MAYO CLINIC LABORATORIES

Test Definition: HL58R

HLA-B*5801 Genotype, Allopurinol Hypersensitivity, Varies

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
- Pharmacogenomic Association Tables
- Multiple Genotype Test List
- Informed Consent for Genetic Testing (Spanish)

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Varies

Specimen Required

Multiple genotype tests can be performed on a single specimen after a single extraction. See Multiple Genotype Test List for a list of tests that can be ordered together.

Submit only 1 of the following specimens:

Container/Tube: Lavender top (EDTA)
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**
Specimen Stability Information: Ambient (preferred) 9 days/Refrigerated 30 days

Specimen Type: Saliva
Supplies: Saliva Swab Collection Kit (T786)
Patient Preparation: Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.
Specimen Volume: 1 Swab

Collection Instructions: Collect and send specimen per kit instructions.
Specimen Stability Information: Ambient 30 days

Specimen Type: Extracted DNA
Container/Tube: 2-mL screw top tube
Specimen Volume: 100 mcL (microliters)
Collection Instructions:
1. The preferred volume is 100 mcL at a concentration of 50 ng/mcL.
2. Provide concentration of DNA and volume on tube.
Specimen Stability Information: Frozen (preferred) 1 year/Ambient/Refrigerated

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:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. If not ordering electronically, complete, print, and send a Therapeutics Test Request (T831) with the specimen.

Specimen Minimum Volume

Blood: 0.35 mL
Saliva, extracted DNA: see Specimen Required

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & 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 1500 different HLA-B alleles identified, one of which is the *HLA-B*58:01* allele. The frequency of the *HLA-B*58:01* allele varies with ethnicity, with a frequency of 10% to 17% in Han Chinese, 6% in Korean, 6% to 8% in Thai, and 3% to 6% in African American populations. This allele is present at a lower frequency (approximately 1%-2%) among the White and Hispanic populations.(1)

Allopurinol is a drug widely used for hyperuricemia-related diseases such as gout, Lesch-Nyhan syndrome, and recurrent urate kidney stones. Allopurinol has been associated with severe cutaneous adverse reactions (SCAR), including drug reaction with eosinophilia and systemic symptoms, toxic epidermal necrolysis, Stevens-Johnson syndrome, and allopurinol hypersensitivity syndrome (AHS). These reactions have a reported mortality rate of 20% to 25%. The

*HLA-B*58:01* allele is associated with a markedly elevated risk for SCAR/AHS.

Guidelines from the Clinical Pharmacogenomics Implementation Consortium 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.(2) In addition, the 2020 American College of Rheumatology Guideline for the Management of Gout recommends testing for the *HLA-B*58:01* allele prior to initiation of allopurinol in patients of Southeast Asian descent (eg, Han Chinese, Korean, Thai) and for African American patients.(3)

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. 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 non-leukoreduced blood transfusions or allogeneic hematopoietic stem cell transplantation. Results from samples obtained under these circumstances may not accurately reflect the recipient's genotype. For individuals who have received blood transfusions, the genotype usually reverts to that of the recipient within 6 weeks. The impact of hematopoietic stem cell 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

1. Gonzalez-Galarza FF, McCabe A, Santos EJ, et al: Allele Frequency Net Database (AFND) 2020 update: gold-standard data classification, open access genotype data, and new query tools. Nucleic Acid Res. 2020;48:D783-D788
2. Saito Y, Stamp L, Caudle K, et al: Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for human leukocyte antigen B (HLA-B) genotype and allopurinol dosing: 2015 update. Clin Pharmacol Ther. 2016 Jan;99(1):36-37. doi: 10.1002/cpt.161
3. FitzGerald JD, Dalbeth N, Mikuls T, et al: 2020 American College of Rheumatology Guideline for the management of gout. Arthritis Rheumatol. 2020 Jun;72(6):879-895
4. Hershfield MS, Callaghan JT, Tassaneeyakul W, et al: Clinical Pharmacogenetics Implementation Consortium guidelines for human leukocyte antigen-B genotype and allopurinol dosing. Clin Pharmacol Ther. 2013 Feb;93(2):153-158
5. Chung WH, Hung SI, Chen YT: Human leukocyte antigens and drug hypersensitivity. Curr Opin Allergy Clin Immunol. 2007;7:317-323

Performance

Method Description
Genomic DNA is extracted from whole blood or saliva. Amplification for the *HLA-B*58:01* allele and an internal control gene is performed by real-time polymerase chain reaction 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) Performed
Monday, Wednesday, Friday

Report Available
3 to 5 days

Specimen Retention Time
Whole blood/Saliva: 2 weeks; Extracted DNA: 2 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
81381

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
HL58R	HLA-B 5801 Genotype, V	79711-8

MAYO CLINIC LABORATORIES

Test Definition: HL58R

HLA-B*5801 Genotype, Allopurinol Hypersensitivity, Varies

Result ID	Test Result Name	Result LOINC® Value
610665	HLA-B *58:01 Genotype	79711-8
610666	HLA-B *58:01 Phenotype	93308-5
610667	Interpretation	69047-9
610668	Additional Information	48767-8
610669	Method	85069-3
610670	Disclaimer	62364-5
610671	Reviewed by	18771-6