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TO: Health care providers
RE: Nitrosamine impurities detected in samples of rifampin and rifapentine
FROM: John Bernardo, MD, Tuberculosis Medical Officer
Jennifer Cochran, Director, Division of Global Populations and Infectious Disease Prevention
Larry Madoff, MD, Medical Director, Bureau of Infectious Disease and Laboratory Sciences
DATE: September 22, 2020

The U.S. Food and Drug Administration (FDA) recently posted an [announcement](#) that nitrosamine impurities have been detected in samples of rifampin and rifapentine. Some compounds in this class of substances (nitrosamines) have been implicated as possible carcinogens in long-term animal studies, with toxicity largely related to cumulative exposure.

At this time, and until additional information becomes available, the Department of Public Health (DPH) recommends:

Treatment of TB disease: Continue use of rifampin in the treatment of TB disease, if acceptable to the patient, as the risk of not taking rifampin likely outweighs any potential risk from nitrosamine impurities.

Treatment of latent TB infection:

- For patients **currently receiving rifampin or rifapentine** for treatment of LTBI, continue this treatment, although a change to isoniazid (INH) is acceptable if preferred by the patient.
- For patients with **newly diagnosed LTBI**, and until more information becomes available, consider alternative treatment strategies. These might include:

Isoniazid (INH) daily for 9 months (6 months is a less effective alternative), recognizing issues with adherence for a 9-month treatment course and toxicity/intolerance of INH.

Rifamycin-containing regimens may be considered for LTBI after evaluating risks and benefits in discussion with individual patients for persons at highest risk of progression to disease such as contacts, converters, immunocompromised individuals, and those who will be receiving certain biologics.

Consider deferring treatment of LTBI for persons at lower risk of disease progression until more data are available from FDA and CDC.

For pregnant or breastfeeding women at low TB risk, treatment may be deferred. Those at high risk may be treated with either rifampin or INH, recognizing increased risk of INH toxicity in late pregnancy and postpartum.

INH is recommended for children.

The origin of these impurities in rifampin and rifapentine currently is unknown. FDA only recently began including testing for nitrosamines, which are potential carcinogens, in rifampin and rifapentine as part of its drug safety requirements. It is possible that nitrosamines were present in rifampin and rifapentine for a substantial time (years or decades) prior to introduction of these tests. The Centers for Disease Control and Prevention (CDC) has subsequently posted a [Dear Colleague](#) letter.

The FDA and CDC believe that the potential risk of cancer in patients receiving these medications for treatment of tuberculosis (TB) or latent TB infection (LTBI) is low. Most nitrosamine exposure in humans comes from dietary sources, such as cured meats and alcoholic beverages.

The FDA and CDC will be monitoring stocks of these drugs from manufacturers while working with manufacturers to reduce nitrosamine levels. Because of the importance of these drugs to public health, FDA is not recalling them, and with CDC, recommends that patients with tuberculosis infection or disease continue to be prescribed these drugs as clinically indicated, subject to drug availability. The FDA has posted information about [nitrosamine impurities in medications](#) for patients, providers, and manufacturers.

Drug supply interruptions may occur. Rifapentine is currently in shortage. Sanofi has announced the discontinuation of rifampin-containing products: Rifadin® (rifampin 150 mg and 300 mg capsules), Rifamate® (a fixed-drug combination of isoniazid and rifampin), and Rifater® (a fixed-drug combination of isoniazid, rifampin, and pyrazinamide). Refer to the [FDA drug shortage](#) website for updates. Drug shortages can also be reported to DPH.

This document may be updated as additional information is available.

Contact the DPH TB Program at 617-983-6970 for additional assistance.