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Subject: Dear Colleague Letter - Update on Rifamycin issues

Dear Colleague:

On August 26, 2020, FDA issued a [statement](#) related to mitigating shortages of rifampin and rifapentine and its interim guidance to continue using these drugs in the treatment of tuberculosis (TB) after nitrosamine-class impurities were detected through recently adopted regulatory standards to assay all medications for nitrosamines. FDA sets standard limits on the concentrations of the impurities and is allowing distribution of rifampin and rifapentine if the concentrations do not exceed interim limits while the impurities are investigated. This letter updates CDC's Division of TB Elimination (DTBE) Dear Colleague Letters of [June 19](#) and [August 19, 2020](#). CDC's DTBE recommends that providers continue prescribing rifampin and rifapentine for all TB and latent TB infection (LTBI) treatment per existing [guidelines](#).

Background

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. DTBE is not aware of any data showing an association between cancer and use of rifamycins in humans. However, DTBE is also not aware of any rigorous studies that have looked for this association.

Information on Rifampin

Unrelated to the detection of nitrosamine impurities, Sanofi announced the discontinuation of three oral 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) in June 2020. Information on drug shortages and discontinuations is available from [FDA](#). FDA is working with other manufacturers to maintain availability of rifampin, and there is no national shortage of rifampin at present. Rifampin should be prescribed as an essential part of a multi-drug regimen for the [treatment of active TB disease](#). Rifampin can also be prescribed, as 3 months of daily isoniazid and rifampin (3HR) or 4 months of daily rifampin (4R), for treating LTBI to prevent the development of active TB disease per current [National TB Controllers Association \(NTCA\)/CDC guidelines](#).

Information on Rifapentine

In June 2020, shipments of rifapentine (supplied as Priftin® 150 mg film-coated tablets manufactured by Sanofi) were paused after a nitrosamine impurity was found. FDA and

Sanofi have not announced when shipments will resume, and [FDA](#) still lists rifapentine as “Currently in Shortage.” Where local supplies of rifapentine are enough for complete regimens, providers can continue to prescribe the 3-month regimen of weekly rifapentine with isoniazid (3HP) for treating LTBI. Where [rifapentine](#) is in shortage, providers can consider other [rifamycin-based regimens](#) such as 3HR or 4R, which have completion rates comparable to 3HP.

Information on Drug Treatment Continuation for LTBI

Patients who are already taking rifampin or rifapentine-containing regimens for LTBI can continue their treatment. If a clinician or a patient prefers to discontinue one of these regimens, a complete regimen of [6 or 9 months of isoniazid](#) can be started, or the original regimen can be completed with a proportionate duration of one of the isoniazid-only regimens. However, isoniazid regimens are associated with increased risk of drug-induced liver injury and lower completion rates. Therefore, CDC does not recommend discontinuing rifamycin-based short-course LTBI treatment in favor of isoniazid-only treatment unless necessitated by another event (e.g., adverse reaction to a rifamycin).

Reporting Rifamycin Supply Issues

Information of drug shortages and discontinuations are available from [FDA](#). DTBE recommends that you periodically assess your rifampin and rifapentine availability with your pharmacy or your suppliers. Please keep your CDC project officer for your jurisdiction’s TB cooperative agreement updated by e-mail message or telephone. If you find a shortage or if you are forecasting a shortage, please notify FDA directly by e-mail (drugshortages@fda.hhs.gov) or telephone (240-402-7770). You also can report a shortage to the National Tuberculosis Controllers Association (NTCA) with a form on its home page, <http://www.tbcontrollers.org/>. Questions related to this letter should be sent to CDC by [email](mailto:tbinfo@cdc.gov) (tbinfo@cdc.gov) or phone (770-488-7100).

CDC will continue to monitor the situation closely and work with our partners at [FDA](#), [NTCA](#), [state and local health departments](#), and the [TB Centers of Excellence for Training, Education, and Medical Consultation](#) to ensure TB patients continue to receive safe and effective treatment.

Sincerely,

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