



Centers for Disease Control
and Prevention (CDC)
1600 Clifton Road NE, MS E-10
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March 4, 2010

Dear Colleagues:

The March 5, 2010 issue of the *Morbidity and Mortality Weekly Report* (MMWR) contains an article entitled *Severe Isoniazid-Associated Liver Injuries Among Persons Being Treated for Latent Tuberculosis Infection — United States, 2004–2008*. The article summarizes data reported to the National Surveillance System for Severe Adverse Events Associated with Latent Tuberculosis Infection. Initiated by the Centers for Disease Control and Prevention (CDC), Division of Tuberculosis Elimination (DTBE) in 2004, this passive surveillance project collects reports of severe adverse events associated with treatment for latent tuberculosis infection (LTBI). For surveillance purposes, a severe adverse event was defined as any drug-associated reaction resulting in a patient's hospitalization or death after at least 1 treatment dose for LTBI. Although the surveillance project collects reports for severe adverse events associated with any LTBI treatment regimen, since 2004 DTBE has received only reports related to the use of isoniazid.

The following is key background information:

- Six to nine months of isoniazid has been the mainstay of treatment for LTBI since the 1960s, but its application has been limited by concerns about the toxicity of isoniazid and the long duration of treatment.
- Historically, isoniazid-associated liver injury has been rare among persons receiving treatment for LTBI, occurring at an estimated rate of 1 per 1,000 patients. However, the lack of specific diagnostic criteria and the unreliability of estimates for the number of persons initiating isoniazid for LTBI treatment prevent an accurate estimation of the rate of isoniazid-associated liver injury.
- CDC's surveillance project is the only national system that collects relevant public health data regarding the appropriateness of testing and treatment for LTBI and monitoring during treatment.

We present these data not to discourage treatment of LTBI, but to remind providers of the need for the careful selection and monitoring of treatment candidates and to increase awareness of CDC's national surveillance project. **We continue to strongly support the treatment of LTBI as a key component of CDC's efforts to eliminate tuberculosis.** Until an equally effective alternative regimen is identified, isoniazid remains the mainstay of LTBI treatment in the United States. Candidates for treatment should be selected according to American Thoracic Society (ATS)/CDC guidelines for the targeted testing and treatment for LTBI. Patients receiving isoniazid for LTBI therapy should be monitored closely according to ATS/CDC recommendations because of the risk of drug-induced hepatotoxicity.

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Providers should counsel patients to terminate isoniazid therapy promptly and seek medical attention if they experience signs and symptoms of liver injury. To learn more about these rare but severe events, CDC encourages reporting to this national passive surveillance project.

This report will be available on the MMWR website at <http://www.cdc.gov/mmwr/> or on DTBE's website at <http://www.cdc.gov/tb> on March 4, 2010. If you have any questions or need additional information, please contact your Program Consultant in the Field Services and Evaluation Branch at DTBE.

Sincerely,



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