Overview

Useful For
The prognostication and clinical management of lymphoplasmacytic lymphoma/Waldenstrom macroglobulinemia

Special Instructions
- Hematopathology Patient Information

Method Name
Only orderable as a reflex. For more information, see LPLFX / Reflexive Testing of MYD88 and CXCR4.

NY State Available
No

Specimen

Specimen Type
Varies

Specimen Required
Only orderable as a reflex. For more information, see LPLFX / Reflexive Testing of MYD88 and CXCR4

Submit only 1 of the following specimens:

Specimen Type: Peripheral blood

Container/Tube: EDTA (lavender top) or ACD solution B (yellow top)

Specimen Volume: 3 mL

Specimen Stability: Ambient (preferred)/Refrigerated

Collection Instructions:
1. Invert several times to mix blood
2. Send specimen in original tube
3. Label specimen as blood

Specimen Type: Bone marrow

Container/Tube: EDTA (lavender top) or ACD solution B (yellow top)

Specimen Volume: 2 mL

Specimen Stability: Ambient (preferred)/Refrigerated
**Collection Instructions:**

1. Invert several times to mix bone marrow
2. Send specimen in original tube
3. Label specimen as bone marrow

**Specimen Type:** Extracted DNA

**Container/Tube:** 1.5- to 2-mL tube with indication of volume and concentration of the DNA

**Specimen Volume:** Entire specimen

**Specimen Stability:** Frozen (preferred)/Refrigerated/Ambient

**Collection Instructions:** Label specimen as extracted DNA and list specimen source. Include indication of volume and concentration of the DNA.

**Specimen Type:** Paraffin-embedded tissue

**Container/Tube:** Paraffin block

**Specimen Stability:** Ambient

**Specimen Type:** Paraffin-embedded bone marrow aspirate clot

**Container/Tube:** Paraffin block

**Specimen Stability:** Ambient

**Specimen Minimum Volume**

Blood, Bone Marrow: 1 mL

Extracted DNA: 20 mcL with a concentration of at least 10 nanograms per mcL

**Reject Due To**

<table>
<thead>
<tr>
<th>Hemolysis</th>
<th>Mild OK; Gross OK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipemia</td>
<td>NA</td>
</tr>
<tr>
<td>Icterus</td>
<td>NA</td>
</tr>
<tr>
<td>Other</td>
<td>B5-fixed tissues, bone marrow biopsies, slides, paraffin shavings, methanol acetic acid (MAA)-fixed pellets, frozen tissue, moderately to severely clotted</td>
</tr>
</tbody>
</table>

**Specimen Stability Information**

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varies</td>
<td>Varies</td>
<td>10 days</td>
</tr>
</tbody>
</table>
Clinical and Interpretive

Clinical Information
Lymphoplasmacytic lymphoma/Waldenstrom macroglobulinemia (LPL/WM) is a B-cell lymphoma that is characterized by an aberrant accumulation of malignant lymphoplasmacytic cells in the bone marrow, lymph nodes and spleen. It is a B-cell neoplasm that can exhibit excess production of serum immunoglobulin-M symptoms related to hyper viscosity, tissue filtration, and autoimmune-related pathology. CXCR4 mutations are identified in approximately 30% to 40% of LPL/WM and are almost always in association with MYD88 L265P, which is highly prevalent in this neoplasm. The status of CXCR4 mutations in the context of MYD88 L265P is clinically relevant as important determinants of clinical presentation, overall survival, and therapeutic response to ibrutinib: A MYD88-L265P/CXCR4-WHIM (C-terminus nonsense/frameshift mutations) molecular signature is associated with intermediate to high bone marrow disease burden and serum IgM levels, less adenopathy, and intermediate response to ibrutinib in previously treated patients, a MYD88-L265P/CXCR4-WT (wild type) molecular signature is associated with intermediate bone marrow disease burden and serum IgM levels, more adenopathy, and highest response to ibrutinib in previously treated patients, and the MYD88-WT/CXCR4-WT molecular signature is associated with intermediate overall survival, lower response to ibrutinib therapy in previously treated patients, and lower bone marrow disease burden in comparison to those harboring a MYD88-L265 mutation. This test is used to aid in the prognostication and therapeutic management of LPL/WM.

Reference Values
Only orderable as a reflex. For more information, see LPLFX / Reflexive Testing of MYD88 and CXCR4

An interpretive report will be provided

Interpretation
Mutations detected or not detected. An interpretive report will be issued under the LPLFX / Reflexive Testing of MYD88 and CXCR4.

Cautions
This test is a targeted assay for the C-terminus end of the CXCR4 gene only. It examines c.898-1059 of the CXCR4 gene (NCBI NM_003467.2 GRCh37) and does not detect variants outside this region. A 1% analytical sensitivity was established at 50-ng DNA input for the hotspot mutations c.1013C->G/A only, which uses bridged nucleic acids (BNA) clamped Sanger sequencing and DNA that does not meet the established criteria can lead to false-negative results. In the extremely rare event that a rare polymorphism or indel may occur at the Sanger sequencing primer binding sites, in cis, with a c.1013C->G/A, data can yield a failed result. Routine Sanger sequencing is used to interrogate other mutations in the tested region with a 15% to 20% analytical sensitivity. The analytical sensitivity of the assay can be affected by a variety of factors, including biologic availability (ie, tumor burden), fixation of paraffin-embedded specimens, rare polymorphisms, or indels at the primer binding sites or nonspecific PCR interferences.

Clinical Reference


Performance

Method Description
The C-terminus end of CXCR4 (NM_003467.2, c.898-1059) is amplified from extracted genomic DNA by polymerase chain reaction, followed by Sanger sequencing and capillary electrophoresis analysis. Review of the sequence data is performed using a combination of automated calls and manual inspection. (Unpublished Mayo method) The hotspot mutations c.1013C->G/A (p.S338X) are examined using bridged nucleic acids (BNA) clamped Sanger sequencing with an analytic sensitivity of 1%. All other genetic variants in the test region are examined by routine Sanger sequencing with an analytic sensitivity of 15% to 20%.

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Friday

Analytic Time
7 days

Specimen Retention Time
DNA 3 months

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 was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.
Test Definition: CXCFX
CXCR4, Gene Mutation, Reflex

CPT Code Information
81479-Unlisted molecular pathology procedure