Corporate Medical Policy

Testing for Diagnosis of Active or Latent Tuberculosis AHS – G2063

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Description of Procedure or Service

Description

Infection by Mycobacterium tuberculosis (Mtb) results in a wide range of clinical presentations dependent upon the site of infection from classic signs and symptoms of pulmonary disease (cough >2 to 3 weeks' duration, lymphadenopathy, fevers, night sweats, weight loss) to silent infection with a complete absence of signs or symptoms(Lewinsohn et al., 2017).

Culture of Mtb is the gold standard for diagnosis as it is the most sensitive and provides an isolate for drug susceptibility testing and species identification (Bernardo, 2018).

Nucleic acid amplification tests (NAAT) use polymerase chain reactions (PCR) to enable sensitive detection and identification of low density infections (M. Pai, Flores, Hubbard, Riley, & Colford, 2004).

Interferon-gamma release assays (IGRAs) are blood tests of cell-mediated immune response which measure T cell release of interferon (IFN)-gamma following stimulation by specific antigens such as *Mycobacterium tuberculosis* antigens (Lewinsohn et al., 2017; Madhukar Pai & Menzies, 2017) used to detect a cellular immune response to *M. tuberculosis* which would indicate latent tuberculosis infection (LTBI) (M. Pai et al., 2014).

Scientific Background

Tuberculosis (TB) continues to be a major public health threat globally, causing an estimated 10.4 million new cases and 1.4 million deaths from TB in 2015 (WHO, 2016), with the emergence of multidrug resistant strains only adding to the threat (Dheda et al., 2014). The lungs are the primary site of infection by Mtb and subsequent TB disease. Onset of symptoms is usually gradual with a persistent cough being most frequently reported (95%) followed by the typical symptoms of fever (75%), night sweats (45%) and weight loss (55%)(Heemskerk, Caws, Marais, & Farrar, 2015). Clinical manifestations include primary TB, reactivation TB, laryngeal TB, endobronchial TB, lower lung field TB infection, and tuberculoma (Bernardo, 2018). Extrapulmonary infection represents approximately 20% of cases of active TB with an additional 7% having concurrent pulmonary and extrapulmonary infections(Peto, Pratt, Harrington, LoBue, & Armstrong, 2009).

In most individuals, initial *Mycobacterium tuberculosis* infection is eliminated, or contained by host defenses while infection remains latent(Barry et al., 2009; Dheda, Schwander, Zhu, van Zyl-Smit, & Zhang, 2010). Persons with latent TB infection (LTBI) are considered to be asymptomatic and not infectious, however, latent Mtb bacilli may remain viable and reactivate to cause active, contagious infection. Identification and treatment of LTBI are important TB control strategies, especially in

settings with a low TB incidence, where reactivation of LTBI often accounts for the majority of nonimported TB disease (ATS, 2000; Landry & Menzies, 2008; M. Pai et al., 2014).

Latent TB Testing

The goal of testing for LTBI is to identify individuals who are at increased risk for the development of tuberculosis (TB) and therefore who would benefit from treatment of latent TB infection. Only those who would benefit from treatment should be tested, so a decision to test presupposes a decision to treat if the test is positive (Madhukar Pai & Menzies, 2017).

Mycobacterial infection results in a predominantly cell mediated immune response (Daniel, 1980). Skin testing (TST) has long been a convenient, cost-effective method for assessing cell-mediated immune responses to a variety of antigens (Snider, 1982), and has been the "gold standard" for diagnostic screening Mycobacterium tuberculosis infections. However, there continue to be multiple factors challenging the accuracy of the skin test, including skill requirements for and variability in placement and reading, cross-reactivity, and underlying illness or immunosuppression (Daniel, 1980; Snider, 1982). The sensitivity of the TST 71%–82% (Francis et al., 1978; Katial et al., 2001; Lewinsohn et al., 2017).

The cell mediated immune response to M. tuberculosis is involves production of gamma interferon (IFN-γ)(Fenton et al., 1997). Interferon-gamma release assays (IGRAs), in vitro culture assays measuring IFN-γ production in response to tuberculin antigen stimulation, have been developed as diagnostic screening tests (Katial et al., 2001; Lein & Von Reyn, 1997) IGRAs have specificity >95 percent for diagnosis of latent TB infection (Menzies, Pai, & Comstock, 2007; M. Pai et al., 2014) and a sensitivity of 80-90 percent.

Clinical Validity and Utility

Diel et al (2012) performed a "meta-analysis critically appraises studies investigating the positive and the negative predictive value (PPV and NPV, respectively) from a test-determined LTBI state for progression to active TB of interferon-γ release assays (IGRAs) and the tuberculin skin test (TST)" and concluded that "The pooled PPV for progression for all studies using commercial IGRAs was 2.7% (95% CI, 2.3%-3.2%) compared with 1.5% (95% CI, 1.2%-1.7%) for the TST (P < .0001)." and "Commercial IGRAs have a higher PPV and NPV for progression to active TB compared with those of the TST".

Ruan et al (2016) further assessed the "diagnostic value of interferon-γ release assays (IGRAs) for latent tuberculosis infection (LTBI) in patients with rheumatic disease before receiving biologic agents." And found "Compared with the tuberculin skin test (TST), the pooled agreements in QFT-G/GIT and T-SPOT.TB were 72 % (95 % confidence interval (CI) 65, 78 %) and 75 % (95 % CI 67, 83 %), respectively. BCG vaccination was positively correlated with positive rates of TST (pooled odds ratio (OR) 1.64, 95 % CI 1.06, 2.53). Compared with TST, IGRAs were better associated with the presentence of one or more tuberculosis (TB) risk factors. Neither steroid nor disease-modifying anti-rheumatic drugs (DMARDs) significantly affect positive IGRA results. In contrast, TST positivity was significantly impacted by the use of steroid (pooled OR 0.45, 95 % CI 0.30, 0.69), but less significantly by the use of DMARDs (pooled OR 0.78, 95 % CI 0.50, 1.21). In conclusion, in rheumatic patients with previous BCG vaccination or currently on steroid therapy, IGRAs would be the better choice to identify LTBI by decreasing the false-positivity and false-negativity rate compared with conventional TST."

Active TB Testing

The diagnosis of TB disease should be suspected in patients with relevant clinical manifestations and exposure history (Lewinsohn et al., 2017). Laboratory testing is an integral part of the rapid and accurate diagnosis of TB to facilitate timely initiation of treatment.

The reference standard for diagnosis of any TB infection is isolation of M.tuberculosis (M. Pai, Nicol, & Boehme, 2016). The isolate recovered should be identified according to the Clinical and Laboratory Standards Institute guidelines (Institute, 2018) and the American Society for Microbiology Manual of Clinical Microbiology (Lewinsohn et al., 2017; Woods, Lin, & Desmond, 2015), and all United States jurisdictions require submission of culture isolates identified as M. tuberculosis for confirmation of identification and drug susceptibility testing (Taylor, Nolan, & Blumberg, 2005). Positive cultures are also reported to public health authorities for oversight and case management (Bernardo, 2018). Cruciani et al (2004) performed a meta-analysis of 10 studies which found that both liquid and solid culture media methods are highly specific (99%). Liquid culture methods are more sensitive (81.5-85.8%) and have a shorter time to detection (13.2-15.2 day) than solid media but are more prone to contamination (4-9%). Solid media has a sensitivity of 76% and averages 25.8 days for detection. The use of both culture methods increases the overall sensitivity to 87.7-89.7%.

Rapid and accurate diagnosis is critical for timely initiation of TB treatment (M. Pai et al., 2016). Although sensitive, culture can take over two weeks to return results (Lewinsohn et al., 2017). The detection of acid-fast bacilli (AFB) on microscopic examination of stained sputum smears is the most rapid and inexpensive technique (Bernardo, 2018), however is limited by its lack of sensitivity especially in extrapulmonary infection or paucibacillary infections in children or as a result of coinfection with HIV(M. Pai et al., 2016). Three specimens should be examined to assure a sensitivity of approximately 70%. The first specimen has a sensitivity of approximately 53.8%, increasing by 11.1% with a second specimen, and another 2-5% with a third (Mase et al., 2007). A first morning specimen increases sensitivity by 12%, and concentrating specimens can increase sensitivity by 18% (Steingart, Ng, et al., 2006). Use of fluoresce microscopy also increases sensitivity 10% over conventional microscopy(Lewinsohn et al., 2017; Steingart, Henry, et al., 2006). The positive predictive value has been reported to be 97.9-100% (Gordin & Slutkin, 1990), but is impacted by non-tuberculosis Mycobacterium species (NTM)(Yajko, Nassos, Sanders, Madej, & Hadley, 1994).

Nucleic acid amplification techniques (NAAT) have been developed for rapid diagnosis of TB. Two major tests are available, the Amplified Mycobacterium tuberculosis Direct (MTD) test and the Xpert MTB/RIF test. NAAT based assays are more sensitive than smear, but less sensitive than culture, with a reported sensitivity of 96% and specificity of 99% (Greco, Girardi, Navarra, & Saltini, 2006; Lewinsohn et al., 2017). NAAT testing has >95% positive predictive value in the setting of AFB smear-positive specimens for distinguishing tuberculous from nontuberculous mycobacteria, and can establish the presence of tuberculosis in 50 to 80% of AFB smear-negative specimens (Cheng, Yew, & Yuen, 2005). NAAT does not replace the roles of AFB smear and culture (Ling, Flores, Riley, & Pai, 2008)in the diagnostic algorithm for tuberculosis and results must be interpreted in conjunction with AFB smear results while mycobacterial culture is pending (CDC, 2009; Lewinsohn et al., 2017).

Sequence based assays provide the genetic identity of a particular mutation and therefore can predict drug resistance with greater accuracy than probe-based assays are available from state public health TB laboratories to the Centers for Disease Control and Prevention for sequence-based molecular detection of drug resistance (MDDR) testing. The testing identifies genetic mutations associated with rifampin and isoniazid resistance as well as resistance to second-line drugs including fluoroquinolones and the injectables amikacin, kanamycin, and capreomycin. Molecular testing results are generally available within days and can be used to guide initial treatment decisions and inform design of prevention regimens for contacts (Bernardo, 2018; Taylor et al., 2005).

Urine testing for mycobacterial cell wall glycolipid (Shah et al., 2010) has been investigated as a point of care assay for diagnosis of TB in HIV infected patients (Nakiyingi et al., 2014). The test was 97.6% specific and 67.9% sensitive in patients with CD4<100. It is useful in addition to routine diagnostic tests for HIV-infected patients with signs and symptoms of TB and CD4 ≤100 cells/microL and for all HIV-infected patients who are seriously ill (Shah et al., 2016; WHO, 2015). Gupta-Wright et al (2018) evaluated via sputum Xpert MTB/RIF with or without urine lipoarabinomannan (LAM) testing. There was no difference in overall mortality, but they found that urine Lam testing might benefit some high-risk subgroups (CD4 <100, severe anaemia, and patients with clinically suspected tuberculosis).

Adenosine deaminase (ADA) and interferon-gamma (IFN- γ) levels in cerebrospinal, pleural, peritoneal, and pericardial fluids have been studied in the diagnosis of extrapulmonary TB. The sensitivity of ADA in these fluids is 79% and the specificity is 83% for TB. The sensitivity of IFN- γ in these fluids is 89% and the specificity is 97% (Lewinsohn et al., 2017). However, neither the ADA level nor the IFN-γ level provide a definitive diagnosis of TB disease.

A panel of six novel serum protein biomarkers was developed from in depth proteomic analysis. It was found to have 90% sensitivity and 80 % specificity (De Groote et al., 2017), but needs further development and evidence of clinical utility.

State and Federal Regulations, as applicable

The Bactec MGIT 960 System was approved by the FDA in 1998 for the detection of mycobacteria growth from clinical specimens (except blood).

In 1994 the FDA approved the Ge-Probe Amplified Mycobacterium Tuberculosis Direct Test as a Nucleic acid-based in vitro diagnostic devices for the detection of Mycobacterium tuberculosis complex in respiratory specimens. These devices are non-multiplexed and intended to be used as an aid in the diagnosis of pulmonary tuberculosis when used in conjunction with clinical and other laboratory findings.

In 2015 the FDA approved the Xpert® MTB/RIF Assay, performed on the GeneXpert® Instrument Systems, as a qualitative, nested real-time polymerase chain reaction (PCR) in vitro diagnostic test for the detection of Mycobacterium tuberculosis complex DNA in raw sputum or concentrated sputum sediment prepared from induced or expectorated sputum. In specimens where Mycobacterium tuberculosis complex (MTB-complex) is detected, the Xpert MTB/RIF Assay also detects the rifampin-resistance associated mutations of the rpoB gene.

The QuantiFERON-TB® assay (CSL Biosciences, Australia) for detection of gamma interferon production is a blood test that has been used in humans in Australia. In November 2001, this test received approval from the U.S. Food and Drug Administration (FDA) in the United States for the following indication:

"The QuantiFERON-TB test is intended as an aid in the detection of latent Mycobacterium tuberculosis infection."

In December of 2004, QuantiFERON-TB® GOLD received FDA approval for the detection of latent TB. This test differs from the first-generation test in that instead of using PPD as the stimulus for interferon production, 2 antigens, ESAT-6 and CFP-10, are used. These antigens are present in mycobacterium tuberculosis but are not present in those exposed to BCG or non-tuberculous mycobacteria.

The QFT-GIT measures IFN-γ plasma concentration using an enzyme-linked immunosorbent assay (ELISA), has been approved by the US Food and Drug Administration (FDA) and has replaced the QuantiFERON-TB Gold (QFT-G) test (Lewinsohn et al., 2017).

The T-SPOT assay enumerates T cells releasing IFN-γ using an enzyme-linked immunospot (ELISPOT) assay. The T-SPOT.TB assay is currently available in Europe, Canada, and has been approved for use in the United States with revised criteria for test interpretation (Lewinsohn et al., 2017).

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

Testing for Diagnosis of Active or Latent Tuberculosis AHS – G2063

BCBSNC will provide coverage for testing for diagnosis of active or latent tuberculosis when it is determined the medical criteria or reimbursement guidelines below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When testing for diagnosis of active or latent tuberculosis is covered

1. Reimbursement is allowed for a gamma interferon blood test to diagnose latent tuberculosis infection in:
   A. individuals 5 years or older who are likely to be infected with Mtb.

   B. individuals who are unlikely to be infected with Mtb, when screening is obliged by law.

2. Reimbursement is allowed for acid fast bacilli (AFB) smear/stain for all suspected tuberculosis infections.

3. Reimbursement is allowed for culture and culture-based drug susceptibility testing of Mycobacteria spp. for all suspected tuberculosis infections.

4. Reimbursement is allowed for direct probe or amplified probe nucleic acid-based testing, including PCR, for the following:
   A. Mycobacteria spp

   B. M. tuberculosis

   C. M. avium intracellulare

5. Reimbursement is allowed for molecular-based drug susceptibility testing for patients whose sputum is AFB smear positive or Hologic Amplified MTD positive and who meet one of the following criteria:

   a. have been treated for tuberculosis in the past
   b. were born in or have lived for at least 1 year in a foreign country with at least a moderate tuberculosis incidence (≥20 per 100 000) or a high primary MDR-TB prevalence (≥2%)

   c. are contacts of patients with MDR-TB

   d. are HIV infected

6. Reimbursement is allowed for cell counts, protein, glucose, and lactate dehydrogenase (LDH) concentrations of cerebrospinal, pleural, peritoneal, pericardial and other fluids in patients with pleural effusion, pericardial effusion, or ascites and suspected tuberculosis infection, respectively.

7. Reimbursement is allowed for urine-based detection of mycobacterial cell wall glycolipid lipoarabinomannan (LAM) in HIV-infected patients with CD4 cell counts ≤100 cells/microL who have signs and symptoms tuberculosis.

When testing for diagnosis of active or latent tuberculosis is not covered

Reimbursement is not allowed for a gamma interferon blood test to diagnose latent tuberculosis infection in healthy children <5 years of age for whom it has been decided that diagnostic testing is warranted. Tuberculosis Skin Test is recommended.t

Reimbursement is not allowed for Gamma Interferon blood test for patients with active tuberculosis.

Quantitative nucleic acid testing for Mycobacteria spp, M. tuberculosis, and M. avium intracellulare is considered investigational.

The technique for quantification of nucleic acid includes both amplification and direct probes; therefore, reimbursement is not allowed for simultaneous coding for both amplification or direct probes.

Whole genome sequencing of mycobacterium spp. for detection of drug resistance is considered investigational.

Reimbursement is not allowed for genotyping of mycobacterium spp.

Adenosine deaminase (ADA) and interferon-gamma (IFN- γ) levels in cerebrospinal, pleural, peritoneal, pericardial and other fluids for the diagnosis of extrapulmonary TB is considered investigational.

Serum protein biomarkers or panels of biomarkers for the detection and diagnosis of TB disease is considered investigational.

Policy Guidelines

Guidelines and Recommendations

Practice Guidelines and Position Statements

World Health Organization

The WHO published recommendations (2016) for the diagnosis of TB which state:

- Mycobacteria can be visually distinguished from other microorganisms by their thick lipidcontaining cell walls, which retain biochemical stains despite decolourization by acid-containing reagents (known as ‘acid fastness’). Given that the examination of two sputum specimens is adequate to identify the majority (95-98%) of smear-positive TB patients, WHO’s current policy on case-finding using microscopy recommends that in settings with appropriate external quality assessment and documented good-quality microscopy two specimens should be examined.

- Direct Ziehl–Neelsen staining of sputum specimens and examination using light microscopy is suitable for use at all levels of laboratory, including peripheral laboratories at primary health-care centres or district hospitals. There is insufficient evidence that processed sputum specimens (for example, those that are concentrated or chemically treated) give better results than direct smear microscopy. Therefore, the use of such methods is not recommended.

- Evidence shows that the diagnostic accuracy of LED microscopy is comparable to that of conventional fluorescence microscopy and it surpasses that of conventional Ziehl–Neelsen microscopy (by an average of 10%). Therefore, WHO recommends replacing conventional fluorescence microscopy with LED microscopy, and that LED microscopy should be phased in as an alternative to conventional Ziehl–Neelsen light microscopy in all settings, prioritizing high-volume laboratories

- Mycobacteria can be cultured in specific solid or liquid media. Bacterial growth can be identified visually (that is, by identifying specific characteristics) or by automated detection of its metabolism. All positive mycobacterial cultures must be tested to confirm the identification of M. tuberculosis complex (MTBC).

- Differentiation of the members of the MTBC is necessary for the treatment of individual patients and for epidemiological purposes, especially in areas of the world where tuberculosis has reached epidemic proportions or wherever the transmission of M. bovis between animals or animal products and humans is a problem. In addition, it can be important to rapidly identify isolates of M. bovis bacillus Calmette-Guérin (BCG) recovered from immunocompromised patients. Differentiation of species with the MTBC can be achieved using either phenotypic26 and/ or genotypic methods.

- The use of rapid immunochromatographic assays (or strip tests for speciation) to identify cultured isolates is recommended because they provide definitive identification of all members of the MTBC (including M. bovis) in 15 minutes.

- WHO recommends that either TST or IGRA can be used to test for LTBI in high-income and upper middle-income countries with estimated TB incidence less than 100 per 100000 population.

- It is strongly recommended that commercial serodiagnostic tests not be used for the diagnosis of pulmonary and extra-pulmonary TB. Currently available commercial serodiagnostic tests (also referred to as serological tests) provide inconsistent and imprecise findings. There is no evidence that existing commercial serological assays improve patient outcomes, and high proportions of false positive and false-negative results may have an adverse impact on the health of patients

- There is no consistent evidence that IGRAs are more sensitive than TST for diagnosis of active TB disease. Studies evaluating the incremental value of IGRAs to conventional microbiological tests show no meaningful contribution of IGRAs to the diagnosis of active TB. IGRAs are considered inadequate as rule-out or rule-in tests for active TB, especially in the context of HIV infection. IGRAs should not be used for the diagnosis of active TB disease.

American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention (Lewinsohn et al., 2017)

The ATS/IDSA/CDC published clinical practice guidelines for diagnosis of TB in 2017 that stated the following:

LTBI:

- We recommend performing an interferon-γ release assay (IGRA) rather than a tuberculin skin test (TST) in individuals 5 years or older who meet the following criteria: (1) are likely to be infected with *Mtb*, (2) have a low or intermediate risk of disease progression, (3) it has been decided that testing for LTBI is warranted, and (4) either have a history of BCG vaccination or are unlikely to return to have their TST read (*strong recommendation, moderate-quality evidence*).

- We suggest performing an IGRA rather than a TST in all other individuals 5 years or older who are likely to be infected with *Mtb*, who have a low or intermediate risk of disease progression, and in whom it has been decided that testing for LTBI is warranted (*conditional recommendation, moderate-quality evidence*).

- There are insufficient data to recommend a preference for either a TST or an IGRA as the first-line diagnostic test in individuals 5 years or older who are likely to be infected with *Mtb*, who have a high risk of progression to disease, and in whom it has been determined that diagnostic testing for LTBI is warranted.

- Guidelines recommend that persons at low risk for *Mtb* infection and disease progression NOT be tested for *Mtb* infection. We concur with this recommendation. However, we also recognize that such testing may be obliged by law or credentialing bodies. If diagnostic testing for LTBI is performed in individuals who are unlikely to be infected with *Mtb* despite guidelines to the contrary:
    - We suggest performing an IGRA instead of a TST in indivduals 5 years or older (*conditional recommendation, low-quality evidence*). Remarks: A TST is an acceptable alternative in settings where an IGRA is unavailable, too costly, or too burdensome.
    - We suggest a second diagnostic test if the initial test is positive in individuals 5 years or older (*conditional recommendation, very low-quality evidence*). Remarks: The confirmatory test may be either an IGRA or a TST. When such testing is performed, the person is considered infected only if both tests are positive.
- We suggest performing a TST rather than an IGRA in healthy children <5 years of age for whom it has been decided that diagnostic testing for LTBI is warranted (conditional recommendation, very low-quality evidence).
- While both IGRA and TST testing provide evidence for infection with Mtb, they cannot distinguish active from latent TB. Therefore, the diagnosis of active TB must be excluded prior to embarking on treatment for LTBI. This is typically done by determining whether or not symptoms suggestive of TB disease are present, performing a chest radiograph and, if radiographic signs of active TB (eg, airspace opacities, pleural effusions, cavities, or changes on serial radiographs) are seen, then sampling is performed, and the patient managed accordingly.

TB Disease:

- We recommend that acid-fast bacilli (AFB) smear microscopy be performed, rather than no AFB smear microscopy, in all patients suspected of having pulmonary TB

- We suggest that both liquid and solid mycobacterial cultures be performed, rather than either culture method alone, for every specimen obtained from an individual with suspected TB disease

- We suggest performing a diagnostic nucleic acid amplification test (NAAT), rather than not performing a NAAT, on the initial respiratory specimen from patients suspected of having pulmonary TB

- We recommend performing rapid molecular drug susceptibility testing for rifampin with or without isoniazid using the respiratory specimens of persons who are either AFB smear positive or Hologic Amplified MTD positive and who meet one of the following criteria: (1) have been treated for tuberculosis in the past, (2) were born in or have lived for at least 1 year in a foreign country with at least a moderate tuberculosis incidence (≥20 per 100 000) or a high primary multidrug-resistant tuberculosis prevalence (≥2%), (3) are contacts of patients with multidrug-resistant tuberculosis, or (4) are HIV infected

- We suggest mycobacterial culture of respiratory specimens for all children suspected of having pulmonary TB

- We suggest that cell counts, and chemistries be performed on amenable fluid specimens collected from sites of suspected extrapulmonary TB

- We suggest that adenosine deaminase levels be measured, rather than not measured, on fluid collected from patients with suspected pleural TB, TB meningitis, peritoneal TB, or pericardial TB

- We suggest that free IFN-γ levels be measured, rather than not measured, on fluid collected from patients with suspected pleural TB or peritoneal TB

- We suggest that AFB smear microscopy be performed, rather than not performed, on specimens collected from sites of suspected extrapulmonary TB

- We recommend that mycobacterial cultures be performed, rather than not performed, on specimens collected from sites of suspected extrapulmonary TB
- We suggest that NAAT be performed, rather than not performed, on specimens collected from sites of suspected extrapulmonary TB
- We suggest that histological examination be performed, rather than not performed, on specimens collected from sites of suspected extrapulmonary TB
- We recommend one culture isolate from each mycobacterial culture-positive patient be submitted to a regional genotyping laboratory for genotyping

United State Preventative Service Task Force (Bibbins-Domingo et al., 2016)

The USPSTF published a recommendation (2016) which found adequate evidence that accurate screening tests for LTBI are available, treatment of LTBI provides a moderate health benefit in preventing progression to active disease, and the harms of screening and treatment are small. The USPSTF has moderate certainty that screening for LTBI in persons at increased risk for infection provides a moderate net benefit.

Infectious Diseases Society of America (IDSA)/American Society of Microbiology (ASM) (Miller et al., 2018)

In the 2018 update to the IDSA/ASM joint guideline, A Guide to Utilization of the Microbiology Laboratory for Diagnosis of Infectious Diseases, concerning Mycobacterium tuberculosis, they recommend AFB smear or AFB culture when performing laboratory diagnosis. They do allow for the use of NAAT for diagnosing M. tuberculosis; however, they state, "A negative result does not rule out Mycobacterium tuberculosis." They also note that currently there is no commercially available, FDA-approved NAAT for mycobacteria for nonrespiratory samples.

In cases of laboratory diagnosis of pulmonary infections in cystic fibrosis due to suspected Mycobacterium spp, they recommend performing a mycobacterial culture from the expectorated sputum, bronchoscopically obtained cultures, or other respiratory cultures.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes; 81099, 81425, 81426, 81479, 82945, 83615, 84157, 84311, 86352, 86480, 86481, 87070, 87077, 87116, 87149, 87150, 87153, 87181, 87184, 87185, 87186, 87187, 87188, 87190, 87206, 87550, 87551, 87552, 87555, 87556, 87557, 87560, 87561, 87562

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

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Policy Implementation/Update Information

4/1/19 New policy developed. BCBSNC will provide coverage for testing for diagnosis of active or latent tuberculosis when it is determined to be medically necessary because the medical criteria and guidelines are met. Medical Director review 4/1/2019. Policy noticed 4/1/2019 for effective date 6/1/2019. (sk)

10/1/19 Policy Statement revised to read: BCBSNC will provide coverage for testing for diagnosis of active or latent tuberculosis when it is determined the medical criteria or reimbursement guidelines below are met. Wording revised in When Covered section. “Medically Necessary” changed to “Reimbursement is allowed…” Wording revised in the Not Covered section. “Not Medically Necessary” changed to read “Reimbursement is not allowed…” Deleted coding grid. Notification given 10/1/2019 for effective date 12/2/2019. (an)