Test Definition: PSYGP
Psychotropic PGx Panel

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 (SSRIs)

Evaluating patients with treatment-resistant depression

Predicting response time to improvement with SSRIs

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), UGT2B15.

CYP2D6 testing is done in 2 tiers when needed. Tier 1 uses a 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) and rarer alleles such as *11, *12, *14A, *14B, and *15. 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; see Special Instructions.

Reflex Tests

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</table>
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Testing Algorithm
If a specimen requires follow-up for CYP2D6, then reflex testing will be performed as appropriate at an additional charge.

See CYP2D6 Comprehensive Cascade Testing Algorithm in Special Instructions.

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

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

Qualitative Allele-Specific Real-Time Polymerase Chain Reaction (PCR)

PCR Followed by Sizing Analysis

NY State Available
Yes

Specimen

Specimen Type
Varies

Necessary Information
Psychotropic Pharmacogenomics Gene Panel Prior Authorization Ordering Instructions is required. See Special Instructions.

Specimen Required
Prior Authorization is available for this test. Submit the required form with the specimen.

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.
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**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

**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 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) 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 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 a Therapeutics Test Request (T831) with the specimen.


**Specimen Minimum Volume**

Blood: 1 mL  
Saliva: 1 swab

**Reject Due To**

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.
Clinical and 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
- **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, where strong FDA guidance has been issued in drug labels, or where peer-reviewed literature strongly suggests that assessment of pharmacogenomic variants may enhance patient care.

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

**Cautions**

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 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:

1A2V / Cytochrome P450 1A2 Genotype, Varies
2C9GV / Cytochrome P450 2C9 Genotype, Varies
2C19V / Cytochrome P450 2C19 Genotype, Varies
2D6CV / Cytochrome P450 2D6 (CYP2D6) Comprehensive Cascade, Varies
3A4V / Cytochrome P450 3A4 Genotype, Varies

3A5V / CYP3A5 Genotype, Varies

CARPB / Carbamazepine Hypersensitivity Pharmacogenomics, Blood

COMTV / Catechol-O-Methyltransferase (COMT) Genotype, Varies

HTR2V / Serotonin Receptor Genotype (HTR2A and HTR2C), Varies

HTT / Serotonin Transporter Genotype, Blood

Clinical Reference


Performance

Method Description
Genomic DNA is extracted from the sample.

Genotyping for the following genes is performed using a 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. (Instruction manual: TaqMan SNP Genotyping Assay, Applied Biosystems Revision A.0 January 2014)

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)


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 to 10 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 Revision B, Applied Biosystems, Carlsbad, CA)

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

No

Day(s) and Time(s) Test Performed

Monday through Thursday; 8 a.m.

Analytic Time

3 days (not reported Saturday or Sunday)

Maximum Laboratory Time

14 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.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
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- 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
81479
81226
81225
81227
81230
81231
81291
81381 x 2

LOINC® Information

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### Test Definition: PSYGP

#### Psychotropic PGx Panel

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### Prior Authorization

**Insurance preauthorization is available for this testing; forms are available in Special Instructions.**

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.