MAYO CLINIC LABORATORIES

Test Definition: 2B6Q

Cytochrome P450 2B6 Genotype, Varies

Overview

Useful For

Aiding in determining therapeutic strategies for drugs that are metabolized by cytochrome P450 (CYP) 2B6

Providing information relevant to bupropion, efavirenz, ketamine, methadone, and nevirapine, as well as other medications metabolized by CYP2B6

Determining the genotype if genotype-phenotype discord is encountered clinically after testing with a less comprehensive genotyping method has occurred

Identifying genotype when required for drug trials and research protocols

Special Instructions

- Informed Consent for Genetic Testing
- Pharmacogenomic Association Tables
- Informed Consent for Genetic Testing (Spanish)

Method Name

Real Time-Polymerase Chain Reaction (RT-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 pharmacogenomics panel.

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

Specimen Required

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) 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: 1 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 cytochrome P450 (CYP) family of enzymes is a group of oxidative/dealkylating enzymes localized in the microsomes of many tissues including the intestines and liver. CYP2B6 is wholly or partially responsible for the metabolism of several commonly prescribed drugs.

The *CYP2B6* gene is highly variable with over 38 named alleles. The gene can have multiple sequence variations. Alleles thought to have an impact upon CYP2B6 enzyme function at the time that this test was developed are included in this test (see Table). Individuals without a detectable gene alteration will be reported as *CYP2B6*1/*1,* but it is possible that these individuals harbor unknown variants that may impact metabolism. In addition, some individuals have genes that are hybrids of *CYP2B6* and the *CYP2B7* pseudogene. The frequency of these hybrids is unknown, and this assay does not test for these hybrids.

Phenotyping is derived from the Pharmacogene Variation Consortium website(1), an exhaustive review of the *CYP2B6* literature, the Clinical Pharmacogenetics Implementation Consortium website(2), and published guidelines.(3) *CYP2B6* genotype results are used to predict metabolizer phenotypes. A *CYP2B6* phenotype is predicted based upon the number of functional, partially functional, and nonfunctional alleles present in a sample. In rare instances where alleles with unknown function are present in a homozygous or compound heterozygous state, an unknown phenotype occurs. It should be noted that other laboratories may use different phenotype prediction methods as there is no consensus on this at this time. However, the method used here represents the findings of the majority of literature available.

Several medications act as substrates of CYP2B6. CYP2B6-metabolized medications with the highest quality of data for the impact of various *CYP2B6* alleles on metabolism are:
-Bupropion
-Efavirenz
-Ketamine
-Methadone
-Nevirapine

Other enzymes may be involved in the metabolism of these drugs. For example, bupropion is also metabolized by CYP2D6. Efavirenz is also metabolized by CYP2A6, although CYP2B6 is the major metabolizing enzyme. Ketamine is also metabolized by CYP2A6, and nevirapine is also metabolized by CYP3A4 and CYP3A5. CYP2A6 testing is not available clinically at the time this document was written, but CYP2D6 (2D6Q / Cytochrome P450 *2D6* Comprehensive Cascade, Varies), CYP3A4 (3A4Q / Cytochrome P450 *3A4* Genotype, Varies), and CYP3A5 (3A5Q / Cytochrome P450 *3A5* Genotype, Varies) testing is available.

There is a variable degree of substrate specificity exhibited by *CYP2B6* alleles on these medications. This means that the same allele (ie, *6) may not metabolize all substrates at exactly the same rate.

Drugs that are metabolized by CYP2B6 may require dosage adjustment based on the individual patient's genotype. For example, patients who are poor metabolizers may require much lower than usual doses to achieve optimal response in the case of drugs that are inactivated by the CYP2B6 enzyme. Alternatively, patients who are ultrarapid metabolizers may benefit from increased doses in the case of drugs that are inactivated by CYP2B6 enzyme. In the absence of clear guidance from the US Food and Drug Administration on dosing for various metabolizer phenotypes, patients with either ultrarapid or poor metabolism may benefit by switching to comparable alternate medications that are not primarily metabolized by CYP2B6 or by therapeutic drug monitoring where applicable.

Table. Enzyme Activity of Individual Star Alleles

Enzyme activity	Examples of *CYP2B6* star alleles
Normal (extensive) activity	*1, *5
Increased activity	*4, *22
Decreased activity	*6, *7, *9, *11, *14, *15, *19, *20, *26, *27, *36
No or null activity	*8, *12, *13, *16 (also known as *18.002), *18, *35, *38
Unknown activity	*27

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.

Cautions

Rare variants may be present that could lead to false-negative or false-positive results.

Samples may contain donor DNA if obtained from patients who received heterologous 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, a pretransplant DNA specimen is recommended for testing.

Genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's genetic status for the genes on this panel.

This test is not designed to provide specific dosing recommendations and is to be used as an aid to clinical decision making only. Drug-label guidance should be used when dosing patients with medications regardless of the predicted phenotype.(4)

Clinical Reference

1. PharmVar. Pharmacogene Variation Consortium. Updated March 3, 2021. Accessed March 22, 2021. Available at www.pharmvar.org/
2. Clinical Pharmacogenetics Implementation Consortium (CPIC). Accessed October 14, 2020. Available at https://cpicpgx.org/
3. Desta Z, Gammal RS, Gong L, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2B6

and Efavirenz-Containing Antiretroviral Therapy. Clin Pharmacol Ther. 2019;106(4):726-733. doi:10.1002/cpt.1477

4. U.S National Library of Medicine: DailyMed. National Institutes of Health. Accessed October 14, 2020. Available at https://dailymed.nlm.nih.gov/dailymed/index.cfm

Performance

Method Description

Genomic DNA is extracted from whole blood or saliva. Genotyping for each allele 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

3 to 8 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

81479

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Cytochrome P450 2B6 Genotype, Varies

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
2B6Q	CYP2B6 Genotype, V	72511-9

Result ID	Test Result Name	Result LOINC® Value
610082	CYP2B6 Genotype	72882-4
610083	CYP2B6 Phenotype	79720-9
610566	CYP2B6 Activity Score	104666-3
610084	Interpretation	69047-9
610085	Additional Information	48767-8
610086	Method	85069-3
610087	Disclaimer	62364-5
610088	Reviewed by	18771-6