

## 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 bone marrow specimens

### Testing Algorithm

This is a second-order test that should be used when the test for the JAK2M / JAK2 V617F Mutation Detection, Bone Marrow test is negative.

See [Myeloproliferative Neoplasm: A Diagnostic Approach to Bone Marrow Evaluation](#) in Special Instructions.

### Special Instructions

- [Myeloproliferative Neoplasm: A Diagnostic Approach to Bone Marrow Evaluation](#)
- [Hematopathology Patient Information](#)

### Method Name

Mutation Detection in cDNA Using Sanger Sequencing

### NY State Available

Yes

## Specimen

### Specimen Type

Bone Marrow

### Ordering Guidance

In all cases being evaluated for JAK2 mutation status, the initial test that should be ordered is JAK2M / JAK2 V617F Mutation Detection, Bone Marrow, a sensitive assay for detection of the mutation. However, if no JAK2 V617F mutation is found, further evaluation of JAK2 may be clinically indicated.

This test is a second-order test that should be ordered when the test for the JAK2M / JAK2 V617F Mutation Detection, Bone Marrow test is negative.

### 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

Container/Tube:

Preferred: EDTA (lavender top)

Acceptable: ACD (yellow top)

Specimen Volume: 4 mL

Collection Instructions:

- 1. Invert several times to mix bone marrow.
- 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

2 mL

Reject Due To

Gross hemolysis	Reject
Other	Moderately to severely clotted

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Bone Marrow	Refrigerated (preferred)	5 days	PURPLE OR PINK TOP/EDTA
	Ambient	5 days	PURPLE OR PINK TOP/EDTA

Clinical & Interpretive

Clinical Information

DNA sequence mutations in the Janus kinase 2 (*JAK2*) gene 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 JAK2M / *JAK2* V617F Mutation Detection, Bone Marrow, 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**

1. Ma W, Kantarjian H, Zhang X, et al: Mutation profile of *JAK2* transcripts in patients with chronic myeloid neoplasias. *J Mol Diagn* 2009;11:49-53
2. Kilpivaara O, Levine RL: *JAK2* and *MPL* mutations in myeloproliferative neoplasms: discovery and science. *Leukemia* 2008;22:1813-1817
3. Kravolics R: Genetic complexity of myeloproliferative neoplasms. *Leukemia* 2008;22:1841-1848

Performance

Method Description

Total RNA is extracted from bone marrow 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 analysis on an automated genetic analyzer.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Saturday

Report Available

5 to 8 days

Specimen Retention Time

RNA 3 months

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & 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 account representative. 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. It has not been cleared or approved by the US 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

Test ID	Test Order Name	Order LOINC® Value
JAKXM	JAK2 Exon 12 Mutation Detection,	80186-0

Test Definition: JAKXM

JAK2 Exon 12 and Other Non-V617F Mutation  
Detection, Bone Marrow

	BM	
Result ID	Test Result Name	Result LOINC® Value
20250	Final Diagnosis:	34574-4
39468	JAK2 Sequencing Result	80186-0