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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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Treatment of Tuberculosis (TB) in HIV/AIDS

August 2014

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

This resource was developed in collaboration with the Southeastern National Tuberculosis Center.
Southeastern National **Tuberculosis** Center

The information contained in this resource has been adapted from the references listed below. Please consult: *www.cdc.gov/tb* for additional up-to-date information on the diagnosis and tx of LTBI and/or active TB.

- Centers for Disease Control and Prevention. Latent Tuberculosis Infection: A Guide for Primary Health Care Providers. Available at: *www.cdc.gov/tb/publications/LTBI/*. Accessed July 25, 2014.
- Centers for Disease Control and Prevention. Treatment of Tuberculosis, American Thoracic Society, CDC, and Infectious Diseases Society of America. MMWR 2003; 52(No. RR-11): [1-77]. Available at: *www.cdc.gov/mmwr/PDF/rr/rr5211.pdf*
- Centers for Disease Control and Prevention. Updated Guidelines for Using Interferon Gamma Release Assays to Detect Mycobacterium tuberculosis Infection-United States, 2010. MMWR 2010; 59 (No. RR-5):[1-24]. Available at: *www.cdc.gov/mmwr/pdf/rr/rr5905.pdf*
- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at: *www.aidsinfo.nih.gov/contentfiles/adultandadolescentgl.pdf*. Pages J12-18 and Tables 17 and 18. Accessed July 25, 2014.
- Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: 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. Available at: *http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf*. Pages F1-27, U41-43. Accessed July 25, 2014.

LATENT TUBERCULOSIS INFECTION

- Latent tuberculosis infection (LTBI) is the presence of *Mycobacterium tuberculosis* in the body without signs and sxs, 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 are at extremely high risk (estimated 3-16% risk per yr) for developing active TB if infected with *M. tuberculosis*
- Test all HIV-infected pts for LTBI at time of entry into care
- All pts with (+) test for LTBI should be evaluated for active TB (i.e., chest x-ray [CXR] and clinical evaluation for pulmonary and extrapulmonary sxs) before starting tx for LTBI

Tuberculin Skin Test

- The Mantoux TST method is recommended and each step must be properly performed to increase accuracy of results
- Pts who will have repeat TST (e.g. healthcare workers, nursing home residents) should have two-step testing done initially. Pts with (-) initial TST should have 2nd test 1-3 weeks later; a (+) 2nd test indicates prior infection (booster effect).

Administration of TST

- Use ¼ to ½ inch 27-gauge needle and tuberculin syringe
- Inject 0.1 mL of tuberculin purified protein derivative (PPD) intradermally into the inner surface of the forearm
- When done correctly, a wheal (pale elevation of skin), 6-10 mm in diameter should be produced
- If wheal not produced, repeat placement on opposite arm or on same arm ≥ 2 inches from original site

Reading of TST

- Reaction measured in 48 to 72 hrs (must be done by properly trained health professional; pt or family/friends should not be allowed to read the test)
  - (+) reaction can be measured accurately for ≤ 7 days, (-) for ≤ 72 hrs
  - Schedule repeat TST or IGRA if pt does not return within 72 hrs
- Measure area of induration (raised palpable, hardened area), not areas of redness, across the forearm
- Report results in mm (not as "positive" or "negative")

Interpretation of TST Results

- Reaction of ≥ 5 mm is considered (+) in HIV-infected persons
- A (-) TST or IGRA result does not exclude LTBI as they may have a compromised ability to react to tests for TB infection
- False (+) may result if:
  - Infection with nontuberculous mycobacteria
  - Prior Bacillus Calmette-Guérin (BCG) vaccine (reactivity wanes over time; use of IGRA preferred)
  - Improper admin and/or interpretation of results

LATENT TUBERCULOSIS INFECTION Continued

- Possible reasons for false (-) (list is not all inclusive):
  - Anergy (inability to react to TST due to immune suppression; anergy testing with "controls" is not recommended)
  - Recent TB infection (2-8 weeks after exposure); treat HIV-infected persons exposed to pulmonary TB regardless of TST or IGRA results
  - Extremes of age (newborns, elderly)
  - Concurrent infections (certain bacterial, fungal, or viral)
  - Overwhelming TB disease
  - Immune suppression due to meds, malignancy, or HIV
  - Recent live virus vaccine (wait 4-6 weeks to admin TST)
  - Problem with tuberculin used (e.g., improper storage), poor admin technique (e.g., subcutaneous instead of intradermal), improper reading or result interpretation

Contraindications to a TST

- Contraindicated for persons with a severe reaction to prior TST (e.g., necrosis, blistering, anaphylactic shock or ulceration)
- Pts with prior (+) TST should not receive TST; CXR or symptomatic cough screen should be done annually

NOTE: TST is NOT contraindicated in infants, children, pregnant women, or persons previously vaccinated with BCG.

Interferon (IFN)-Gamma Release Assays (IGRAs)

- IGRAs are *in vitro* assays that detect IFN-gamma release in response to *Mycobacterium tuberculosis* specific antigens. Specificity of IGRA ranges 92%-97%, compared to 56%-95% for TST. Two FDA approved assays are available:
  - QuantiFERON® - TB Gold In-Tube (Cellestis Limited)
  - T-SPOT® TB Test (Oxford Immunotec Limited)
- It is important that test samples be drawn, transported, processed, and interpreted according to each manufacturer's recommendations
  - Blood samples must be processed within 8-16 hrs after collection (time requirements differ among assays) so that the white blood cells remain viable
- Additional information about IGRAs can be found online at: *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 when a TST is recommended with some preferences noted below
- IGRA is preferred in:
  - Persons who have received BCG whether as a vaccination or as cancer tx
  - Groups that have low rates of return for TST read (e.g., homeless persons, drug-users, and those who failed to return within 72 hrs for TST read in the past)

LATENT TUBERCULOSIS INFECTION Continued

Repeat Testing for LTBI Recommended When: Continued

- CD4 increases to > 200 cells/mm³ in response to ART since false (-) TST or IGRA may occur when severely immunocompromised
- Exposed to an active TB case; retest at the time of exposure and again in 8-10 weeks
- Pt is identified to have a risk factor for infection with *M. tuberculosis* (incarcerated or lived in a congregate setting)
- Abused IV drugs, been homeless, or living in a shelter
- Born in or traveled to a country where active TB disease is common (most countries in Latin America, the Caribbean, Africa, Asia, Eastern Europe and Russia)
- Worked in a migrant farm camp
- Been in close contact with recent immigrants from high-prevalence countries
- Had sxs suggestive of active TB disease

NOTE: Annual testing is recommended for pts who have ongoing risks such as those listed. Pts with a history (hx) of (+) TST or IGRA should have annual CXR or TB symptom screen.

TREATMENT FOR LTBI

- LTBI is the presence of *Mycobacterium tuberculosis* in the body without signs and symptoms, or radiographic or bacteriologic evidence of tuberculosis (TB) disease
- All pts with a (+) test (TST or IGRA) for TB infection should have a CXR and clinical evaluation to rule out active pulmonary and extrapulmonary TB disease prior to initiating LTBI tx
- Treat HIV-infected pts for LTBI if:
  - (+) diagnostic test for LTBI with no sxs of active TB and (-) cultures for *M. tuberculosis* **or**
  - Close contact of person with infectious pulmonary TB even if TST or IGRA are (-) **or**
  - Inadequately treated TB (e.g., old fibrotic changes on CXR)
- Completion of full tx course for LTBI is important due to high risk of progression to active TB
- Collaborate with local health department to provide directly observed therapy (DOT) if needed
- **Preferred LTBI regimens:**
  - Isoniazid (INH) 5 mg/kg (max of 300 mg) po once daily **plus** pyridoxine 25 mg po once daily for 9 months (AII) **or**
  - INH 15 mg/kg (max of 900 mg) po twice weekly **via directly observed tx (DOT) plus** pyridoxine 25 mg po once daily for 9 months (BII)
- **Alternative LTBI regimens:**
  - Rifampin (RIF) 10 mg/kg (max 600 mg) po once daily for 4 months (BIII) **or**
  - Rifabutin (RFB) (dose adjusted per ART) for 4 months (BIII) **or**
  - INH 15 mg/kg (max of 900 mg) **plus** rifapentine (RPT) (900 mg [if ≥ 50 kg] or 750 mg [if 32.1-49.9 kg]) po once weekly **via DOT** for 12 weeks **only if pt is otherwise healthy, not pregnant, and *not on ART* (AIII)**
- **For those exposed to drug resistant TB, consult expert (AII)**

LATENT TUBERCULOSIS INFECTION Continued

Monitoring Patients Treated for LTBI

- Monitor all pts clinically at least monthly including physical exam, side effect and adherence assessment
- Perform baseline LFTs (AST or ALT) and total bilirubin in all pts and check monthly in pts with risk factors for hepatotoxicity (e.g., liver disease, regular alcohol use, pregnant or < 3 months post-partum, receiving ART)
- Perform CBC with diff and platelets at baseline if rifampin used and repeat testing if results abnormal or pt has sxs suggestive of hematologic adverse reaction
- Instruct pt to seek medical attention for the following: fever, yellow eyes, dizziness, rash, or aches or > 1 day of nausea, vomiting, weakness, abdominal pain, loss of appetite
- Rash and flu-like sxs may be sign of serious hypersensitivity reaction to a rifamycin
- Discontinue INH-RPT if ALT ≥ 5x ULN (even if no sxs) or ALT ≥ 3x ULN with sxs

ACTIVE TUBERCULOSIS

Initiating ART in HIV-infected Patients with Active TB

- All HIV-infected pts with active TB should start ART
- See *Adult/Adolescent Antiretroviral guidelines (pages J12-J18,* accessed July 25, 2014) for recommendations regarding timing of ART initiation (all CD4 cell counts are in cells/mm^3):
  - CD4 < 50 (AI): start ART within 2 weeks of starting TB tx
  - CD4 50 to 200 (BI) or > 200 (BIII) with severe TB disease (e.g., low Karnofsky score, low body mass index, low Hgb, low albumin, organ dysfunction or extensive disease): start ART within 2-4 weeks of starting TB tx
  - CD4 50 - 500 (AI) or > 500 (BIII) without severe clinical disease, ART can be deferred > 2-4 weeks but should be started within 8-12 weeks

NOTE: Adult/Adolescent OI Guidelines indicate to start ART in ART-naive pts within 2 weeks of starting TB tx if CD4 < 50 and by 8-12 weeks for all others (AI) (*See page F-8 of the OI guidelines.* Accessed July 25, 2014).

Diagnosis of Active Tuberculosis Infection

- Evaluate all pts with a (+) TB test (TST or IGRA) for active TB
- Test for TB in all pts suspected of having active TB; a (-) test does not rule out active TB, particularly in immunocompromised pts
- Sxs of active pulmonary TB:
  - Prolonged productive cough (usually > 3 weeks), chest pain, hemoptysis, fever/chills, night sweats, decreased appetite/weight loss, fatigue
- Pts with HIV are more likely to have extrapulmonary TB compared to those without HIV. Sxs and clinical presentation depend on the site of infection. **Consult a TB/HIV expert for the management of extrapulmonary TB.**
- CXR: Abnormalities usually seen in upper lobe. Pts with HIV may have atypical CXR appearance, including a normal CXR despite pulmonary disease.
- Sputum smear and culture:
  - 3 sputum specimens (8-12 hrs apart) should be sent for smear examination (AFB stain and nucleic acid amplification test [NAAT]) and culture (even if smear is [-])

NOTE: In extrapulmonary TB, sputum smear and culture are usually (-) until late in disease.

Treatment of Drug-Susceptible Active Pulmonary TB in HIV-infected Patients

Southeastern National Tuberculosis Center

Consult a TB/HIV expert for the assistance in the management of extrapulmonary TB, drug-resistant TB, adverse effects, or drug-drug interactions. Call the 24-hour TB Hotline at 1.800.4TB.INFO (1.800.482.4636) for assistance.

- All HIV pts should receive directly observed tx (DOT)
- All pts with presumed or confirmed active TB should be started on a 4-drug regimen of isoniazid (INH), (rifampin [RIF] or rifabutin [RFB]), pyrazinamide (PZA), and ethambutol (EMB)
  - Rifabutin is often substituted for rifampin in HIV-infected pts since it is a less potent inducer of drug metabolism and can be used with most ART (see drug interaction table)
  - Rifapentine is a long-acting rifamycin that is dosed once weekly, but should not be used in HIV-infected pts due to higher rates of relapse and resistance
- **Initial phase:** INH + (RIF or RFB) + PZA + EMB po once daily for 2 months (discontinue EMB prior to 2 months if susceptible to INH, RIF/RFB, PZA) (AII)
- **Continuation phase:** INH + (RIF or RFB) 5-7 days per week or 3 times per week po via DOT for 4-7 months (AII)
  - Extend the continuation phase from 4 to 7 months if the sputum culture remains (+) at 2 months (send repeat sputum for susceptibility testing and consult an expert if resistant to INH and/or RIF)

Adult Dose of Agents for Active TB

INH = isoniazid | **RIF** = rifampin | **RFB** = rifabutin
PZA = pyrazinamide | **EMB** = ethambutol

		INH	RIF[1]	RFB[1]	PZA	EMB
Daily	mg/kg	5	10	5	15-30	15-25
	max	300	600	300	2000	1600
3 times per week	mg/kg	15	10	5	50-70	30
	max	900	600	300	3000	2400

1. See Drug Interactions table for interactions and dosing recommendations with ART.

Monitoring Therapy for Pulmonary TB

- Monitor pt clinically at least monthly
- Sputum for smear and culture monthly until 2 consecutive (-) culture results:
  - If initially smear (+), test more frequently (e.g., every 2 weeks) to assess tx response

ACTIVE TUBERCULOSIS Continued

Monitoring Therapy for Pulmonary TB Continued

- Repeat CXR after 2 months of tx (not essential if cultures [+] at diagnosis but if [-] at diagnosis and CXR improving, presumptive diagnosis of TB can be made). End of tx CXR recommended by most to document end of tx baseline.
- Repeat drug susceptibility testing if culture (+) after 3 months of tx. Consider tx failure if (+) culture at 4 months. Consult a TB/HIV specialist for pts who fail tx and/or have drug resistance.

Monitoring for Drug Adverse Effects (AEs)

Baseline:

- Obtain hx for risk factors for AEs (e.g., diabetes, renal failure, hepatitis, alcohol use) and concurrent medications
- Obtain baseline labs - LFTs, TBili, uric acid, BUN/Cr, CBC with differential
- If pt is to be on EMB, obtain baseline eye exam for both acuity and color discrimination
- Educate pt on the signs and sxs of hepatitis
- Encourage pt to immediately report sxs of hepatitis or changes in vision

Monthly:

- Interview pt for AEs, changes in medications, and screen for possible drug interactions
  - Vomiting - (increases risk for drug resistance)
    - Change time of TB Rx dose, have pt eat 2 hrs before dosing
    - Add metoclopramide 5 to 10 mg or promethazine 25 mg 30 min before TB drugs
    - Persistent cases may require lorazepam 0.5 to 1 mg 30 min before TB meds
  - Peripheral neuropathy (INH) - Ensure pt is receiving pyridoxine (vitamin B6) 25-50 mg po once daily
  - Itching - add antihistamine 30 min before TB Rx and prn
- If on EMB, do eye exam for acuity and color. If decreased, stop the EMB. Check dose, renal function, serum drug levels, refer to ophthalmologist. Consult TB/HIV expert for TB regimen modification.
- LFTs, TBili (INH, RIF/RFB, PZA) - Continue Rx unless AST > 3x ULN and symptomatic, AST ≥ 5x ULN and asymptomatic, or significant increases in bilirubin and/or alkaline phosphatase. Consult a TB/HIV expert for management of these cases.

Periodically during tx:

- Uric acid levels do not need to be followed unless symptomatic (e.g., gouty arthritis). If symptomatic may add allopurinol, NSAIDS.
- If at risk or otherwise indicated, do lab work for renal function, CBC with differential
- Consider therapeutic drug monitoring for TB, HIV (NNRTI, PI, integrase inhibitor, maraviroc) and other interacting drugs if signs of AEs, renal or hepatic disease or possible tx failure

Immune Reconstitution Inflammatory Syndrome (IRIS)

- Pts may have worsening or new onset sxs of active TB following initiation (more common in pts with CD4 < 50 cells/mm^3 and pts with higher pre-ART HIV viral load)
- Continue both ART and anti-TB tx while managing IRIS
- Mild cases can be treated with NSAIDs while more severe cases may require corticosteroid tx
- Consult a TB/HIV expert as needed for IRIS

Therapeutic Drug Monitoring (TDM)

- Interactions can be complex and difficult to predict in individual pts
- Consider TDM in pts who are slow to respond to tx or have complex drug-drug interactions
- TDM should be considered for most pts with renal insufficiency or on dialysis
- Consider TDM in pts on cycloserine
- Consult an TB/HIV expert for assistance in managing these pts
- Call the 24-hour TB Hotline 1.800.4TB.INFO (1.800.482.4636) for assistance
- HIV and TB drug levels are available through many commercial labs as well as the Infectious Disease Pharmacokinetic Laboratory at the University of Florida in Gainesville (*http://idpl.cop.ufl.edu/*) where expert interpretation and consultation regarding results is available

Drug-drug Interactions with Rifamycins and ART

NOTE: Rifpentine is not recommended for use in pts on ART.

RIFAMPIN (RIF)[3]-based Regimen with ART

NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIs)

Efavirenz (EFV) 600 mg po every night (standard) or consider ↑ to 800 mg po every night (pts > 60 kg). Consider TDM

Do not use RIF with etravirine (ETR), nevirapine (NVP), or rilpivirine (RPV)

PROTEASE INHIBITORS (PIs)

Due to significant interactions and/or need for high doses of ritonavir (RTV) to overcome the interactions, it is impractical to use RIF with a PI-containing regimen (boosted or unboosted) and it is not recommended

INTEGRASE STRAND TRANSFER INHIBITORs (INSTIs)

Increase dolutegravir (DTG) to 50 mg po bid. Use alternative to RIF if INSTI-exp with certain INSTI-associated resistance substitutions or clinically suspected INSTI resistance.

Increase raltegravir (RAL) to 800 mg po bid

Do not combine RIF with Stribild® (elvitegravir/cobicistat/emtricitabine/tenofovir)

CCR5 INHIBITOR

Not recommended, but if maraviroc (MVC) used:
MVC 300 mg po bid (with potent CYP3A inhibitor);
MVC 600 mg po bid (without potent CYP3A inhibitor)

RIFABUTIN (RFB)-based Regimen with ART

NNRTIs

NNRTI	Rifabutin (RFB)
EFV (standard dose)	RFB 450-600 mg po once daily **or** 600 mg po 3 times per week (if no PI in the regimen)
ETR (standard dose)	RFB 300 mg po once daily (standard dose). Do not combine ETR with RFB if used with a RTV-boosted PI.
NVP (standard dose)	RFB 300 mg po once daily or 3 times per week (standard dose)
RPV	Increase RPV to 50 mg po once daily[4]

PIs

Ritonavir(r)-boosted PIs	
Atazanavir (ATV)/r	RFB 150 mg po once daily or 300 mg po 3 times per week. Monitor for antimycobacterial efficacy and consider TDM.
Darunavir/r	
Fosamprenavir (FPV)/r	
Lopinavir/r	
Saquinavir/r	
Tipranavir/r	

Unboosted PIs	
ATV	RFB 150 mg po once daily or 300 mg po 3 times per week
FPV	

INSTIs

No dosage adjustments for DTG or RFB

No dosage adjustments recommended for RAL or RFB

Do not combine RFB with Stribild® (elvitegravir/cobicistat/emtricitabine/tenofovir) if avoidable. If used together RFB 150 mg po once daily or 3 times per week with TDM for dose adjustments.

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)

3. All are with RIF standard dose.

4. Edurant® [package insert] Titusville, NJ: Janssen Therapeutics; revised May 2014.

Drugs Used for Treatment of Drug-Susceptible Active TB and LTBI

NOTE: Consult a TB/HIV expert for pts with renal insufficiency (e.g., CrCL < 30 mL/min) and/or hepatic impairment (e.g., LFTs > 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. **Call the 24-hour TB Hotline 1.800.4TB.INFO (1.800.482.4636) for assistance.**

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 hrs after a meal)	• Avoid antacids for 2 hrs 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 hr prior to or 2 hrs after meal); may open cap and mix in food (applesauce)	• Most common/severe AEs: GI disturbances, 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)[2]	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, 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 weeks), hepatotoxicity, arthralgias/myalgias, ↑ uric acid, rare hematologic reactions (thrombocytopenia, porphyria, sideroblastic anemia)

2. Priftin® [package insert]. Bridgewater, NJ: Sanofi-Aventis; revised May, 2010.