MAYO CLINIC LABORATORIES

Test Definition: 2C19R

Cytochrome P450 2C19 Genotype, Varies

Overview

Useful For

Identifying patients who may be at risk for altered metabolism of drugs that are modified by cytochrome P450 2C19

Predicting anticoagulation response to clopidogrel

Special Instructions

- Informed Consent for Genetic Testing
- Pharmacogenomic Association 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

Ordering Guidance

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 needed, consider PGXQP / Focused Pharmacogenomics Panel, Varies.

If genotype testing for psychotropic medications is requested, order PSYQP / 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 for a list of tests that can be ordered together.

Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube:

Preferred: Lavender top (EDTA)
Acceptable: None
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
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: 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)/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 1 of the following forms with the specimen:
-Neurology Specialty Testing Client Test Request (T732)
-Therapeutics Test Request (T831)
-Cardiovascular Test Request (T724)

Specimen Minimum Volume

Blood: 0.4 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

Primary metabolism of many drugs is performed by the cytochrome P450 (CYP) enzymes, a group of oxidative/dealkylating enzymes localized in the microsomes of many tissues including the intestines and liver. One of these CYP 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 (ie, poor metabolizers). The frequency of *CYP2C19* variants (formerly known as polymorphisms) depends on ethnicity. *CYP2C19* variants that produce poor metabolizers are found with frequencies of 2% to 5% in the White population, 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. Enzyme Activity of Individual Star Alleles

***CYP2C19* allele**	**cDNA nucleotide change (NM_000769.1)**	**Effect on enzyme activity**
**1*	None (wild type)	Normal (extensive) activity
**2*	c.681G>A	No activity
**3*	c.636G>A	No activity
**4*	c.1A>G	No activity
**5*	c.1297C>T	No activity
**6*	c.395G>A	No activity
**7*	c.819+2T>A	No activity
**8*	c.358T>C	No activity
**9*	c.431G>A	Decreased activity
**10*	c.680C>T	Decreased activity
**17*	c.-806C>T	Enhanced activity
**35*	c.332-23A>G in the absence of c.681G>A	No activity

CYP2C19 drug metabolism is dependent on the specific genotype detected and also on the number and type of drugs administered to the patient. Phenotyping is derived from the Pharmacogene Variation Consortium website(1), the Clinical Pharmacogenetics Implementation Consortium website(2), published guidelines(3-8), and an exhaustive review of the CYP2C19 literature(9-10). 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. 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 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. For individuals who have received allogeneic hematopoietic stem cell 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
1. PharmVar: Pharmacogene Variation Consortium. Updated November 5, 2024. Accessed November 14, 2024. Available at www.pharmvar.org/

2. Clinical Pharmacogenetics Implementation Consortium (CPIC). Updated September 23, 2022. Accessed November 14, 2024. Available at https://cpicpgx.org/
3. Scott SA, Sangkuhl K, Stein CM, et al. Clinical Pharmacogenetics Implementation Consortium guidelines for CYP2C19 genotype and clopidogrel therapy: 2013 update. Clin Pharmacol Ther. 2013;94(3):317-323. doi:10.1038/clpt.2013.105
4. Lima JJ, Thomas CD, Barbarino J, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for CYP2C19 and proton pump inhibitor dosing. Clin Pharmacol Ther. 2021;109(6):1417-1423. doi:10.1002/cpt.2015
5. Moriyama B, Obeng AO, Barbarino J, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for CYP2C19 and voriconazole therapy. Clin Pharmacol Ther. 2017;102(1):45-51. doi:10.1002/cpt.583. Erratum in: Clin Pharmacol Ther. 2018 Feb;103(2):349
6. Hicks JK, Bishop JR, Sangkuhl K, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for CYP2D6 and CYP2C19 genotypes and dosing of selective serotonin reuptake inhibitors. Clin Pharmacol Ther. 2015;98(2):127-134. doi:10.1002/cpt.147
7. Hicks JK, Sangkuhl K, Swen JJ, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther. 2017;102(1):37-44. doi:10.1002/cpt.597
8. Blaisdell J, Mohrenweiser H, Jackson J, et al. Identification and functional characterization of new potentially defective alleles of human CYP2C19. Pharmacogenetics. 2002;12(9):703-711. doi:10.1097/00008571-200212000-00004
9. Mega JL, Close SL, Wiviott SD, et al. Cytochrome p-450 polymorphisms and response to clopidogrel. N Engl J Med. 2009;360(4):354-362. doi:10.1056/NEJMoa0809171

Performance

Method Description
Genomic DNA is extracted from whole blood or saliva. Genotyping for *CYP2C19* alleles is performed using a polymerase chain reaction (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.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
2 to 4 days

Specimen Retention Time
Whole blood: Refrigerate; Saliva: Ambient; Extracted DNA: Frozen

Performing Laboratory Location
Rochester

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

81225

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
2C19R	CYP2C19 Genotype, V	57132-3

Result ID	Test Result Name	Result LOINC® Value
610089	CYP2C19 Genotype	57132-3
610090	CYP2C19 Phenotype	79714-2
610567	CYP2C19 Activity Score	104667-1
610091	Interpretation	69047-9
610092	Additional Information	48767-8
610093	Method	85069-3
610094	Disclaimer	62364-5
610095	Reviewed by	18771-6