MAYO CLINIC LABORATORIES

Test Definition: PSYQP

Psychotropic Pharmacogenomics Gene Panel, Varies

Overview

Useful For

Individualizing selection and dosage of medications prescribed for treatment of depression and other psychiatric disorders based on genetic variation

Identifying genetic variation in genes known to be associated with response and/or risk of toxicity with psychotropic medications

Evaluating patients who have failed therapy with selective serotonin reuptake inhibitors (SSRI)

Evaluating patients with treatment-resistant depression

Predicting response time to improvement with SSRI

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
2D61Z	CYP2D6 Full Gene Sequence	No, (Bill Only)	No
2D62Z	CYP2D6 GEN CYP2D6-2D7 Hybrid	No, (Bill Only)	No
2D63Z	CYP2D6 GEN CYP2D7-2D6 Hybrid	No, (Bill Only)	No
2D64Z	CYP2D6 Nonduplicated Gene	No, (Bill Only)	No
2D65Z	CYP2D6 5' Gene DUP/MLT	No, (Bill Only)	No
2D66Z	CYP2D6 3' Gene DUP/MLT	No, (Bill Only)	No

Genetics Test Information

This test includes targeted testing to evaluate the following genes: *ANKK1, ADRA2, CHRNA3, COMT, CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, DRD2, EPHX1, GRIK4, HLA-A*31:01, HLA-B*15:02, HTR2A, HTR2C, MTHFR, OPRM1, SCN1A, SLC6A4 (5-HTT),* and *UGT2B15.*

CYP2D6 testing is done in 2 tiers when needed. Tier 1 uses a polymerase chain reaction (PCR)-based 5'-nuclease assay to determine the variants present. All samples also have copy number determined by PCR-based 5'-nuclease assay. Testing in tier 1 allows for the detection of all common *CYP2D6* variants (eg, **2, *3, *4, *5, *6, *7, *8, *9, *10, *17, *29, *35, *41, *59*) and rarer alleles such as **11*, **12, *14, *15*, and **114*. Duplications and multiplications of alleles are also identified. Unitary and tandem *CYP2D7-2D6* (**13*) alleles and *CYP2D6-2D7* (eg, **4N*, **36*, and **68*) alleles can also be detected. Tier 2 testing involves sequencing using fluorescent dye-terminator chemistry and is only done if an ambiguous phenotype results from tier 1 testing. Approximately 3% of samples require tier 2 testing.

Prior Authorization is available for this assay.

Testing Algorithm

If a specimen requires follow-up for *CYP2D6*, then reflex testing will be performed as appropriate at an additional charge.

For more information see *CYP2D6* Comprehensive Cascade Testing Algorithm.

Special Instructions

- Informed Consent for Genetic Testing
- CYP2D6 Comprehensive Cascade Testing Algorithm
- Pharmacogenomic Association Tables
- Informed Consent for Genetic Testing (Spanish)
- Psychotropic Pharmacogenomics Gene Panel (PSYQP) Prior Authorization Ordering Instructions

Method Name

Real-Time Polymerase Chain Reaction (RT-PCR) with Allelic Discrimination Analysis/Qualitative Allele-Specific RT-PCR/PCR followed by Sizing Analysis

NY State Available

Yes

Specimen

Specimen Type

Varies

Necessary Information

Prior Authorization is available, **but not required**, for this test. If proceeding with the prior authorization process, submit the required form with the specimen.

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: 2 Swabs, use 2 kits for collection
Collection Instructions: Collect and send specimen per kit instructions.
Additional Information: Due to lower concentration of DNA yielded from saliva, testing cannot proceed to reflex testing for CYP2D6 sequencing and will stop after initial testing is complete.
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. Psychotropic Pharmacogenomics Gene Panel Prior Authorization Ordering Instructions
3. 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

This panel provides a comprehensive analysis for multiple genes that have strong pharmacogenomic associations with

medications used in the treatment of psychiatric disorders, including depression. Each sample is tested for specific variations with known functional impact. Pharmacogenomic data for the following specific variants are reviewed and reported (if present):
-*ADRA2A* rs1800544
-*ANKK1* (*DRD2* associated) rs1800497
-*CHRNA3* rs1051730
-*COMT* rs4680
-*CYP1A2 *1F*, *1K*, *6*, and *7*
-*CYP2B6 *4, *5, *6, *7, *8, *9, *11, *12, *13, *14, *15, *16* (also known as *18.002*), *18, *19, *20, *22, *26, *27, , *35, *36, and *38*
-*CYP2C9 *2*, *3*, *4*, *5*, *6*, *8*, *9*, *11*, *12*, *13*, *14*, *15*, *16*, *17*, *18*, *25*, *26*, *28*, *30*, *33*, and *35*
-*CYP2C19 *2*, *3*, *4*, *5*, *6*, *7*, *8*, *9*, *10*, *17*, and *35*
-*CYP2D6 *2*, *3*, *4*, *4N*, *5*, *6*, *7*, *8*, *9*, *10*, *11*, *12*, *13*, *14A* (now known as *114*), *14B* (now known as *14*),*15*, *17*, *29*, *35*, *36*, *41*, *59, *68*, and *CYP2D6* gene duplication; additional *CYP2D6* variants may be detected through the reflex testing process
-*CYP3A4 *8*, *11*, *12*, *13*, *16*, *17*, *18*, *22*, and *26*
-*CYP3A5 *3*, *6*, *7*, *8*, and *9*
-*DRD2* rs1799978
-*EPHX1* rs2234922
-*GRIK4* rs1954787
-*HLA-A*31:01*
-*HLA-B*15:02*
-*HTR2A* rs7997012
-*HTR2C* rs3813929 and rs1414334
-*MTHFR* rs1801131 and rs1801133
-*OPRM1* rs1799971
-*SCN1A* rs3812718
-*SLC6A4* linked polymorphic region (LPR), a 44-base pair promoter insertion/deletion polymorphism
-*UGT2B15* rs1902023

Based on the results of each assay, a genotype is assigned, and a phenotype is predicted for each gene. Assessment of multiple genes may assist the ordering clinician with personalized drug recommendations, avoidance of adverse drug reactions, and optimization of drug treatment.

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided that focuses on medications and genes with published pharmacogenomic practice guidance by the Clinical Pharmacogenetics Implementation Consortium or other professional organizations,(1-3) where strong US Food and Drug Administration guidance has been issued in drug labels,(4) or where peer-reviewed literature strongly suggests that assessment of pharmacogenomic variants may enhance patient care.(5-8)

For additional information regarding pharmacogenomic genes and their associated medications, see Pharmacogenomic Associations 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 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.

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.

For additional information, see the following tests:
-1A2Q / Cytochrome P450 *1A2* Genotype, Varies
-2C9QT / Cytochrome P450 *2C9* Genotype, Varies
-2C19R / Cytochrome P450 *2C19* Genotype, Varies
-2D6Q / Cytochrome P450 *2D6* Comprehensive Cascade, Varies
-3A4Q / Cytochrome P450 *3A4* Genotype, Varies
-3A5Q / Cytochrome P450 *3A5* Genotype, Varies
-CARBR / Carbamazepine Hypersensitivity Pharmacogenomics, Varies
-COMTQ / Catechol-O-Methyltransferase (*COMT*) Genotype, Varies

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. Hicks JK, Sangkuhl K, Swen JJ, et al. Clinical Pharmacogenetics Implementation Consortium guideline (CPIC) 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
4. U.S National Library of Medicine: DailyMed. National Institutes of Health. Accessed November 14, 2024. Available at https://dailymed.nlm.nih.gov/dailymed/index.cfm
5. Bradley P, Shiekh M, Mehra V, et al. Improved efficacy with targeted pharmacogenetic-guided treatment of patients with depression and anxiety: A randomized clinical trial demonstrating clinical utility. J Psychiatr Res. 2018;96:100-107
6. Brennan FX, Gardner KR, Lombard J, et al. A naturalistic study of the effectiveness of pharmacogenetic testing to guide treatment in psychiatric patients with mood and anxiety disorders. Prim Care Companion CNS Disord. 2015;17(2). doi:10.4088/PCC.14m01717
7. Perez V, Salavert A, Espadaler J, et al. Efficacy of prospective pharmacogenetic testing in the treatment of major

depressive disorder: results of a randomized, double-blind clinical trial. BMC Psychiatry. 2017;17(1):250
8. Reynolds GP, McGowan OO, Dalton CF. Pharmacogenomics in psychiatry: the relevance of receptor and transporter polymorphisms. Br J Clin Pharmacol. 2014;77(4):654-672
9. Crews KR, Monte AA, Huddart R, et al. Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6, OPRM1, and COMT Genotypes and Select Opioid Therapy. Clin Pharmacol Ther. 2021;110(4):888-896. doi:10.1002/cpt.2149

Performance

Method Description

Genomic DNA is extracted from the sample.

Genotyping for the following genes is performed using a polymerase chain reaction (PCR)-based 5'-nuclease assay. Fluorescently labeled detection probes anneal to the target DNA: *ANKK1*, *ADRA2, CHRNA3, COMT, CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, DRD2, EPHX1, GRIK4, HTR2A, HTR2C, MTHFR, OPRM1, SCN1A,* and *UGT2B15.* 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)

Amplification for the *HLA-B*15:02* and *HLA-A*31:01* alleles and an internal control gene is performed by real-time PCR 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)

SLC6A4 is performed utilizing PCR amplification of the region surrounding the polymorphism followed by size separation of the products.(Lesch KP, Bengel D, Heils A, et al. Association of anxiety-related traits with a polymorphism in the serotonin transporter gene regulatory region. Science. 1996;274[5292]:1527-1531)

CYP2D6 Copy Number Assay:
This assay utilizes a duplex real-time PCR, which includes 1 copy number probe and a reference assay per reaction. Each copy number probe detects the genomic sequence of interest and the reference assay detects a sequence that is known to be present in 2 copies in a diploid genome. Relative quantitation is used to determine the relative copy number of the target of interest in a genomic DNA (gDNA) sample normalized to10 ng/mcL for each probe. Each probe is normalized to the known copy number of the reference sequence, and compared to a calibrator sample with known copies of the target sequence included with each run.(Package insert: Taqman Copy Number Assays. Applied Biosystems; Revision D, 02/2019)

2D6 Sequencing Assays (Tier 2, as needed):
The *CYP2D6* allele of interest is amplified by PCR. The PCR product is then purified and sequenced in both directions using fluorescent dye-terminator chemistry. Sequencing products are separated on an automated sequencer and trace files analyzed for variations in the exons and intron/exon boundaries of all 9 exons using mutation detection software and visual inspection.(Unpublished Mayo method)

PDF Report
Supplemental RE

Day(s) Performed
Tuesday

Report Available
3 to 14 days

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

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
81418

Prior Auhtorization
Insurance preauthorization is available for this testing; forms are available.
Patient financial assistance may be available to those who qualify. Patients who receive a bill from Mayo Clinic Laboratories will receive information on eligibility and how to apply.

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PSYQP	Psychotropic PGx Panel, V	94753-1

Result ID	Test Result Name	Result LOINC® Value
610209	ADRA2A rs1800544 Genotype	94401-7
610210	ANKK1 rs1800497 Genotype	94402-5
610211	CHRNA3 rs1051730 Genotype	94403-3

610212	COMT rs4680 Genotype	74511-7
610213	CYP1A2 Genotype	72884-0
610214	CYP1A2 Phenotype	94254-0
610215	CYP2B6 Genotype	72882-4
610216	CYP2B6 Phenotype	79720-9
610573	CYP2B6 Activity Score	104666-3
610217	CYP2C19 Genotype	57132-3
610218	CYP2C19 Phenotype	79714-2
610574	CYP2C19 Activity Score	104667-1
610219	CYP2C9 Genotype	46724-1
610220	CYP2C9 Phenotype	79716-7
610575	CYP2C9 Activity Score	104668-9
610221	CYP2D6 Genotype	40425-1
610222	CYP2D6 Phenotype	79715-9
610576	CYP2D6 Activity Score	104669-7
610227	DRD2 rs1799978 Genotype	94411-6
610228	EPHX1 rs2234922 Genotype	94412-4
610229	GRIK4 rs1954787 Genotype	94413-2
610230	HLA-A*31:01 Genotype	79712-6
610231	HLA-B*15:02 Genotype	57979-7
610232	HTR2A rs7997012 Genotype	93190-7
610233	HTR2C rs3813929 Genotype	93191-5
610234	HTR2C rs1414334 Genotype	93192-3
610235	MTHFR Genotype	94414-0
610236	OPRM1 rs1799971 Genotype	94415-7
610237	SCN1A rs3812718 Genotype	94416-5
610238	SLC6A4 5HTTLPR Genotype	94417-3
610239	UGT2B15 rs1902023 Genotype	94418-1
610240	Interpretation	69047-9
610241	Additional Information	48767-8
610242	Method	85069-3
610243	Disclaimer	62364-5
610244	Reviewed by	18771-6
610223	CYP3A4 Genotype	81139-8
610224	CYP3A4 Phenotype	81145-5
610225	CYP3A5 Genotype	81140-6
610226	CYP3A5 Phenotype	79717-5