Overview

Useful For
Aiding in the prognostication and clinical management of lymphoplasmacytic lymphoma/Waldenstrom macroglobulinemia

Genetics Test Information
This test detects gene variants within the C-terminal end of the CXCR4 gene that are commonly found in association with MYD88 L265P variants in cases of lymphoplasmacytic lymphoma/Waldenstrom macroglobulinemia (LPL/WM).

Highlights
This test offers highly sensitive detection of the well-characterized hotspot variants c.1013C->G/A, p.S338X and routine Sanger sequencing for other variant in the C-terminus region. It is strongly recommended that this test be used in the context of the MYD88 / MYD88, L265P, Somatic Gene Mutation, DNA Allele-Specific PCR assay during evaluation of lymphoplasmacytic lymphoma/Waldenstrom macroglobulinemia (LPL/WM).

Special Instructions
- Hematopathology Patient Information

Method Name
Mutation Detection in DNA using BNAClamp Sanger Sequencing Technology and Routine Sanger Sequencing

(BNAClamp is utilized pursuant to a license agreement with BNA Inc)

NY State Available
Yes

Specimen

Specimen Type
Varies

Shipping Instructions
Specimen must arrive within 10 days of collection.

Necessary Information
The following information is required:

1. Pertinent clinical history
2. Clinical or morphologic suspicion
3. Date and time of collection
4. Specimen source

Specimen Required
Submit only 1 of the following specimens:
Specimen Type: Blood

Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable: Yellow top (ACD)

Specimen Volume: 3 mL

Collection Instructions:

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

Specimen Stability Information: Ambient (preferred)/Refrigerated

Specimen Type: Bone marrow aspirate

Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable: Yellow top (ACD)

Specimen Volume: 2 mL

Collection Instructions:

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

Specimen Stability Information: Ambient (preferred)/Refrigerated

Specimen Type: Extracted DNA from blood or bone marrow

Container/Tube: 1.5- to 2-mL tube

Specimen Volume: Entire specimen

Collection Instructions: Label specimen as extracted DNA from blood or bone marrow and provide indication of volume and concentration of the DNA

Specimen Stability Information: Frozen (preferred)/Refrigerated/Ambient
Test Definition: CXLPL
CXCR4 Mutation in B-cell Lymphoma

Specimen Type: Paraffin-embedded tissue

Container/Tube: Paraffin block

Specimen Stability Information: Ambient

Specimen Type: Tissue

Slides: Unstained slides

Specimen Volume: 10 slides

Additional Information: Tissue must demonstrate involvement by a hematologic neoplasm (e.g., acute myelocytic leukemia), not solid tumors.

Specimen Stability Information: Ambient

Forms
1. Hematopathology Patient Information (T676) in Special Instructions
2. If not ordering electronically, complete, print, and send a Hematopathology/Cytogenetics Test Request (T726) with the specimen.

Specimen Minimum Volume
Blood, Bone marrow: 1 mL
Extracted DNA: at least 20 mcL with a concentration of at least 10 nanograms per mcL

Reject Due To

<table>
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<tr>
<th>Condition</th>
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<tbody>
<tr>
<td>Hemolysis</td>
<td>Mild OK; Gross reject</td>
</tr>
<tr>
<td>Lipemia</td>
<td>NA</td>
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<tr>
<td>Icterus</td>
<td>NA</td>
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<tr>
<td>Other</td>
<td>B5 fixed tissues, decalcified bone marrow core biopsies, paraffin shavings, frozen tissue, methanol acetic acid (MAA) fixed pellets, moderately to severely clotted</td>
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Specimen Stability Information

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

Clinical Information
Lymphoplasmacytic lymphoma/Waldenstrom macroglobulinemia (LPL/WM) is a B-cell lymphoma 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 IgM symptoms related to hyperviscosity, tissue filtration,
and autoimmune-related pathology. CXCR4 variants are identified in approximately 30% to 40% of LPL/WM patients and are almost always associated with MYD88 L265P, which is highly prevalent in this neoplasm. The status of CXCR4 variants 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 variants) 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. A MYD88-WT/CXCR4-WT molecular signature is associated with inferior 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 variant.

**Reference Values**

Variants present or absent in the test region of the CXCR4 gene (NCBI NM_003467.2, GRCh37).

**Interpretation**

Variants detected or not detected. An interpretive report will be issued.

**Cautions**

This test is a targeted assay for the C-terminal 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 variants c.1013C->G/A only, which uses 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, insertion, or deletion 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 variants 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, insertions or deletions at the primer binding sites, or nonspecific PCR interferences.

**Clinical Reference**


**Performance**

**Method Description**

The C-terminal 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%. (Unpublished Mayo method)

**PDF Report**

No

**Day(s) and Time(s) Test Performed**

Monday through Friday

**Analytic Time**

7 days

**Maximum Laboratory Time**

10 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.

**CPT Code Information**

81479-Unlisted molecular pathology procedure

**LOINC® Information**
### Test Definition: CXLPL

**CXCR4 Mutation in B-cell Lymphoma**

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