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Recurrent Nationwide Shortage of Tuberculin Skin Test Antigen Solutions: CDC Recommendations for Patient Care and Public Health Practice

Summary: In HAN 345 (<http://emergency.cdc.gov/HAN/han00345.asp>), April 2013, CDC reported that TUBERSOL®, a product of Sanofi Pasteur Limited, was in shortage nationwide. Although supplies were restored in early June 2013, TUBERSOL® is in shortage again until at least the middle of October 2013. At the current time, the 5 tuberculin units/0.1 mL, 5 mL (50 tests), multiple dose vials are unavailable. The 5 tuberculin units/0.1 mL, 1 mL (10 tests), multiple dose vials are in limited supply. **This notice updates and supersedes the advice in HAN 345 and advises public health officials, clinicians, and workers in occupational health and infection control about how to adapt testing protocols to the recurrent shortage.**

TUBERSOL® is one of two purified-protein derivative (PPD) tuberculin antigen solutions that are licensed by the United States Food and Drug Administration (FDA). JHP Pharmaceuticals, LLC, manufactures APLISOL®, the other PPD tuberculin product that is licensed by FDA. JHP Pharmaceuticals, LLC, has notified FDA that APLISOL® is on allocation, meaning that historical customers have precedence for buying the product, and APLISOL® is available in restricted quantity. Regional shortages of APLISOL® have been reported since healthcare providers switched from TUBERSOL® to APLISOL®.

Background

Two kinds of immunological methods are used for detecting *Mycobacterium tuberculosis* infection: tuberculin skin tests (TSTs) and interferon- γ release assay (IGRA) blood tests. The indications for using these tests are the same for both methods, although one or the other method is preferred for certain populations (1). When setting testing priorities because of the current shortage of antigen, these preferences may be considered as factors when one of the methods is unavailable. Together, these tests are the only means for detecting latent *M. tuberculosis* infection, and they contribute to diagnosing tuberculosis (TB) disease. When findings such as chest radiography and mycobacterial cultures are sufficient for confirming or excluding the TB diagnosis, the results from a TST or an IGRA blood test might be unnecessary (2). Nevertheless, most TB cases in the United States are diagnosed with a set of findings including results from one of these tests. When TB disease is strongly suspected, specific treatment should be started regardless of results from TST or an IGRA blood test (1,3).

In cross-sectional controlled studies, TUBERSOL® and APLISOL® give similar results for most patients. The agreement between results from a TST and an IGRA blood test or between results from the two commercial IGRA blood tests is lower (1).

Recommendations

CDC recommends any of three general approaches for addressing the shortages of tuberculin skin test antigens:

1. Substitute IGRA blood tests for TSTs. The cost associated with using the blood tests can be greater than the cost of TST because the per-unit cost of the IGRA test materials is greater than for those of TST and, unlike TST, IGRAs entail services external to the point of care in some settings. The blood tests require phlebotomy, preparation of blood specimens, and specific laboratory services for analysis; therefore, these tests are not available in all practice settings. Clinicians who use the IGRA blood tests should be aware that the criteria for test interpretation are different from the criteria for interpreting TSTs (1). IGRAs do not utilize the risk-stratified cut-off measurements that are used for TST. Both IGRA products that are licensed in the United States can give indeterminate results, and one of these can also give borderline results (results between positive and negative). TST does not yield indeterminate or borderline results (1).

2. Substitute APLISOL® for TUBERSOL® for skin testing if APLISOL® is available. In studies, the two products give similar results for most patients. The fixed availability of APLISOL® has created a relative shortage because of increased demand at sites where TUBERSOL® is unavailable, thus limiting the feasibility of this approach.

3. Allocate TSTs to priority usages, such as TB contact investigations, as determined by public health authorities. Priorities can be set in accordance to relative TB risks (4) and local TB epidemiology. A priority strategy might require deferment of testing some persons, and it might require modification of public health rules, regulations, or policies. CDC does not recommend testing persons who are not at risk for TB (4).

Some surveillance programs for TB infection control rely on routine serial TSTs. Switching products or methods might make serial changes in test results difficult to interpret. The apparent conversions of results from negative to positive or reversions from positive to negative could be caused by inherent inter-product or inter-method discordance (1,5). In settings with a low likelihood of TB exposure, the deferment of routine serial testing should be considered in consultation with public health and occupational health authorities.

Updates about the shortages of tuberculin skin test solutions are posted by the FDA Center for Biologics Evaluation and Research at

<http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/Shortages/ucm351921.htm>.

References

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