Overview

Useful For
Identifying patients who may be at risk for altered metabolism of drugs that are modified by CYP2C19

Predicting anticoagulation response to clopidogrel

Special Instructions

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

Method Name
Real-Time Polymerase Chain Reaction (PCR) with Allelic Discrimination Analysis

NY State Available
Yes

Specimen

Specimen Type
Varies

Advisory Information
Testing is available as the single gene assay (this test) and as a part of a psychotropic or focused pharmacogenomics panel.

If multiple pharmacogenomic genotype testing is desired, order PGXFP / Focused Pharmacogenomics Panel, Varies.

If genotype testing for psychotropic medications is desired, order PSYGP / Psychotropic Pharmacogenomics Gene Panel, Varies.

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

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 specimen in original tube.

**Specimen Stability Information:** Ambient (preferred) 9 days/Refrigerated 30 days

**Specimen Type:** Saliva

**Patient Preparation:** Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.

**Supplies:** Saliva Swab Collection Kit (T786)

**Specimen Volume:** 1 swab

**Collection Instructions:** Collect and send specimen per kit instructions.

**Specimen Stability Information:** Ambient 30 days

**Specimen Type:** 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. Include concentration and volume on tube.

**Specimen Stability Information:** Frozen (preferred)/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 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)
   - [Cardiovascular Test Request](T724)
   - [Neurology Specialty Testing Client Test Request](T732)
   - [Therapeutics Test Request](T831)

**Specimen Minimum Volume**

Blood: 0.4 mL
Saliva: 1 swab
Test Definition: 2C19V
CYP2C19 Genotype

Reject Due To

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

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varies</td>
<td>Varies</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Clinical and Interpretive

Clinical Information

Primary metabolism of many drugs is performed by the cytochrome P450 (CYP450) enzymes, a group of oxidative/dealkylating enzymes localized in the microsomes of many tissues including the intestines and liver. One of these CYP450 enzymes, CYP2C19, participates in the metabolism of a wide variety of drugs, including the activation of the anticoagulant clopidogrel and the inactivation of citalopram.

CYP2C19 drug metabolism is variable among individuals. Some individuals have CYP2C19 genetic variants that lead to severely diminished or absent CYP2C19 catalytic activity (i.e., poor metabolizers). The frequency of CYP2C19 variants (also referred to as polymorphisms) depends on ethnicity. CYP2C19 variants that produce poor metabolizers are found with frequencies of 2% to 5% in Caucasians, 4% in African Americans, 13% to 23% in Asians, and 38% to 79% in Polynesians and Micronesians.

The following table displays the CYP2C19 variants detected by this assay, the corresponding star allele, and the effect on CYP2C19 enzyme activity:

<table>
<thead>
<tr>
<th>CYP2C19 Allele</th>
<th>cDNA Nucleotide Change</th>
<th>Effect on Enzyme Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>*1</td>
<td>None (wild type)</td>
<td>Normal (extensive) activity</td>
</tr>
<tr>
<td>*2</td>
<td>681G-&gt;A</td>
<td>No activity</td>
</tr>
<tr>
<td>*3</td>
<td>636G-&gt;A</td>
<td>No activity</td>
</tr>
<tr>
<td>*4</td>
<td>1A-&gt;G</td>
<td>No activity</td>
</tr>
<tr>
<td>*5</td>
<td>1297C-&gt;T</td>
<td>No activity</td>
</tr>
<tr>
<td>*6</td>
<td>395G-&gt;A</td>
<td>No activity</td>
</tr>
<tr>
<td>*7</td>
<td>819+2T-&gt;A</td>
<td>No activity</td>
</tr>
<tr>
<td>*8</td>
<td>358T-&gt;C</td>
<td>No activity</td>
</tr>
<tr>
<td>*9</td>
<td>431G-&gt;A</td>
<td>Decreased activity</td>
</tr>
<tr>
<td>*10</td>
<td>680C-&gt;T</td>
<td>Minimal activity</td>
</tr>
<tr>
<td>*17</td>
<td>-806C-&gt;T</td>
<td>Enhanced activity</td>
</tr>
<tr>
<td>*35</td>
<td>332-23A-&gt;G in the absence of 681G-&gt;A</td>
<td>No activity</td>
</tr>
</tbody>
</table>
CYP2C19 drug metabolism is dependent on the specific genotype detected and also on the number and type of drugs administered to the patient. Individuals without a detectable CYP2C19 variant will have the predicted phenotype of an extensive drug metabolizer and are designated as CYP2C19 *1/*1. If an individual is homozygous or compound heterozygous for alleles with no activity, the individual is predicted to be a poor metabolizer. If an individual is heterozygous for an allele with no activity, the individual is predicted to be an intermediate metabolizer. Individuals with the CYP2C19*17 allele (in the absence of any inactive or decreased activity alleles) may have enhanced metabolism of drugs. In some cases, a range of potential phenotypes may be given, depending on the combination of alleles identified.

Patients who are poor metabolizers may benefit from dose alteration or selection of a comparable drug that is not primarily metabolized by CYP2C19. It is important to interpret the results of testing in the context of other coadministered drugs.

Reference Values
An interpretive report will be provided.

Interpretation
An interpretive report will be provided.

The genotype, with associated star alleles, is assigned using standard allelic nomenclature as published by the Pharmacogene Variation (PharmVar) Consortium.(1)

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

Drug-drug interactions and drug-metabolite inhibition must be considered when treating intermediate metabolizers. It is important to interpret the results of testing and dose adjustments in the context of hepatic and renal function and patient age.

Cautions
Rare variants may be present that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings (phenotype), additional testing should be considered.

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 recipient's genotype. For individuals who have received blood transfusions, the genotype usually reverts to that of the recipient within 6 weeks. For individuals who have received allogeneic blood or marrow transplantation, a pretransplant DNA specimen is recommended for testing.

CYP2C19 genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's CYP2C19 status.

This method may not detect all variants that result in altered CYP2C19 activity. Therefore, absence of a detectable variant does not rule out the possibility that a patient has altered CYP2C19 metabolism due to other CYP2C19 variants that cannot be detected with this method. Furthermore, when 2 or more variants are identified, the cis-/trans-status (whether the variants are on the same or opposite chromosomes) is not always known.

This test is designed to detect only the variants specified above. Other variants in the primer binding regions can affect testing and, ultimately, the genotype and phenotype predictions made.
Clinical Reference


Performance

Method Description
Genomic DNA is extracted from whole blood or saliva. Genotyping for CYP2C19 alleles is performed using a PCR-based 5'-nuclease assay. Fluorescently labeled detection probes anneal to the target DNA. PCR is used to amplify the section of DNA that contains the variant. If the detection probe is an exact match to the target DNA, the 5'-nuclease polymerase degrades the probe, the reporter dye is released from the effects of the quencher dye, and a fluorescent signal is detected. Genotypes are assigned based on the allele-specific fluorescent signals that are detected. (User Guide: TaqMan SNP Genotyping Assay, Applied Biosystems, Revision A.0 January 2014)

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Friday; 8 a.m.

Analytic Time
1 day (not reported Saturday or Sunday)

Maximum Laboratory Time
5 days

Specimen Retention Time
Whole Blood/Saliva Swab: 2 weeks Extracted DNA: 2 months

Performing Laboratory Location
Rochester

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
Test Definition: 2C19V
CYP2C19 Genotype

- 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
81225

LOINC® Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2C19V</td>
<td>CYP2C19 Genotype</td>
<td>57132-3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA0103</td>
<td>CYP2C19 Genotype</td>
<td>57132-3</td>
</tr>
<tr>
<td>BA0104</td>
<td>CYP2C19 Phenotype</td>
<td>79714-2</td>
</tr>
<tr>
<td>BA0105</td>
<td>Interpretation</td>
<td>69047-9</td>
</tr>
<tr>
<td>BA0106</td>
<td>Additional Information</td>
<td>48767-8</td>
</tr>
<tr>
<td>BA0191</td>
<td>Method</td>
<td>49549-9</td>
</tr>
<tr>
<td>BA0192</td>
<td>Disclaimer</td>
<td>62364-5</td>
</tr>
<tr>
<td>BA0107</td>
<td>Reviewed by</td>
<td>18771-6</td>
</tr>
</tbody>
</table>