

TREATMENT INFORMATION

This card is intended as a convenient, but not a complete reference for health care providers managing the care of HIV-infected patients with drug susceptible TB. As HIV and TB treatment guidelines change frequently, consult <http://www.cdc.gov/tb> and <http://aidsinfo.nih.gov> for up-to-date information in addition to the references listed below.

- TB treatment regimens should be directly observed to assure patient adherence, and therapy should be prolonged if there is a delay in clinical or bacteriological response. The continuation phase should be extended from 4 to 7 months (9 months of total treatment) if the 2-month treatment culture is positive and if cavitation is seen in the chest x-ray after 4 months of treatment.
- Although the principles of TB treatment are similar for children and adults, there are unique considerations in the treatment of HIV and TB co-infected children. Children should be treated without delay. However, consultation with a specialist experienced in managing co-infected children is advised because indications for antiretroviral therapy, dosing of medications, and optimal length of TB therapy in children can vary.
- To prevent acquired rifamycin resistance in persons with advanced HIV infection (CD4⁺ T-cell counts <100/mm³) and TB, use more frequent therapy (3x weekly or daily) with RIF or RBT-based therapies.
- Rifapentine, a long-acting rifamycin, is not recommended for the treatment of TB in HIV-infected persons because of its association with acquired rifamycin resistance.

For complete treatment information, consult the following references:

- CDC. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. *MMWR* 1998; 47.
- CDC. Updated guidelines for the use of rifabutin or rifampin for the treatment and prevention of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. *MMWR* 2000; 49:185-9.
- CDC. Updated guidelines for the use of rifamycins for the treatment of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. *MMWR* 2004; 53:37.
- CDC. Treatment of tuberculosis. *MMWR* 2003; 52 (RR-11).
- American Academy of Pediatrics, Committee on Infectious Diseases. Tuberculosis. In L.K. Pickering (Ed.), 2006 *Red Book: Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2006:678-704.



NEW JERSEY
MEDICAL SCHOOL
GLOBAL
TUBERCULOSIS
INSTITUTE

TB INFOLINE: 1-800-4TB-DOCS WEBSITE: <http://www.umdnj.edu/globaltb>

225 Warren Street
Newark, NJ 07101-1709
(973) 972-3270

Treatment of Tuberculosis (TB) in Adult and Adolescent Patients Co-infected with the Human Immunodeficiency Virus (HIV) 2007

Highly active antiretroviral therapy (HAART) is frequently recommended for TB and HIV co-infected patients. The management of these patients is complex and should be undertaken by experienced health care providers. Drug interactions make TB treatment in HIV-infected patients taking nonnucleoside reverse transcriptase inhibitors (NNRTI) and protease inhibitors (PI) more difficult. Rifamycins induce cytochrome P450 (CYP450) hepatic enzymes that accelerate the metabolism of PIs and NNRTIs and may significantly reduce the serum levels of these drugs. If a rifamycin is excluded from the TB treatment regimen, this may result in delayed sputum conversion, prolong the duration of therapy, and possibly result in a poorer outcome. Rifabutin has been shown to be an effective substitute for rifampin, and because of its lesser effect on CYP450 induction is used *preferably* in the treatment for patients on PIs and NNRTIs. No dose adjustments are needed while using rifamycins and nucleoside/nucleotide reverse transcriptase inhibitors (NRTI/NNRTI) nor for fusion inhibitors.

RECOMMENDATIONS FOR CO-ADMINISTRATION OF RIFAMYCINS AND NNRTIs AND PIs

Rifabutin (RBT)-Based Regimen

Nonnucleoside reverse transcriptase inhibitors

RBT	NNRTI ¹
450-600 mg/day or 600 mg 3x/week	Efavirenz (standard dose)
300 mg/day or 300 mg 3x/week	Nevirapine (standard dose)

Protease Inhibitors

RBT	Single PI
150 mg/day or 300 mg 3x/week	Amprenavir/fos-amprenavir (usual dose)
150 mg/day or 300 mg 3x/week	Indinavir 1000 mg TID
150 mg/day or 300 mg 3x/week	Nelfinavir 1250 mg BID
150 mg alternate days or 3x/week	Atazanavir (usual dose)
150 mg alternate days or 3x/week	Ritonavir (usual dose)
RBT	Dual PI
150 mg alternate days or 3x/week	Lopinavir/ritonavir (usual dose)
150 mg alternate days or 3x/week	Ritonavir (any dose) booster with saquinavir, indinavir, amprenavir, fos-amprenavir, atazanavir, or tipranavir
150 mg alternate days	Ritonavir + darunavir (usual dose)

Do not use delavirdine and unboosted saquinavir with RBT

¹These recommendations apply to regimens that do not include PIs, which can substantially increase RBT levels.

Rifampin (RIF)-Based Regimen

Nonnucleoside reverse transcriptase inhibitors

RIF	NNRTI
600 mg/day	Efavirenz 800 mg/day (max) ²

Do not use nevirapine and delavirdine with RIF.

Protease Inhibitors

Do not use amprenavir, atazanavir, fos-amprenavir, indinavir, lopinavir/ritonavir, nelfinavir, ritonavir, or boosted/unboosted saquinavir with RIF.

²If efavirenz 800 mg cannot be tolerated, reduce to 600 mg.

ANTI-TB TREATMENT REGIMENS (TB-DRUG SENSITIVE) FOR PATIENTS RECEIVING HAART

Initiation of HAART for co-infected patients is based on HIV RNA levels (viral load), CD4⁺ T-cell counts, and a history of certain HIV-associated clinical conditions. Clinicians and patients need to also consider other existing medical issues (e.g., drug interactions and toxicities, ability to adhere to two complex treatment regimens, and laboratory abnormalities). A staggered initiation of anti-TB treatment and HAART for patients not currently on HAART might promote greater adherence to both treatment regimens and reduce any associated drug toxicity. This strategy might include starting HAART at the end of the 2-month induction phase of TB therapy or after TB therapy is completed. For some patients, switching from a RIF-based regimen to a RBT-based regimen will be necessary if HAART is initiated before the completion of anti-TB treatment. However, the potent effect of RIF as a CYP450 inducer continues up to at least 2 weeks following the discontinuation of RIF. Thus, clinicians need to plan for a 2-week “washout” period between the last dose of RIF and first doses of PIs and/or NNRTIs. Alternatively, if HAART will be initiated during anti-TB treatment, the induction phase should include RBT instead of RIF.

Induction Phase		Continuation Phase		
Drugs Daily mg/kg [maximum dosage]	Duration	Drugs Daily mg/kg [maximum dosage]	Drugs 3x weekly mg/kg [maximum dosage]	Duration
Isoniazid (INH): 5 [300] ¹	2 months (8 weeks)	INH: 5 [300]	INH: 15 [900]	4 months (18 weeks)
Rifampin (RIF): 10 [600] ²		RIF: 10 [600]	RIF: 10 [600]	
OR		OR		
Rifabutin (RBT): 5 [300] ^{2,3}		INH: 5 [300]	INH: 15 [900]	
Pyrazinamide (PZA):-- ⁴ [2 g]		RBT: 5 [300]	RBT: 5 [300]	
Ethambutol (EMB):-- ⁴ [1.6 g]				

¹Pyridoxine (vitamin B6) 50 mg/day should be given to all HIV-infected patients taking INH.

²Rifamycins have significant interactions with methadone, oral contraceptives, and other drugs. See MMWR 2003; 52 (RR-11), p. 47.

³RBT dosage is based on weight and class of co-administered HIV drugs (i.e., NNRTI and/or PI) in the HAART regimen. Maximum RBT dosage varies when administered with efavirenz.

⁴See weight-based dosing charts in MMWR 2003; 52 (RR-11), p. 6.