Decrease™
TB LAM
AG TEST

TECHNICAL INFORMATION NOTE

Ensuring an uninterrupted supply of quality-assured, affordable anti-TB drugs and diagnostics to the world.

stoptb.org/gdf
TECHNICAL INFORMATION NOTE

DETERMINE™ TB LAM AG TEST

Diagnosis of TB in people living with HIV (PLHIV) using sputum-based tests is challenging, given the frequency of extrapulmonary TB in such patients combined with their frequent inability to expectorate sputum adequately. In PLHIV with advanced immunodeficiency, disseminated TB with renal involvement can result in the lipoarabinomannan (LAM) antigen being present in the urine. A urine-based test to detect LAM therefore has important utility among these patients. In November 2015, WHO issued policy guidance on the urine-based LAM assay, based on the evaluation of the commercially available Determine™ TB LAM Ag test. As a simple dipstick test with minimal biosafety hazards and training needs, it is currently the only truly point-of-care test for TB.

SUPPLY INFORMATION

<table>
<thead>
<tr>
<th>PRODUCT NAME</th>
<th>Determine™ TB LAM Ag test</th>
</tr>
</thead>
<tbody>
<tr>
<td>GDF ITEM NUMBER</td>
<td>106642 (available in the GDF diagnostics catalogue)</td>
</tr>
<tr>
<td>MANUFACTURER</td>
<td>Abbott Laboratories, Lake Bluff, USA (formerly Alere Inc, Waltham, USA)</td>
</tr>
<tr>
<td>COST</td>
<td>USD $3.50 / test strip (packaged in kits of 100 test strips: USD $350)</td>
</tr>
<tr>
<td>SHELF LIFE</td>
<td>18 months</td>
</tr>
<tr>
<td>STORAGE CONDITIONS</td>
<td>2 – 30°C</td>
</tr>
</tbody>
</table>

For more information or to place an order contact gdf@stoptb.org
To forecast the number of LAM test strips to procure for an initial shipment, data from HIV registers on numbers of patients stratified by CD4 count at planned implementation sites (hospitals and/or peripheral sites) should be used, if available:

<table>
<thead>
<tr>
<th>ITEMS INDICATED IN PACKAGE INSERT</th>
<th>GDF ITEM NUMBER</th>
<th>GDF ITEM DESCRIPTION</th>
<th>COST (IN USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sputum containers</td>
<td>106525</td>
<td>80 ml each; 1,000 cups per pack</td>
<td>$83.30</td>
</tr>
<tr>
<td>Pipette capable of delivering 60 µl</td>
<td>106055</td>
<td>Pipette capable of delivering 10-100 µl</td>
<td>$226.94</td>
</tr>
<tr>
<td>Disposable pipette tips</td>
<td>106388</td>
<td>Pipette tips capable of delivering 10-100 µl; 1,000 tips per pack</td>
<td>$72.75</td>
</tr>
<tr>
<td>Timer</td>
<td>106570</td>
<td>Mechanical timer</td>
<td>$1.11</td>
</tr>
</tbody>
</table>

In settings where CD4 testing is routine, the number of patients registered annually with CD4 counts ≤ 100 cells/µl at the implementation sites should be multiplied by a factor to arrive at the number of people in this population group who would be evaluated for TB annually based on presence of signs or symptoms of TB or danger signs, and therefore in need of a LAM test.

- In the absence of country-specific data to calculate the factor, 0.6 may be used as a default estimate of the proportion of this population group who would have signs or symptoms of TB or danger signs in a given year.

- The calculated number of tests may be used as a conservative estimate for the size of an initial order, given seriously ill patients with unknown CD4 counts would also be eligible for testing, and considering the 18 month shelf life of the test strips.

- Data from any in-country pilot studies or verification studies should be used to refine the initial forecast.
In the absence of data from registers or in settings where CD4 testing is not routine, data from any in-country studies on estimated numbers of patients stratified by CD4 count should be extrapolated to the planned implementation sites. The proportion of this population group with CD4 counts ≤ 100 cells/μl who would be expected to have signs or symptoms of TB or danger signs in a given year would need to be estimated in order to calculate the number of tests needed annually.

- Alternatively, any data available from studies on the proportion or number of PLHIV classified as having advanced HIV disease (AIDS) may be used.

For subsequent forecasting exercises, the number of PLHIV estimated nationwide to have CD4 counts ≤ 100 cells/μl multiplied by the aforementioned factor (default estimate of 0.6) should be considered as a target to phase in over time when implementation sites include all hospitals and peripheral sites. Data that become available on actual test consumption rates should be used to refine the forecast.

Operational research may also be considered using the test with a threshold of CD4 counts ≤ 200 cells/μl or as a screening tool among all PLHIV admitted to hospitals.

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1 WHO proposes a default factor of 0.3 to estimate the proportion of all PLHIV who would have signs or symptoms of TB in a given year, assuming patients are clinically screened on average twice a year and 15% of screened patients would have signs or symptoms (WHO Framework of indicators and targets for laboratory strengthening under the End TB Strategy, 2016, WHO/HTM/TB/2016.18). The higher default factor of 0.6 proposed herewith is due to the target patient group having low CD4 counts.
WHO POLICY RECOMMENDATIONS 
(NOVEMBER 2015)

WHO recommends use of the LAM test to assist in the diagnosis of TB in two specific population groups:

- People living with HIV who have signs or symptoms of TB and a CD4 count ≤ 100 cells/µl

- People living with HIV who are “seriously ill” regardless of CD4 count or if the CD4 count is unknown. “Seriously ill” is defined based on 4 danger signs: respiratory rate >30/min, temperature >39°C, heart rate > 120/min and unable to walk unaided.

The LAM test is not recommended for TB screening or for diagnosis of active TB disease in the general population.

RESOURCES AVAILABLE: CURRENT NORMATIVE AND PRACTICAL GUIDANCE

- 2015 WHO Global TB Programme Guidelines on use of the LAM assay

- 2017 WHO HIV Department Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy: Includes the LAM test as a component of the package of care for people with advanced HIV disease

- 2017 GLI Model TB Diagnostic Algorithms: Includes the LAM test in Algorithm #4, for evaluating persons for TB among PLHIV who are seriously ill with danger signs or have CD4 counts ≤ 100 cells/µl (see next page)

- 2016 GLI Information Note: Describes a study finding LAM-guided TB treatment initiation reduces mortality in HIV-positive hospital inpatients; includes case studies on use of the LAM test

- 2017 TAG Activist’s Guide to the TB LAM Test and TAG Webinar on Expanding its Use
Persons to be evaluated for TB who are HIV-positive or unknown and are seriously ill with danger signs or have CD4 counts <100 cells/μl

- Collect 1 specimen and conduct Xpert MTB/RIF (preferred test)
- Consider using the urine lateral flow lipoarabinomannan (LF-LAM) assay
- Conduct additional clinical evaluations for TB
  - Initiate treatment with antibiotics for bacterial infections
  - Consider treatment for Pneumocystis pneumonia
  - Chest X-ray if available

Xpert MTB/RIF, MTB detected

- Follow Algorithm 1 for interpretation of Xpert MTB/RIF result and follow-up
- Initiate TB treatment

Xpert MTB/RIF, MTB not detected or no test available

- TB is not ruled out
- Evaluate the clinical response after 3–5 days of antibiotic treatment

Clinical worsening or no improvement

- TB is likely
- Start presumptive TB treatment if patient is seriously ill with danger signs
- Conduct additional investigations for TB and other HIV-related diseases
- Complete the course of parenteral antibiotics

Clinical improvement

- TB is unlikely, but is not ruled out
- Conduct additional investigations for TB and other HIV-related diseases
- Consider isoniazid preventive therapy
- Complete the course of parenteral antibiotics

STOP TB PARTNERSHIP
GLOBAL DRUG FACILITY