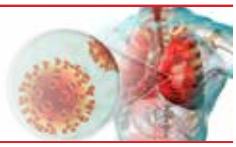
THE PATHCARE NEWS

XPERT MTB/XDR TESTING



PathCare introduces Xpert MTB/XDR testing as a reflex test for rapid molecular drug susceptibility testing of rifampicin-resistant Mycobacterium tuberculosis (RR-TB) positive clinical samples

South Africa remains one of the top 30 high-burden countries for multidrug-resistant/rifampicin-resistant *Mycobacterium tuberculosis* (MDR-TB/RR-TB) (WHO, 2022). The National Department of Health (NDOH) has published updated guidelines for the management of RR-TB which recommends early access to a bedaquiline, pretomanid, linezolid and levofloxacin (BPaL-L) treatment regimen and early detection of second-line drug resistance, especially fluoroquinolone (FLQ) resistance, for optimal therapy (NDOH, 2023). Subsequently, reflex testing on direct RR-TB positive samples, within the public sector, has been implemented. Whilst the private sector has been constrained with re-imbursement challenges, it remains important to comply with guidelines, and to provide standard of care as we acknowledge that current conventional methods to detect second-line resistance, utilizing line probe assays on culture isolates, can cause severe delays and this practice has been phased out in the public sector.

The Xpert MTB/XDR (Cepheid, USA) PCR assay is able to rapidly detect resistance-associated mutations to isoniazid (INH), ethionamide (ETH), fluoroquinolones (FLQ) including levofloxacin and moxifloxacin and second-line injectable agents (SLIDs) such as amikacin (AMK), kanamycin (KAN) and capreomycin (CAP) in confirmed MDR-TB/RR-TB positive specimens. The WHO has endorsed the use of this assay as a reflex test on positive RR-TB samples to identify resistance as a low-complexity test without the delay to wait for subsequent testing on positive culture isolates (WHO, 2021). The reported sensitivity for *Mycobacterium tuberculosis* (MTB) detection among sputum smear positive and smear negative samples is 99.5% and 94.7% respectively and an overall specificity of 100%. The sensitivity for detecting drug resistance mutations correlating to phenotypic DST is >90% for isoniazid (INH), fluoroquinolones (FLQ), amikacin, kanamycin and capreomycin. Lower sensitivity for ethionamide is apparent at 65.9% (Omar et al, 2024).

Following the incorporation of this reflex testing in the public sector as per NDOH guidelines, PathCare offers this test as a reflex on positive RR-TB samples. Following detection of RR-TB/MDR-TB on a clinical sample, reflex testing will be performed following discussion with the attending clinician and treated as an add-on request to the sample.

Patients with RR-TB qualify for a BPaL-L treatment regimen. Additional phenotypic susceptibility testing for bedaquiline and linezolid, will be performed on all positive culture isolates. In the presence of FLQ mutations, levofloxacin should be omitted from the regimen and where INH and FLQ resistance mutations are detected together, pretomanid susceptibility testing is required. The laboratory will reflex further phenotypic testing as per the national algorithm.

The cost of the reflex testing will be 1x PCR billing code and will not be repeated on positive culture isolates. For specimens testing MTB negative on initial PCR testing but subsequently becomes culture positive with RR-TB, routine second-line testing will continue as per norm.

For further discussion please contact your local Clinical Microbiologist.

References

1. NDOH, 2023. *Clinical management of rifampicin resistant tuberculosis.* Available at: https://www.health.gov.za/wp-content/uploads/2023/10/Updated-RR-TB-Clinical-Guidelines-September-2023.pdf
2. WHO, 2021. *WHO consolidated guidelines on tuberculosis. Module 3: diagnosis - rapid diagnostics for tuberculosis detection, 2021 update.* Available at: https://www.ncbi.nlm.nih.gov/books/NBK572344/
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4. Omar, SV et al., 2024. Performance evaluation of the Xpert MTB/XDR test for the detection of drug resistance to Mycobacterium tuberculosis among people diagnosed with tuberculosis in South Africa. *Journal of Clinical Microbiology*, 62(8), pp.e00229-24.

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