitivity reaction to a rifamycin; consult TB HIV expert

NOTE: COVID-19 vaccines should not be delayed because of testing or treatment for TB infection. Though current COVID-19 vaccines do NOT contain live virus, preferably perform TST or IGRA before or during the same encounter as COVID-19 vaccination.

COVID-19 vaccine and TB testing information:

https://www.cdc.gov/tb/topic/testing/tbtesttypes.htm

TABLE 1. TREATING LTBI TO PREVENT TB DISEASE

- Both LTBI treatment and ART decrease the risk of TB disease and are recommended to prevent TB disease.
- Rule out TB disease before LTBI treatment.

INDICATIONS FOR LTBI TREATMENT:

- (+) TST or IGRA and no prior history of completing treatment for active or latent TB;
- Close contact with infectious TB, regardless of TST or IGRA result.

LTBI TREATMENT REGIMENS:

PREFERRED:

- **3HP**: 3 mos (12 wks) of once-weekly isoniazid (**INH**) plus rifapentine (**RPT**) for pts either not receiving ART or virally-suppressed persons receiving a once-daily dolutegravir (**DTG**), efavirenz (**EFV**), or raltegravir (**RAL**)-based regimen without tenofovir alafenamide (**TAF**).
  Doses: **INH** 15 mg/kg (900 mg max) PO weekly plus
  RPT: if weight 32.1-49.9 kg, use 750 mg PO weekly; if weight > 50.0 kg, use 900 mg (max) PO weekly plus **B6** (pyridoxine): 25-50 mg PO weekly
- **3HR**: 3 mos (12 wks) of **INH** daily plus rifampin (**RIF**) daily plus **B6** daily
  Doses: **INH** 300 mg PO daily plus RIF 600 mg PO daily plus **B6** 25-50 mg PO daily

ALTERNATIVES:

- **Isoniazid**: 6 to 9 months of daily **INH**
  Doses: **INH** 300 mg PO daily plus **B6** 25-50 mg PO daily
- 4R: 4 mos of daily **RIF**; 4RIF is strongly recommended for adults without HIV, but there is limited evidence available for effectiveness in those with HIV. Ensure no TB by symptom eval, CXR and culture.
  Dose: **RIF** 600 mg PO daily
- **1HP**: 4 wks of daily **INH**, **RPT** and **B6**. This is only recommended as an alternative regimen for patients receiving efavirenz-based ARV.
  Doses: **INH** 300 mg PO daily plus **RPT**(max dose 600 mg): if weight <35 kg use 350 mg PO daily; 35-45 kg: 450 mg PO daily, >45 kg: 600 mg PO daily plus **B6**: 25-50 mg PO daily

For detailed information about rifamycin (RIF, RFB and RPT) interactions with ARVs see Table 5 and:

- www.hiv-druginteractions.org or
- https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/overview?view=full

TUBERCULOSIS DISEASE

DIAGNOSIS OF ACTIVE TUBERCULOSIS DISEASE

- Symptoms of **pulmonary TB disease**:
  - Prolonged productive cough (> 3 wks), chest pain, hemoptysis, fever/chills, night sweats, decreased appetite/weight loss, fatigue;
  - Clinical presentation can be atypical or subtle in pts with HIV
- Pts with HIV have increased risk **of extrapulmonary TB**; Symptoms and clinical presentation depend on the site of infection. **Consult a TB/HIV expert especially if CNS disease**.
- Aggressively pursue diagnosis when pulmonary and/or extrapulomary TB is suspected to confirm TB vs. other diagnosis and enable TB drug susceptibility testing (DST).
- If pulmonary or extrapulmonary TB is suspected:
  - Obtain PA and lateral CXR. Abnormalities often seen in upper lobe, but pts with HIV and TB disease may have atypical or normal CXR appearance despite pulmonary disease.
  - Obtain 3 sputum specimens 8-24 hours apart for AFB smear and culture. Consider sputum induction/bronchoscopy to obtain specimen.
  - Obtain nucleic acid amplification testing (NAAT) on >1 respiratory specimen, even if smear (-).
  - If NAAT (+), obtain GeneXpert, HAIN, or other rapid molecular test for rifampin (RIF) resistance; if RIF resistance detected obtain full molecular testing for drug resistance through CDC. Contact your state TB program.
  - If indicated, collect other fluid or tissue specimens and request AFB smear, culture and NAAT (even if smear [-])
  - Obtain culture-based DST on initial TB culture isolate from any source.
- TST and IGRA indicate that M.tb infection may be present, but do not rule out or confirm TB disease.
- Aggressively pursue diagnosis when TB is suspected to enable TB susceptibility testing and confirm TB vs. other diagnosis.

NOTE: In extrapulmonary TB, sputum smear, NAAT, and culture should always be done even when (-) CXR to detect subtle TB disease.

Treatment of Drug-Susceptible TB Disease in Patients with HIV

- After collection of appropriate specimens, start TB treatment guided by molecular DST.
- If clinical and radiographic presentation suggest TB disease but NAAT/PCR is (-), consider empirical treatment while cultures pending.
- For drug-susceptible TB disease, use a 4-drug regimen of isoniazid (INH), (rifampin [RIF] or rifabutin [RFB]), pyrazinamide (PZA), and ethambutol (EMB)
  - RFB is often substituted for RIF in pts with HIV since it is a less potent inducer of drug metabolism and can be used with most ART (See Table 5 for information about drug interactions)
  - Rifapentine (RPT) is a long-acting rifamycin that is dosed once-weekly, but should NOT be used to treat TB disease in pts with HIV due to higher rates of relapse and resistance.

TB treatment includes 2 phases:

- **Initial phase**:
  - INH + (RIF or RFB) + PZA + EMB PO once-daily (5-7 days per wk) for 2 mos
  - Discontinue EMB prior to 2 mos if susceptible to INH, RIF/RFB, PZA
  - Pts should complete 8 wks of PZA
- **Continuation phase**:
  - INH + (RIF or RFB) 5-7 days per wk for 4 mos;
  - Extend continuation phase to ≥ 7 mos (e.g. 9 mos total treatment) if:
    - pt is not on ART
    - cavity on chest X-ray, and/or the sputum culture remains (+) at 2 mos.
    - 8 wks of PZA is not completed
  - Completion of TB therapy is based on number of doses received as well as duration in wks.
- Use DOT for all pts treated for TB disease: video DOT (VDOT) may be appropriate (consult public health).
- Use case management interventions during treatment of pts with TB disease (pt education and counseling, field and home visits, integration and coordination of all providers, pt reminders, and incentives and enablers).

NOTE: If sputum culture remains positive after 2 mos of TB treatment, send repeat sputum for rapid molecular DST (GeneXpert, etc.), assess adherence, consider serum drug levels, and consult a TB/HIV expert.

Initiating ART in Patients with HIV with TB disease

- All pts with HIV with TB disease should start ART if:
  - CD4 < 50, start ART within 2 wks of starting TB therapy
  - CD4 ≥ 50, start ART within 8 wks of starting TB therapy

NOTE: If TB meningitis is suspected, do not start ART early due to risk of Immune Reconstitution Inflammatory Syndrome (IRIS). Corticosteroids recommended with TB therapy. Consult a TB/HIV expert for management.

TABLE 2. ADULT DOSE OF AGENTS FOR TB DISEASE

	Isoniazid	Rifampin	Rifabutin
Dose (mg/kg)	5	10	5
Usual Daily Dose	300 mg	600 mg	300 mg
Ethambutol (Suggested Doses Using Whole Tablets)			
Weight (kg)	40-55	56-75	76-90
Daily Dose	800	1200	1600
Pyrazinamide (Suggested Doses Using Whole Tablets)			
Weight (kg)	40-55	56-75	76-90
Daily Dose	1000	1500	2000

NOTES:
1. Dose based on actual body weight if not obese (i.e. > 20% above ideal body weight [IBW]). If obese, use IBW (MD+CALC https://www.mdcalc.com/ideal-body-weight-adjusted-body-weight) and consider obtaining serum drug levels and TB/HIV expert consultation.
2. Doses are for pts with normal renal and hepatic function. Consult a TB/HIV expert for pts with abnormal renal and/or hepatic function.
3. Daily therapy is 5-7 days per wk via DOT.
4. See Table 5 for drug interactions and ART dosing recommendations

Monitoring Treatment for Pulmonary TB Disease

- See Table 3 for recommended baseline and periodic assessments
- As part of the baseline and monthly clinical assessment, assess concurrent medications for drug-drug interactions
- **Consult a TB/HIV expert for pts who fail treatment (e.g. (+) sputum culture after 4 mos of treatment) and/or have drug resistance**

Possible Adverse Effects of TB Drugs

Consult a TB/HIV expert for management of significant adverse effects or cases requiring changes in TB regimen.

- If a TB drug is stopped for intolerance or toxicity, the regimen must still include at least 2 effective drugs.
- Maintain either RIF or RBT if at all possible; consult an expert if RIF/RBT cannot be used.
- If PZA is not used for 8 wks or RIF/RBT not used throughout, treatment duration must be extended.

Recommendations for managing adverse effects of TB drugs can be found at:

- ATS/CDC/IDSA 2016 TB treatment guidelines https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf
- CDC and NTCA Testing and Treatment of Latent Tuberculosis Infection in the United States: Clinical Recommendations http://www.tbcontrollers.org/resources/tb-infection/clinical-recommendations/#.YGSWji2caqA
- Official ATS Statement: Hepatotoxicity of Antituberculosis Therapy and other clinical resources https://www.thoracic.org/statements/resources/mtpi/hepatotoxicity-of-antituberculosis-therapy.pdf

Immune Reconstitution Inflammatory Syndrome (IRIS)

- TB IRIS is diagnosis of exclusion. TB treatment failure, drug resistance, and other new diagnoses must be ruled out.
- IRIS can manifest as worsening symptoms suggesting TB treatment failure, or can unmask undetected TB disease following ART treatment initiation.
- Continue both ART and TB therapy while managing IRIS.
- Mild IRIS can be treated with NSAIDs; severe IRIS (e.g., CNS symptoms, compromised airway or swallowing, sterile abscesses, uncomfortable lymph nodes) may require corticosteroids.
  - Steroid dosing option: Prednisone 1.5 mg/kg/day for 2 wks followed by 0.65 mg/kg/day for 2 wks (some pts may require higher doses or slower duration of taper)
- Consult a TB/HIV expert for assistance.

Therapeutic Drug Monitoring (TDM)

- Serum drug levels ensure safe and effective drug doses are used:
  - If TB HIV drug interactions exist
  - If pt develops an adverse effect
  - If pt has renal or hepatic disease
  - If pt has risk for malabsorption (e.g. HIV and diabetes)
  - If pt remains culture (+) after 2 mos of appropriate TB therapy or is clinically slow to improve
  - If 2nd-line TB drugs used (e.g., fluoroquinolones, linezolid, etc.)
- TDM for HIV and TB drugs available through the Infectious Disease Pharmacokinetic Laboratory at U. Florida (http://idpl.cop.ufl.edu/)
- Call TB Hotline 1.800.4TB.INFO (1.800.482.4636) for expert interpretation and consultation regarding TDM.

TABLE 3. MONITORING TREATMENT FOR ACTIVE TB DISEASE IN PATIENTS WITH HIV
X=recommended in all pts, O=optional or recommended in certain situations (see footnotes)

Activity	Baseline	Month of Treatment Completed								End of Treatment
		1	2	3	4	5	6	7	8	
Microbiology										
Sputum smears and culture[1]	X	X	X	O	O					O
Sputum NAAT[2]	X			O						
Drug susceptibility testing[3]	X			O						
Imaging										
CXR or other imaging[3]	X		O							O
Clinical Assessment										
Weight[4]	X	X	X	X	X	X	X	X	X	
Symptom and adherence review[5]	X	X	X	X	X	X	X	X	X	
Vision assessment[6]	X	X	X	O	O	O	O	O	O	
Laboratory Testing										
AST, ALT, bilirubin, alkaline phosphatase[7]	X	X	X	X	X	X	X	X	X	
Platelet count[8]	X	O	O	O	O	O	O	O	O	
Creatinine[8]	X	O	O	O	O	O	O	O	O	
HIV testing[9]	X									
Hepatitis B and C screen[10]	X									
Diabetes Screen[11]	O									

1. If pulmonary TB, obtain sputa for smear and culture monthly until 2 consecutive (-) culture results. Obtain sputa more frequently early in therapy to assess for treatment response (optional).
2. Test at least one baseline specimen using a rapid molecular test.
2. Drug susceptibility testing for INH, RIF, EMB, and PZA is recommended. Repeat susceptibility testing if pt remains culture (+) after completing 3 mos of treatment. Molecular resistance testing recommended for pts at risk for drug resistance.
3. Repeat CXR at 2 mos in pts who were culture (-) at diagnosis. Presumptive diagnosis of TB can be made if CXR is improving on treatment. End of treatment CXR is optional.
4. Monitor weight monthly and adjust medication dose(s) as indicated.
5. Assess adherence and monitor improvement in TB symptoms (e.g., cough, fever, fatigue, night sweats). Assess for development of medication adverse effects (e.g., jaundice, dark urine, nausea, vomiting, abdominal pain, fever, rash, anorexia, malaise, neuropathy, arthralgias).
6. Required for pts on EMB. Baseline testing for visual acuity (Snellen test) and color discrimination. Inquire about visual disturbances and perform color discrimination testing monthly.
7. Recommended monthly for pts at increased risk for hepatotoxicity, including pts with HIV.
8. Monitoring beyond baseline only if abnormalities or as clinically indicated.
9. CD4 and HIV RNA viral load in pts infected with HIV.
10. Pts with HIV are at increased risk for Hepatitis B or C coinfection.
11. Fasting glucose or hemoglobin A1c for pts with diabetes risk factors (age > 45, BMI > 25 kg/m^2, 1st degree relative with diabetes, and race/ethnicity of African American, Asian, Hispanic, American Indian/Alaskan Native, or Hawaiian Native/Pacific Islander.

TABLE 4. DRUGS USED FOR TREATMENT OF DRUG-SUSCEPTIBLE TB DISEASE AND LTBI

NOTE: Consult a TB/HIV expert for pts with renal insufficiency (e.g., CrCL < 30 mL/min or on dialysis) and/or hepatic impairment (e.g., AST/ALT > 2 ULN). Although the guidelines provide empiric dosage adjustment recommendations, some experts do not recommend empiric dosage adjustment as TDM is often required to optimize dosing. See the TB Guidelines and call the 24-hour TB Hotline 1.800.4TB.INFO (1.800.482.4636) for assistance in managing pts with renal and/or hepatic impairment.

DRUG	DOSAGE FORM	FOOD RESTRICTIONS	IMPORTANT POINTS
Isoniazid (INH)	100, 300 mg tab; 50 mg/5 mL oral soln; injection (100 mg/mL)	Empty stomach (30 mins before or 2 hours after a meal)	Avoid antacids for 2 hours before and after INH Most common/severe AEs: hepatotoxicity, peripheral neuropathy, optic neuritis, rare hematologic or dermatologic reactions Co-admin pyridoxine (vitamin B6) 25-50 mg once-daily to prevent neuropathy
Rifabutin (RFB)	150 mg cap	With or without food, may open cap and mix in food (applesauce)	Most common/severe AEs: red-orange discoloration of body fluids (e.g., urine, sweat, tears), rash, flu-like syndrome, arthralgias, hematologic reactions (anemia, neutropenia, thrombocytopenia), uveitis (dose-related), hepatotoxicity
Rifampin (RIF)	150, 300 mg cap; injection (600 mg vial)	Empty stomach (1 hour prior to or 2 hours after meal); may open cap and mix in food (applesauce)	Most common/severe AEs: GI upset, red-orange discoloration of body fluids (e.g., urine, sweat, tears), rash, flu-like syndrome, hematologic reactions (hemolytic anemia, leukopenia, thrombocytopenia), hepatotoxicity, hypersensitivity reaction (dermatologic manifestations including urticaria or rash; renal manifestations including ↑ BUN, ↑ uric acid, acute renal failure)
Rifapentine (RPT)	150 mg tab	Take with food	Most common/severe AEs: red-orange discoloration of body fluids (e.g., urine, sweat, tears), rash, flu-like syndrome, pyuria, hematologic reactions (anemia, neutropenia, thrombocytopenia), hepatotoxicity
Ethambutol (EMB)	100, 400 mg tab	Take with food to ↓ GI upset	Most common/severe AEs: GI upset (nausea, vomiting, anorexia), optic neuritis (pt should report visual changes), peripheral neuropathy, arthralgias, hepatotoxicity, ↑ uric acid, hyperuricemia, rash, hypersensitivity reaction
Pyrazinamide (PZA)	500 mg tab	With or without food	Most common/severe AEs: nausea and vomiting (usually improves after a few wks), hepatotoxicity, arthralgias/myalgias, ↑ uric acid, rare hematologic reactions (thrombocytopenia, porphyria, sideroblastic anemia)

TABLE 5. DRUG-DRUG INTERACTIONS WITH RIFAMYCINS AND ART
For additional details see the drug-drug interactions tables in the Adult/Adolescent ARV guidelines at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/overview?view=full and www.hiv-druginteractions.org

RIFAMPIN (RIF)[1]-BASED REGIMEN WITH ART
NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIS)
Do not use RIF with tenofovir alafenamide (TAF) containing regimens unless benefits outweigh the risks. See other sections of table for other ART interactions with TAF.
INTEGRASE STRAND TRANSFER INHIBITORS (INSTIS)
Do not use RIF with bictegravir/emtricitabine/TAF (Biktarvy)
Do not use RIF with cabotegravir (CAB) PO or IM (CAB) (Vocabria or Cabenuva)
Increase dolutegravir (DTG) to 50 mg po bid. Use alternative to RIF if INSTI-experienced with certain INSTI-associated resistance substitutions or clinically suspected INSTI resistance.
Do not use RIF with elvitegravir (EVG) containing regimens (Genvoya or Stribild)
Increase raltegravir (RAL) from 400 mg po bid to 800 mg po bid. Do not use once-daily RAL with rifampin
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIS)
Efavirenz (EFV) 600 mg po every night (standard). Consider TDM.
Do not use RIF with doravirine (DOR)[2], etravirine (ETR), nevirapine (NVP), or rilpivirine (RPV) PO or IM.
PROTEASE INHIBITORS (PIS)
Do not use RIF with any PI (boosted or unboosted) containing regimen.
CCR5 INHIBITOR
Use MVC 600 mg bid with RIF, or 300 mg bid if used with RIF and a strong CYP3A inhibitor
CAPSID INHIBITOR
Do not use RIF with lenacapavir (LEN)
RIFABUTIN (RFB)-BASED REGIMEN WITH ART
NRTIs
Do not use RFB with TAF containing regimens unless benefits outweigh risks. (i.e. Biktarvy, Descovy, Genvoya, Odefsey)
INSTIs
No dosage adjustments for DTG or RFB[2]
No dosage adjustments for RAL or RFB[2]
Do not use RFB with CAB/RPV (Cabenuva). No interaction expected between RFB and CAB (Vocabria).[2]
Do not use RFB with bictegravir/emtricitabine/TAF (Biktarvy)
Do not use RFB with EVG-containing regimens (Stribild or Genvoya).
NNRTIs

NNRTI	Rifabutin (RFB)
DOR	Increase DOR to 100 mg po bid. RFB standard dose.
EFV	RFB 450–600 mg PO once-daily; with EFV 600 mg PO once-daily (if EFV is not coadministered with a PI).
ETR	Do not combine ETR with RFB if used with a RTV-boosted PI. Standard dose for ETR and RFB if no boosted PI in regimen.
NVP	Standard doses for NVP and RFB.
RPV	Increase RPV from 25 mg PO once-daily to 50 mg po once-daily. RFB standard dose. RPV IM contraindicated

PIs (all standard dose with modified RFB dose as listed below)	
Ritonavir (/r) or Cobicistat (/c) boosted PIs[2]	
Atazanavir (ATV)/r	RFB 150 mg PO once-daily Monitor for antimycobacterial efficacy, adverse effects, and consider TDM
Darunavir (DRV)/r	
Lopinavir/r	
Do not use RFB with cobicistat (/c) boosted PIs (ATV/c or DRV/c)	

CCR5 INHIBITOR
MVC 150 mg PO bid (with potent CYP3A inhibitor); MVC 300 mg po bid (without potent CYP3A inhibitor or inducer); Dose RFB based on other drugs in regimen (consider TDM)
CAPSID INHIBITOR
Do not use RFB with LEN
RIFAPENTINE (RPT)-BASED REGIMEN WITH ART
Once-weekly RPT can be used in a regimen to treat LTBI in virally-suppressed persons receiving a once-daily DTG, EFV, or RAL-based regimen without TAF (unless benefit outweighs risk). Once-daily RPT regimen for LTBI treatment can only be used if patient is receiving EFV-based ART.
nRTIS
No dose adjustment with EFV
Do not use RPT with DOR, ETR, NVP, or RPV (IM or PO)
INSTIs
For once-weekly rifapentine, RAL 400 mg twice-daily (standard twice-daily dose) can be used. Do not use RAL with once-daily rifapentine.
With once-weekly rifapentine, DTG 50 mg daily may be used in patients with viral suppression on daily DTG. Monitor for virologic efficacy. Do not use RPT in patients who require twice-daily DTG. Do not use DTG with once-daily rifapentine.
Do not use RPT with BIC, EVG/c, or CAB (PO and IM)
NRTIs
No dose adjustment with TDF
Do not use with TAF unless benefits outweigh risks.
PIS
Do not use RPT with any PI (boosted or unboosted) containing regimen.
CCR5 INHIBITOR
Do not use RPT with MVC
CAPSID INHIBITOR
Do not use RPT with LEN

1. All are with RIF standard dose.
2. If boosted PI included in regimen, see dosing recommendations listed above.