Test Definition: TBPZA

Susceptibility, Mtb Complex, PZA

Overview

Useful For

Susceptibility testing of *Mycobacterium tuberculosis* complex isolates growing in pure culture against pyrazinamide

Confirming *Mycobacterium tuberculosis* complex resistance to pyrazinamide

Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
MTBVP	Mtb PZA Confirmation, pncA Sequence	No, (Bill Only)	No

Additional Tests

Test ID	Reporting Name	Available Separately	Always Performed
STVP	Susceptibility, Mtb Complex, PZA	No, (Bill Only)	Yes

Testing Algorithm

When this test is ordered the additional test will always be performed and charged separately.

If resistance to Pyrazinamide is detected, the reflex test for confirmation of resistance will be performed and charged separately.

Special Instructions

- Infectious Specimen Shipping Guidelines

Method Name

Broth Dilution at Critical Drug Concentrations

NY State Available

Yes

Specimen

Specimen Type

Varies

Additional Testing Requirements

CTB / Mycobacteria and *Nocardia* Culture or CTBID / Culture Referred for Identification, *Mycobacterium* and *Nocardia* must also be ordered and will be charged separately unless identification of organism is provided.

Shipping Instructions

1. See Infectious Specimen Shipping Guidelines in Special Instructions.

2. Place specimen in a large infectious container (T146) and label as an etiologic agent/infectious substance.

Necessary Information

Specimen sourceand suspected organism identification are required.

Specimen Required

Specimen Type: Organism

Supplies: Infectious Container, Large (T146)

Container/Tube: Middlebrook 7H10 agar slant

Specimen Volume: Isolate

Collection Instructions: Organism must be in pure culture, actively growing.

Forms

If not ordering electronically, complete, print, and send a Microbiology Test Request (T244) with the specimen.

Reject Due To

Other	Agar plate

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		
	Refrigerated		

Clinical and Interpretive

Clinical Information

Primary treatment regimens for *Mycobacterium tuberculosis* complex often include isoniazid, rifampin, ethambutol, and pyrazinamide (PZA). Susceptibility testing of each *Mycobacterium tuberculosis* complex isolate against these first-line antimycobacterial agents is a key component of patient management.

The Clinical and Laboratory Standards Institute (CLSI) provides consensus protocols for the methods, antimycobacterial agents, and critical concentrations of each agent to be tested in order to permit standardized interpretation of *Mycobacterium tuberculosis* complex susceptibility test results. Current recommendations indicate that laboratories should use a rapid broth method in order to obtain *Mycobacterium tuberculosis* complex susceptibility data as quickly as possible to help guide patient management. According to the CLSI, resistance can be confirmed by another method or by another laboratory at the discretion of the testing laboratory.

This test uses an FDA-cleared commercial system for rapid broth susceptibility testing of *Mycobacterium tuberculosis* complex against PZA. Since the literature indicates that broth testing of PZA can, at times, produce falsely resistant results, resistance to PZA by the broth method is automatically confirmed by *pncA* DNA sequencing.

The *pncA* gene of *Mycobacterium tuberculosis* complex is responsible for activation of the prodrug PZA and hence PZA activity. Mutations in the *pncA* gene and upstream promoter region have been reported to account for the majority (70%-97%) of PZA-resistant isolates. However, 3% to 30% of PZA-resistant isolates do not have a corresponding *pncA* mutation and other genes (eg, *rpsA*) may also play a role.

A separate test is available for testing of the other first-line agents (isoniazid, rifampin and ethambutol).

Reference Values

Results are reported as susceptible or resistant.

Interpretation

Mycobacterium tuberculosis complex isolates are reported as susceptible or resistant to pyrazinamide at the critical concentration.

Cautions

For resistant organisms, confirmatory testing using *pncA* DNA sequencing is automatically performed and the presence or absence of *pncA* mutations associated with pyrazinamide resistance is reported.

In vitro susceptibility does not guarantee clinical response. Therefore, the decision to treat with a particular agent should not be based solely on the antimicrobial susceptibility testing result.

Susceptibility testing should be performed on pure culture isolates of *Mycobacterium tuberculosis* complex.

Some mutations associated with pyrazinamide resistance that may occur outside of the *pncA* promoter and gene region and may therefore not be confirmed by DNA sequencing of this target.

Clinical Reference

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2. Woods GL, Lin S-Y G, Desmond EP: Susceptibility test methods: *Mycobacteria, Nocardia* and other Actinomycetes. In Manual of Clinical Microbiology.10th edition. Edited by J Versalovic, KC Carroll, G Funke, et al. Washington, DC, ASM Press, 2011, pp 1215-1238

3. Dormandy J, Somoskovi A, Kreiswirth BN, et al: Discrepant results between pyrazinamide susceptibility testing by the reference BACTEC 460TB method and pncA DNA sequencing in patients infected with multidrug-resistant W-Beijing Mycobacterium tuberculosis strains. Chest 2007;131:497-501

4. Chedore P, Bertucci L, Wolfe J: Potential for Erroneous Results Indicating Resistance When Using the BACTEC MGIT 960 System for Testing Susceptibility of Mycobacterium tuberculosis to Pyrazinamide. J Clin Microbiol 2010 Jan;48(1):300-301

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6. Shi W, Zhang X, Jiang X, et al: Pyrazinamide inhibits trans-translation in Mycobacterium tuberculosis. Science 2011;333:1630-1632

7. CLSI, Susceptibility Testing of *Mycobacteria*, *Nocardiae*, and Other *Actinomycetes*; Approved Standard. CLSI document M24-A2. CLSI, Wayne, PA, 2011

8. LaBombardi VJ: Comparison of the ESP and BACTEC Systems for testing susceptibilities of *Mycobacterium tuberculosis* complex isolates to pyrazinamide. J Clin Microbiol 2002;40:2238-2239

9. Espasa M, Salvado M, Vicente E, et al: Evaluation of the VersaTREK system compared to the Bactec MGIT 960 system for first-line drug susceptibility testing of Mycobacterium tuberculosis. J Clin Microbiol 2012;50:488-491

10. Somoskovi A, Dormandy J, Parson LM, et al: Sequencing of the pncA gene in members of the Mycobacterium tuberculosis complex has important diagnostic applications: Identification of a species-specific pncA mutation in "Mycobacterium canettiiâ€• and the reliable and rapid predictor of pyrazinamide resistance. Confirmation of pyrazinamide resistance is done using Sanger dideoxy sequencing of approximately 700bp of the *pncA* gene and promoter region. J Clin Microbiol 2007;45:595-599

11. Jureen P, Werngren J, Toro JC, Hoffner S: Pyrazinamide resistance and pncA gene mutations in Mycobacterium tuberculosis. Antimicrob Agents Chemother 2008;52:1852-1854

Performance

Method Description

This test method is based on presence or absence of growth of *Mycobacterium tuberculosis* in broth cultures with the presence of critical concentrations of the antimycobacterial drug pyrazinamide. One of 2 FDA-cleared platforms may be used.

The VersaTrek platform uses the presence or absence of a pressure increase inside broth vials containing *Mycobacterium tuberculosis* in the presence of critical concentrations of the antimycobacterial drug pyrazinamide. Increasing pressure indicates the presence of actively growing *M tuberculosis* that is resistant pyrazinamide at 300 mcg/mL. Low or undetectable pressure increases in the presence of critical drug concentration suggests a lack of *M tuberculosis* growth and susceptibility to pyrazinamide 300 mcg/mL.(Package insert: VersaTREK Mycobacteria Detection and Susceptibility Testing system, TREK Diagnostics, Cleveland, OH 2014)

The BACTEC MGIT 960 platform uses the production and measurement of fluorescence within a Mycobacterial Growth Indicator Tube (MGIT) in the presence of actively growing *M tuberculosis* complex isolates in the presence of critical concentration of the antimycobacterial drug pyrazinamide. Low or undetectable levels of fluorescence in the presence of critical drug concentrations suggests lack of *M tuberculosis* growth and susceptibility to pyrazinamide at 100 mcg/mL. Increased fluorescence suggests active growth of *M tuberculosis* and resistance to pyrazinamide at 100 mcg/mL.(Package insert: BACTEC MGIT 960 SIRE Kit, BD Diagnostics, Sparks, MD 2016)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Sunday; Varies

Analytic Time

10-15 days

Maximum Laboratory Time

21 days

Specimen Retention Time

1 year

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test has been cleared or approved by the U.S. Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

87188-Susceptibility, *Mycobacterium tuberculosis* Complex, Pyrazinamide

87153-Mtb PZA Confirmation, pncA Sequencing (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
TBPZA	Susceptibility, Mtb Complex, PZA	56026-8

Result ID	Test Result Name	Result LOINC Value
TBPZA	Susceptibility, Mtb Complex, PZA	56026-8