

## Key Messages on the 12-dose Treatment Regimen for Latent Tuberculosis Infection

- On December 9, 2011 the Centers for Disease Control and Prevention (CDC) released recommendations on the use of a new treatment regimen for latent tuberculosis (TB) infection.
  - CDC. Recommendations for Use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent Mycobacterium tuberculosis Infection. *MMWR* 2011;60:1650-1653.  
[http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s\\_cid=mm6048a3\\_w](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_w)
- This new regimen, referred to as the 12-dose regimen, represents a major advancement in preventing future cases of TB disease and puts us closer to our goal of TB elimination.
- The 12-dose regimen is a combination regimen of isoniazid and rifapentine given in 12 once-weekly doses under directly observed therapy (DOT).
- The 12-dose regimen reduces the required treatment for latent TB infection from 270 daily doses over 9 months to 12 once-weekly doses given over 3 months.
- CDC's recommendations are a result of a recent large randomized control trial which found the 12-dose regimen to be as effective for preventing TB as other regimens. The new regimen is also more likely to be completed than the current U.S. standard regimen of 9 months of daily isoniazid given without directly observed therapy.
  - Two additional studies also found the 12-dose regimen to be as effective as other regimens in preventing new cases of TB disease.
- The 12-dose regimen does not replace other recommended latent TB infection treatment regimens; the 12-dose regimen is another effective regimen.
- The 12-dose treatment guideline also does not replace the current latent TB infection treatment guidelines (<http://www.cdc.gov/MMWR/PDF/rr/rr4906.pdf>); it is a supplement guideline.
- The choice between the 12-dose regimen and other approved latent TB infection treatment regimens depends on several factors, including:

- Feasibility of DOT,
  - Resources for drug procurement,
  - Program operations including patient monitoring,
  - Expectance of treatment completion considering medical and social circumstances of the patient, and
  - Preferences of the patient and the prescribing physician.
- Although the new regimen will initially be more expensive for TB programs to administer (including the cost of the drugs and DOT), the public health benefits associated with the new regimen will be that more people will actually complete treatment to prevent progression to TB disease (therefore, also avoiding the potential cost of treating future cases of TB disease).
  - The 12-dose regimen is recommended as an equal option to previous regimens for treating latent TB infection in otherwise healthy people, 12 years of age and older, who were recently in contact with infectious TB or who had tuberculin skin test conversions or positive blood test for TB infection.
    - HIV-infected people who are otherwise healthy and not taking anti-retroviral medicines are included in this category.
  - The 12-dose regimen can be considered for other groups when it offers practical advantages, such as completion within a limited timeframe.
  - The 12-dose regimen is NOT recommended for:
    - Children younger than 2 years of age,
    - People with HIV/AIDS who are taking anti-retroviral therapy,
    - Pregnant women or women who expect to become pregnant during treatment, and
    - People who are presumed to have been infected with isoniazid-resistant or rifampin-resistant *M. tuberculosis*.
  - The preferred regimen for children aged 2 to 11 years old is 9 months of daily isoniazid.
  - Evidence for broader usage of the 12-dose regimen is currently being gathered.
  - DOT is recommended for the 12-dose regimen. Additional studies on self-administration of the 12-dose regimen are underway.

- DOT workers should be trained on how to educate patients about adverse effects and how to inquire about adverse effects.
  - Patients using the 12-dose regimen should undergo monthly clinical monitoring, including inquiries about side effects and a physical assessment for signs of adverse effects.
  - While the 12-dose regimen was well tolerated in the three reported treatment trials, severe adverse effects (defined as effects requiring hospital admission or fatalities) should be reported to FDA MedWatch and local and state health departments immediately for inclusion in CDC's latent TB infection treatment adverse effects surveillance system.
- The American Thoracic Society, Infectious Diseases Society of America, and CDC are revising the comprehensive joint guidelines for diagnosing and treating latent TB infection.

### **Overarching Messages about Latent TB Infection**

- Treating latent TB infection to prevent progression to TB disease is a cornerstone of the U.S. strategy for TB elimination.
- More than 11 million people in the United States have latent TB infection, which is about 4 percent of the total population.
- Certain individuals with latent TB infection, such as those with weakened immune systems (due to HIV, a recent organ transplant, or other reasons) and persons recently infected with TB, are at increased risk of developing TB disease.
- About 5 to 10 percent of people with latent TB infection will develop TB disease if not treated. This equates to approximately 550,000 to 1.1 million people who will develop TB at some point in their life, unless they receive adequate treatment for latent TB infection.
- Treating latent TB infection is essential to controlling and eliminating TB in the United States, because it substantially reduces the risk that the infection will progress to TB disease.
  - Of those with latent TB infection, an estimated 300,000 to 400,000 people begin preventive treatment each year in the United States.
  - Among those who begin treatment, up to 60 percent never complete the current treatment regimen. Patients are more likely to complete a once-weekly, shorter duration regimen. Clinicians may also be more likely to prescribe a shorter regimen.

- Every effort should be made to ensure people with latent TB infection who also have risks for TB disease begin — and complete — the entire course of treatment.
  - Stopping treatment, or missing a significant number of doses, can lead to the development of TB disease.
- More information about latent TB infection, treatment options, and the 12-dose regimen is available at [www.cdc.gov/tb](http://www.cdc.gov/tb).