Overview

Useful For
Identifying individuals with an increased risk of severe cutaneous adverse reactions to allopurinol based on the presence of the human leukocyte antigen HLA-B*58:01 allele

Special Instructions
- Informed Consent for Genetic Testing
- Multiple Whole Blood EDTA Genotype Tests
- Pharmacogenomic Associations Tables
- Informed Consent for Genetic Testing (Spanish)

Method Name
Qualitative Allele-Specific Real-Time Polymerase Chain Reaction (PCR)

NY State Available
Yes

Specimen

Specimen Type
Whole Blood EDTA

Specimen Required
Multiple genotype tests can be performed on a single specimen after a single extraction. See Multiple Whole Blood EDTA Genotype Tests in Special Instructions for a list of tests that can be ordered together.

Container/Tube: Lavender top (EDTA)

Specimen Volume: 3 mL

Collection Instructions: Send specimen in original tube.

Forms
1. New York Clients-Informed consent is required. Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

   - Informed Consent for Genetic Testing (T576)
   - Informed Consent for Genetic Testing-Spanish (T826)

2. If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

   - Pharmacogenomics Test Request (T797)
   - Therapeutics Test Request (T831)

Specimen Minimum Volume
0.35 mL
Test Definition: HLA58
HLA-B 5801 Genotype, Allopurinol, B

Reject Due To
No specimen should be rejected.

Specimen Stability Information

<table>
<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 EDTA</td>
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<tr>
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Clinical and Interpretive

Clinical Information
The human leukocyte antigen (HLA) genes help the immune system recognize and respond to foreign substances (such as viruses and bacteria). The HLA-B gene encodes a class 1 HLA molecule in the major histocompatibility complex (MHC), which acts by presenting peptides to immune cells. There are more than 1,500 different HLA-B alleles identified, one of which is the HLA-B*58:01 allele. Frequency of the HLA-B*58:01 allele varies with ethnicity, with a frequency of 6% to 7% in Asian populations, and 1% in Caucasian populations.

Allopurinol is a drug widely used for hyperuricemia-related diseases such as gout, Lesch-Nyhan syndrome, and recurrent urate kidney stones. However, this drug is one of the most common causes of severe cutaneous adverse reactions (SCAR), an umbrella term encompassing drug hypersensitivity syndrome, Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN). These reactions have a reported mortality rate of 20% to 25%. For individuals taking allopurinol, the presence of the HLA-B*58:01 allele has been strongly associated with allopurinol-induced SCAR.

Guidelines from the Clinical Pharmacogenomics Implementation Consortium (CPIC) recommend HLA-B*58:01 genotyping be performed when considering prescribing allopurinol, and that allopurinol should not be prescribed to patients who test positive for the allele due to the increased risk of SCAR.(1) In addition, guidelines developed by the 2012 American College of Rheumatology for Management of Gout recommend that HLA-B*58:01 testing should be considered in select patient subpopulations at an elevated risk for allopurinol-induced SCAR. Those of Korean descent, especially those with stage 3 or higher chronic kidney disease, or of Han Chinese or Thai descent, irrespective of renal function, should be tested.(2)

Reference Values
An interpretive report will be provided.

Interpretation
Positivity for HLA-B*58:01 confers increased risk for hypersensitivity to allopurinol.

For additional information regarding pharmacogenomic genes and their associated drugs, see the Pharmacogenomic Associations Tables in Special Instructions. This resource also includes information regarding enzyme inhibitors and inducers, as well as potential alternate drug choices.

Cautions
Samples may contain donor DNA if obtained from patients who received heterologous blood transfusions or allogeneic blood or marrow transplantation. Results from samples obtained under these circumstances may not accurately reflect the recipientâs genotype. For individuals who have received blood transfusions, the
genotype usually reverts to that of the recipient within 6 weeks. The impact of blood or marrow transplantation on risk of severe cutaneous adverse reactions with allopurinol is not defined in the literature.

Rare or novel variants may be present that could lead to false-negative or false-positive results. This assay also detects closely related rare alleles including HLA-B*57:05, *58:04, *58:05, *58:09, *58:10, *58:11, *58:12, *58:13, *58:15, *58:17, *58:19, *58:21, *58:22, *58:23, *58:24, and *58:28. There are currently no data indicating whether these or any other alleles or subtypes are associated with allopurinol-induced severe cutaneous adverse reactions.

**Clinical Reference**


**Performance**

**Method Description**
Genomic DNA is extracted from whole blood. Amplification for the HLA-B*58:01 allele and an internal control gene is performed by real-time PCR in the presence of SYBR green, which fluoresces when bound to double-stranded DNA. A genotype is assigned based on the allele-specific SYBR green fluorescent signals that are detected.(Unpublished Mayo method)

**PDF Report**
No

**Day(s) and Time(s) Test Performed**
Monday, Wednesday, Friday; 9 a.m.

**Analytic Time**
1 day (Not reported Saturday or Sunday)

**Maximum Laboratory Time**
8 days

**Specimen Retention Time**
Whole Blood: 2 weeks; Extracted DNA: 2 months

**Performing Laboratory Location**
Rochester
Test Definition: HLA58
HLA-B 5801 Genotype, Allopurinol, B

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 using an analyte specific reagent. Its performance characteristics were 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
81381

LOINC® Information

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