Overview

Useful For
Second-order testing to aid in the distinction between a reactive cytosis and a myeloproliferative neoplasm, particularly when a diagnosis of polycythemia is being entertained; for use with blood specimens

Testing Algorithm
This is a second-order test that should be used when the test for the JAK2B / JAK2 V617F Mutation Detection, Blood test is negative. The sensitivity of this assay is much less than that of the JAK2B test. This is because the sequencing technique is required to evaluate for many potential mutations. The sensitive JAK2B test should always be performed first, as the JAK2 mutation burden may be very low in some specimens. If the JAK2B test is negative, then this assay should be performed for detection of non-V617F JAK2 mutations.

The following algorithms are available in Special Instructions:

- Myeloproliferative Neoplasm: A Diagnostic Approach to Peripheral Blood Evaluation
- Erythrocytosis Evaluation Testing Algorithm

Special Instructions

Method Name
Mutation Detection in cDNA Using Sanger Sequencing

NY State Available
Yes

Specimen Type
Whole blood

Advisory Information
In all cases being evaluated for JAK2 mutation status, the initial test that should be ordered is JAK2B / JAK2 V617F Mutation Detection, Blood, a sensitive assay for detection of the mutation. However, if no JAK2 V617F mutation is found, further evaluation of JAK2 may be clinically indicated.

Shipping Instructions
1. Specimen must arrive within 5 days (120 hours) of collection.
2. Draw and package specimen as close to shipping time as possible.

Necessary Information
Date of collection is required.

Specimen Required
Test Definition: JAKXB
JAK2 Exon 12 Mutation Detection, B

Container/Tube:

Preferred: EDTA (lavender top)

Acceptable: ACD (yellow top)

Specimen Volume: 10 mL

Collection Instructions:

1. Invert several times to mix blood.

2. Send specimen in original tube.

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

4 mL

Specimen Stability Information

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<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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<tbody>
<tr>
<td>Whole blood</td>
<td>Refrigerated (preferred)</td>
<td>5 days</td>
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<tr>
<td></td>
<td>Ambient</td>
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Clinical and Interpretive

Clinical Information

DNA sequence mutations in the Janus kinase 2 gene (JAK2) are found in the hematopoietic cells of several myeloproliferative neoplasms (MPN), most frequently polycythemia vera (close to 100%), essential thrombocythemia (approximately 50%), and primary myelofibrosis (approximately 50%). Mutations in JAK2 have been reported at much lower frequency in other MPN, chronic myelomonocytic leukemia and mixed MPN/myelodysplastic syndromes, but essentially never in chronic myelogenous leukemia (CML), reactive cytoses, or normal patients. Mutations are believed to cause constitutive activation of the JAK2 protein, which is an intracellular tyrosine kinase important for signal transduction in many hematopoietic cells. Since it is often difficult to distinguish reactive conditions from the non-CML MPN, identification of a JAK2 mutation has diagnostic value. Potential prognostic significance of JAK2 mutation detection in chronic myeloid disorders has yet to be clearly established.

The vast majority of JAK2 mutations occur as base pair 1849 in the gene, resulting in a JAK2 V617F protein change. In all cases being evaluated for JAK2 mutation status, the initial test that should be ordered is JAK2B / JAK2 V617F Mutation Detection, Blood, a sensitive assay for detection of the mutation. However, if no JAK2 V617F mutation is found, further evaluation of JAK2 may be clinically indicated. Over 50 different mutations have now been reported.
within exons 12 through 15 of JAK2 and essentially all of the non-V617F mutations have been identified in polycythemia vera. These mutations include point mutations and small insertions or deletions. Several of the exon 12 mutations have been shown to have biologic effects similar to those caused by the V617F mutation such that it is currently assumed other nonpolymorphic mutations have similar clinical effects. However, research in this area is ongoing.

This assay for non-V617F/alternative JAK2 mutations is designed to obtain the sequence for JAK2 exons 12 through the first 90% of exon 15, which spans the region containing all mutations reported to date.

**Reference Values**
An interpretive report will be provided.

**Interpretation**
The results will be reported as 1 of 2 states:

1. Negative for JAK2 mutation
2. Positive for JAK2 mutation

If the result is positive, a description of the mutation at the nucleotide level and the altered protein sequence is reported.

Positive mutation status is highly suggestive of a myeloproliferative neoplasm, but must be correlated with clinical and other laboratory features for a definitive diagnosis. Negative mutation status does not exclude the presence of a myeloproliferative or other neoplasm.

**Cautions**
A positive result is not specific for a particular diagnosis and clinico-pathologic correlation is necessary in all cases. A negative result does not exclude the presence of a myeloproliferative or other neoplasm.

If this test is ordered in the setting of erythrocytosis and suspicion of polycythemia vera, interpretation requires correlation with a concurrent or recent prior bone marrow evaluation.

**Supportive Data**
Analytical sensitivity is approximately 20% meaning there must be about 20% of the mutated DNA in the sample for reliable detection.

**Clinical Reference**

**Performance**

**Method Description**
Total RNA is extracted from whole blood and cDNA synthesized from JAK2 mRNA. A fragment spanning exons 12 through 15 is then amplified using standard PCR and the sequence is obtained using Sanger sequencing with
Test Definition: JAKXB
JAK2 Exon 12 Mutation Detection, B

analysis on an automated genetic analyzer. (Unpublished Mayo method)

PDF Report
No

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

Analytic Time
5 days

Maximum Laboratory Time
8 days

Specimen Retention Time
RNA 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
0027U-JAK2 (Janus kinase 2) (eg, myeloproliferative disorder), exon 12 sequence and exon 13 sequence, if performed

LOINC® Information

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