Health Advisory

KITSAP PUBLIC HEALTH DISTRICT

June 24, 2020

Tuberculosis Infection Management

Actions Requested

- Be aware of an international shortage of Rifapentine (supplied as Priftin® 150 mg film-coated tablets manufactured by Sanofi), used in combination with isoniazid (H3P) to treat latent tuberculosis infection.
- Continue Rifapentine in H3P treatment for latent TB if therapy is already established.
- Initiate an alternative treatment course for patients beginning latent TB therapy until Rifapentine supply has been replenished locally.
- Consult our new Tuberculosis Infection Nurse at Kitsap Public Health District, available for providers and community tuberculosis infection support.
    - TB screening, resources, and consults
    - Latent tuberculosis (LTBI) diagnosis and treatment consults
    - TB infection risk and exposure management

      Debbie Rassa, RN-BSN
      Tuberculosis Infection Nurse
      Debbie.rassa@kitsappublichealth.org
      (360) 728-2276
- Report active tuberculosis disease immediately to Kitsap Public Health.
- Reporting of Latent tuberculosis infections is not required.
- For questions, please contact our Communicable Disease staff at 360-728-2235.

Background

- Rifapentine (supplied as Priftin® 150 mg film-coated tablets manufactured by Sanofi) is part of a 3-month regimen with isoniazid (3HP) for treating latent tuberculosis infection (LTBI) and preventing TB disease. It has also been used in several recent and ongoing CDC-funded clinical trials. Priftin® is the only rifapentine product approved by the U.S. Food and Drug Administration (FDA). In June 2020, Sanofi detected low levels of an impurity in some rifapentine drug substance and in some market-ready Priftin® drug product batches at production facilities in Italy. Distribution of rifapentine is currently suspended, this pause is in addition to the ongoing shortage that has affected the U.S. supplies of Priftin® since late 2019.
- The impurity, 1-cyclopentyl-4-nitrosopiperazine, is a nitrosamine and a potential carcinogen. Neither FDA nor Sanofi have issued a recall and have do not recommend that patients presently taking Priftin® as part of 3HP for treating LTBI discontinue this regimen. If a clinician or a patient prefers to discontinue 3HP, treatment for LTBI can be restarted with a complete alternative regimen, or it can be completed with a proportionate duration of an alternative regimen. More background information about nitrosamine impurities in drug products is available on the FDA website.

Resources

- WA DOH TB Provider Toolkit: https://www.doh.wa.gov/YouandYourFamily/IllnessandDisease/Tuberculosis/TBProviderToolkit
- WA DOH latent TB: https://www.doh.wa.gov/Portals/1/Documents/Pubs/343-158-LTBI%20guidance%20in%20WA.pdf
- WA TB Project ECHO Consultations: https://www.doh.wa.gov/YouandYourFamily/IllnessandDisease/Tuberculosis/TrainingandEducation/TBECHO
- CDC latent TB treatment guidelines: https://www.cdc.gov/tb/topic/treatment/ltbi.htm
- CDC clinical considerations for healthcare providers: https://www.cdc.gov/tb/publications/ltbi/default.htm
- FDA nitrosamine impurities: https://www.fda.gov/drugs/drug-safety-and-availability/information-about-nitrosamine-impurities-medications

Attachment

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30341-3724

June 19. 2020

Dear Colleague,

Rifapentine (supplied as Priftin® 150 mg film-coated tablets manufactured by Sanofi) is part of a 3-month regimen with isoniazid (3HP) for treating latent tuberculosis infection (LTBI) and preventing TB disease. It has also been used in several recent and ongoing CDC-funded clinical trials. Priftin® is the only rifapentine product approved by the U.S. Food and Drug Administration (FDA). In June 2020 Sanofi alerted the Division of Tuberculosis Elimination, other health agencies, and stakeholders worldwide about a newly detected impurity in Priftin®. The impurity, 1-cyclopentyl-4-nitrosopiperazine, is a nitrosamine and a potential carcinogen. It was detected through testing based upon recently adopted regulatory standards to assay all medications for nitrosamines. (1,2) Low levels of the impurity have been detected in some rifapentine drug substance and in some market-ready Priftin® drug product batches at production facilities in Italy. The company is investigating the source of this impurity and any safety implications, and has communicated with FDA. A follow-up submission of the results of Sanofi's investigation for discussion with FDA (including a benefit-risk evaluation) is anticipated in July. More background information about nitrosamine impurities in drug products is available on the FDA website. (3)

As a precautionary measure, Sanofi has paused the release of Priftin® from its production sites. This is expected to affect availability of the drug in the United States. This pause is in addition to the ongoing shortage that has affected the U.S. supplies of Priftin® since late 2019, and which was attributed to increased global demand. The investigation underway is the result of chemical testing of drug product and drug substance, and not a consequence of any observed safety signal in the pharmacovigilance databases. At this time, neither FDA nor Sanofi has requested a recall of the Priftin® supply that has already been distributed. FDA has not issued any new advisory about Priftin®. Neither FDA nor Sanofi has recommended that patients presently taking Priftin® as part of 3HP for treating LTBI discontinue this regimen. If a clinician or a patient prefers to discontinue 3HP, treatment for LTBI can be restarted with a complete alternative regimen, or it can be completed with a proportionate duration of an alternative regimen.

The 3HP treatment regimen should not be started for new patients until shipments of Priftin® resume and local supplies are reestablished. Other short-course regimens for treating LTBI — 4 months of daily rifampin or 3 months of daily isoniazid and rifampin — are recommended for their effectiveness and tolerability, per CDC's updated guidelines on treating LTBI. (4) When directly observed therapy (DOT) is preferred, regimens of 6 or 9 months of isoniazid administered twice weekly can be considered because the intermittent dosing schedule is useful for DOT. However,

these twice-weekly regimens have long durations and unconfirmed tolerability and efficacy.

Please share this notice with your partners in TB prevention such as clinicians at community health centers or correctional facilities. We will send updates about Priftin® when Sanofi and FDA share new information. Please coordinate your efforts with jurisdictional TB control authorities, https://www.cdc.gov/tb/links/default.htm. Send questions by e-mail to RPTqueries@cdc.gov. We will monitor this mailbox daily including weekends.

Sincerely,

Terence Chorba, MD, DSc
Chief, Field Services Branch, Division of Tuberculosis Elimination
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Centers for Disease Control and Prevention
1600 Clifton Road NE (US 12-4), Atlanta, GA 30329

References:

1. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/m7r1-assessment-and-control-dna-reactive-mutagenic-impurities-pharmaceuticals-limit-potential

2. https://database.ich.org/sites/default/files/Q3A%28R2%29%20Guideline.pdf and https://database.ich.org/sites/default/files/Q3B%28R2%29%20Guideline.pdf

3. https://www.fda.gov/drugs/drug-safety-and-availability/information-about-nitrosamine-impurities-medications

4. Available at: https://www.cdc.gov/mmwr/volumes/69/rr/rr6901a1.htm.