MAYO CLINIC LABORATORIES

Test Definition: HL57R

HLA-B*57:01 Genotype, Pharmacogenomics, Varies

Overview

Useful For

Identifying individuals with an increased risk of hypersensitivity reactions to abacavir, based on the presence of the human leukocyte antigen *HLA-B*57:01* allele

Identifying individuals taking pazopanib who have an increased risk of elevated alanine aminotransferase (ALT) levels based on the presence of an *HLA-B*57:01* allele

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
_STR1	Comp Analysis using STR (Bill only)	No, (Bill only)	No
_STR2	Add'l comp analysis w/STR (Bill Only)	No, (Bill only)	No
MATCC	Maternal Cell Contamination, B	Yes	No

Testing Algorithm

Cord blood:

For cord blood specimens that have an accompanying maternal blood specimen, maternal cell contamination studies will be performed at an additional charge.

See Abacavir Hypersensitivity Testing and Initial Patient Management Algorithm

For additional information regarding pharmacogenomic genes and their associated drugs, see the Pharmacogenomic Associations Tables.

Special Instructions

- Informed Consent for Genetic Testing
- Abacavir Hypersensitivity Testing and Initial Patient Management Algorithm
- 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.

Patient Preparation: A previous hematopoietic stem cell transplant or liver transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a hematopoietic stem cell or liver transplant.

Submit only 1 of the following specimens:

Specimen Type: Whole blood
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**.
3. Whole blood collected postnatal from an umbilical cord is also acceptable. See Additional Information
Specimen Stability Information: Ambient (preferred) 4 days/Refrigerated 4 days/Frozen 4 days
Additional Information:
1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.
2. To ensure minimum volume and concentration of DNA are met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.
3. For postnatal umbilical cord whole blood specimens, maternal cell contamination studies are recommended to ensure test results reflect that of the patient tested. A maternal blood specimen is required to complete maternal cell contamination studies. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on both the cord blood and maternal blood specimens under separate order numbers.

Specimen Type: Saliva
Patient Preparation: Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.
Supplies:
DNA Saliva Kit High Yield (T1007)
Saliva Swab Collection Kit (T786)

Container/Tube:
Preferred: High-yield DNA saliva kit
Acceptable: Saliva swab
Specimen Volume: 1 Tube if using T1007 or 2 swabs if using T786
Collection Instructions: Collect and send specimen per kit instructions.
Specimen Stability Information: Ambient (preferred) 30 days/Refrigerated 30 days
Additional Information: Saliva specimens are acceptable but not recommended. Due to lower quantity/quality of DNA yielded from saliva, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.

Specimen Type: Extracted DNA
Container/Tube:
Preferred: Screw Cap Micro Tube, 2 mL with skirted conical base
Acceptable: Matrix tube, 1 mL
Collection Instructions:
1. The preferred volume is at least 100 mcL at a concentration of 75 ng/mcL.
2. Include concentration and volume on tube.
Specimen Stability Information: Frozen (preferred) 1 year/Ambient/Refrigerated
Additional Information: DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). Our laboratory has experience with Chemagic, Puregene, Autopure, MagnaPure, and EZ1 extraction platforms and cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied. If applicable, specific gene regions that were unable to be interrogated due to DNA quality will be noted in the report.

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

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 I HLA molecule in the major histocompatibility complex, which acts by presenting peptides to immune cells. There are many HLA-B alleles identified, one of which is the *HLA-B*57:01* allele. Frequency of the *HLA-B*57:01* allele varies across ancestral populations, with a frequency of 6% to 7% in European populations and up to 20% in Southwest Asian populations.

The *HLA-B*57:01* allele has been associated with hypersensitivity to abacavir, a highly effective nucleoside analog reverse-transcriptase inhibitor used to treat HIV infection and AIDS. Per the Clinical Pharmacogenomics Implementation Consortium (CPIC) guideline for abacavir and *HLA-B*, individuals who are positive for the *HLA-B*57:01* allele are at an increased risk for abacavir hypersensitivity, and it is not recommended for use in treating these individuals.

Hypersensitivity reactions, which generally occur during the first 6 weeks of treatment, are often nonspecific and include skin rashes, gastrointestinal symptoms (eg, nausea, vomiting, diarrhea, abdominal pain), and respiratory symptoms. Fatalities have been reported with abacavir hypersensitivity. Prospective testing for the *HLA-B*57*:*01* genotype and excluding *HLA-B*57*:*01*-positive individuals from treatment with abacavir decreases the incidence of abacavir hypersensitivity.

Pazopanib is a kinase inhibitor indicated for the treatment of patients with advanced renal cell carcinoma and advanced soft tissue sarcoma who have received prior chemotherapy. In clinical trials with pazopanib, hepatotoxicity was observed, manifested as increases in serum transaminases such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin. This hepatotoxicity can be severe and fatal. Patients older than 65 years are at greater risk for hepatotoxicity. Transaminase elevations occur early in the course of treatment (92.5% of all transaminase elevations of any grade occurred in the first 18 weeks).

Patients who are *HLA-B*57:01* carriers and are taking pazopanib are at increased risk of elevated ALT levels.(1,2) According to the US Food and Drug Administration (FDA) label for pazopanib, in an analysis of data from 31 clinical studies of pazopanib administered as either monotherapy or in combination with other agents, elevation in ALT to levels greater than 3 times the upper limit of normal occurred in 32% (42/133) of *HLA-B*57:01* allele carriers as compared to 19% (397/2101) of noncarriers. Furthermore, elevation in ALT to levels greater than 5 times the upper limit of normal occurred in 19% (25/133) of *HLA-B*57:01* allele carriers and in 10% (213/2101) of noncarriers. All patients taking pazopanib should have hepatic function monitored, regardless of *HLA-B*57:01* carrier status, and administration of pazopanib should be interrupted, reduced, or discontinued according to recommendations in the FDA label if hepatic function is impaired.

UGT1A1 genotype is also relevant to pazopanib-induced hyperbilirubinemia and testing may also be warranted. For more information see U1A1Q / Uridine Diphosphate (UDP) Glucuronosyltransferase 1A1 TA Repeat Genotype, *UGT1A1*, Varies.

Flucloxacillin is an antibiotic and can lead to liver injury in a subset of individuals; however, this medication is no longer used in the United States. Individuals who are positive for *HLA-B*57:01* allele have an 80-fold higher risk of

flucloxacillin-induced liver injury.(3) While the overall incidence is low, the Royal Dutch Pharmacists Association Pharmacogenetics Working Group recommends regular monitoring of liver function for *HLA-B*57:01* positive individuals prescribed flucloxacillin. For those who develop an elevation of liver enzymes or bilirubin, consideration of alternative medication is recommended. Other *HLA-B* alleles may also be associated with flucloxacillin-induced liver injury.

Reference Values

Negative
An interpretive report will be provided.

Interpretation

Positivity for human leukocyte antigen allele *HLA-B*57:01* confers high risk for hypersensitivity to abacavir and higher risk of elevated alanine aminotransferase (ALT) levels in patient taking pazopanib.

For more information see Abacavir Hypersensitivity Testing and Initial Patient Management Algorithm.

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

Cautions

Specimens may contain donor DNA if obtained from patients who received non-leukoreduced blood transfusions or allogeneic hematopoietic stem cell transplantation. Results from specimens obtained under these circumstances may not accurately reflect the recipient's genotype. For individuals who have received non-leukoreduced blood transfusions, the genotype usually reverts to that of the recipient within 6 weeks. The impact of hematopoietic stem cell or liver transplantation on risk of severe cutaneous adverse reactions with allopurinol is not defined in the literature. Risk is unknown for stem cell or liver transplant recipients with mismatch of the *HLA-B*57:01* allele.

The US Food and Drug Administration (FDA) recommends screening for the *HLA-B*57:01* allele before initiating therapy with abacavir. Genotyping is also critical when there is a clinical history of, or when the physician suspects, an abacavir hypersensitivity reaction. However, FDA guidance states that, regardless of *HLA-B*57:01* status, abacavir should be permanently discontinued if hypersensitivity cannot be ruled out, even when other diagnoses are possible. Although the negative predictive value of the test is high, a negative *HLA-B*57:01* result does not preclude the development of a hypersensitivity response to abacavir and cannot substitute for clinical vigilance whenever abacavir therapy is administered. Since symptoms of abacavir hypersensitivity are often nonspecific and can imitate other conditions commonly seen in HIV patients on antiretroviral therapy, the phenotypic diagnosis of abacavir hypersensitivity can be challenging. There is significant variability among patients identified as hypersensitive to abacavir. Not all individuals who are positive for *HLA-B*57:01* will have a hypersensitivity reaction.

All patients taking pazopanib should have hepatic function monitored, regardless of *HLA-B*57:01* carrier status, and administration of pazopanib should be interrupted, reduced, or discontinued according to recommendations in the FDA label if hepatic function is impaired.

Rare or novel variants may be present that could lead to false-negative or false-positive results. There may be rare or novel HLA-B alleles that could interfere with this assay. Currently, there isn't data indicating whether any other allele or subtype is associated with abacavir hypersensitivity or pazopanib hepatotoxicity.

Supportive Data

Sensitivity of this assay for detecting the human leukocyte antigen *HLA-B*57:01* allele approaches 100% with specificity near 96%.(4)

Clinical Reference

1. Xu CF, Johnson T, Wang X, et al. HLA-B*57:01 confers susceptibility to pazopanib-associated liver injury in patients with cancer. Clin Cancer Res. 2016;22(6):1371-1377
2. Pazopanib. Package insert. Novartis Pharmaceuticals; Updated January 3, 2025. Accessed August 11, 2025. Available at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=eeaaaf38-fb86-4d9f-a19d-0f61daac2fd7
3. Nicoletti P, Aithal GP, Chamberlain TC, et al. Drug-induced liver injury due to flucloxacillin: relevance of multiple human leukocyte antigen alleles. Clin Pharmacol Ther. 2019;106(1):245-253
4. Saag M, Balu R, Brachman P, et al. High sensitivity of HLA-B*5701 in whites and blacks in immunologically-confirmed cases of abacavir hypersensitivity. Fourth IAS Conference on HIV Pathogenesis, Treatment, and Prevention. July 22-25, 2007. Sydney. Abstract WEAB305
5. Martin MA, Hoffman JM, Freimuth RR, et al. Clinical Pharmacogenetics Implementation Consortium Guidelines for HLA-B genotype and abacavir dosing: 2014 update. Clin Pharmacol Ther. 2014;95(5):499-500
6. Faruki H, Heine U, Brown T, Koester R, Lai-Goldman M. HLA-B*5701 clinical testing: early experience in the United States. Pharmacogenet Genomics. 2007;17(10):857-860
7. Sun HY, Hung CC, Lin PH, et al. Incidence of abacavir hypersensitivity and its relationship with HLA-B*5701 in HIV-infected patients in Taiwan. J Antimicrob Chemother. 2007;60(3):599-604. doi:10.1093/jac/dkm243

Performance

Method Description

Genomic DNA is extracted from the sample. Amplification for the *HLA-B*57:01* 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.(Hammond E, Mamotte C, Nolan D, Mallal S. HLA-B*5701 typing: evaluation of an allele-specific polymerase chain reaction melting assay. Tissue Antigens. 2007;70[1]:58-61)

PDF Report

No

Day(s) Performed

Varies

Report Available

3 to 7 days

Specimen Retention Time

Whole blood: 28 days (if available); Saliva: 30 days (if available); Extracted DNA: 3 months

Test Definition: HL57R

HLA-B*57:01 Genotype, Pharmacogenomics, Varies

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
HL57R	HLA-B 5701 Genotype, V	50956-2

Result ID	Test Result Name	Result LOINC® Value
610672	HLA-B *57:01 Genotype	50956-2
610673	HLA-B *57:01 Phenotype	93308-5
610674	Interpretation	69047-9
610675	Additional Information	48767-8
610676	Method	85069-3
610677	Disclaimer	62364-5
610678	Reviewed by	18771-6