**Cytochrome P450 2D6 Genotyping**

**TESTS** | **RESULT** | **FLAG** | **UNITS** | **REFERENCE INTERVAL** | **LAB**
---|---|---|---|---|---
Cytochrome P450 2D6 Genotyping |  |  |  |  |  
2D6 Genotype: | *1/*1 |  |  |  |  
2D6 Metabolic Activity: | Normal |  |  |  |  

**Description of Predicted Metabolic Activity Types:**

Ultrarapid metabolizers (UM) have elevated enzyme activity. For drugs that are active when administered, ultrarapid metabolizers may not reach therapeutic levels due to rapid clearance. For drugs that require activation, ultrarapid metabolizers may be at increased risk for adverse reactions due to higher than expected concentrations of active metabolite.

Normal (extensive) metabolizers (EM) are anticipated to have normal enzyme activity. For CYP2D6, there is a range of enzyme activity within this category. The distinction between normal and intermediate metabolizer differs between publications and may differ depending on the drug in question.

Intermediate to normal metabolizers (IM-EM) are anticipated to have a range of reduced to normal enzyme activity.

Intermediate metabolizers (IM) have reduced enzyme activity, and may experience some, or none, of the consequences similar to poor metabolizers.

Poor metabolizers (PM) have significantly reduced or absent enzyme activity. Drugs are metabolized slowly or not at all. For drugs that are active when administered, poor metabolizers may have increased concentrations of active drug with potential for serious side effects. For drugs that require activation, poor metabolizers may have lower than expected concentrations of active metabolite and limited effect of the therapy.
The metabolism of drugs is also influenced by ethnicity, diet, and other drugs. All factors should be considered prior to initiating new therapy. This testing does not rule out the possibility of variant alleles in other drug metabolism pathways.

Cytochrome P450 CYP2D6 is involved in the metabolism of up to 25-30% of all clinically used drugs. Variants in the CYP2D6 gene can result in ultrarapid (UM), normal (EM), intermediate to normal (IM-EM), intermediate (IM) and poor metabolizer (PM) phenotypes. Certain alleles of P450 genes may enhance drug metabolism while others may slow it. In some cases, this may adversely affect treatment outcomes. This should be considered prior to initiating or modifying treatment or supplementing with additional drugs.

Common drugs metabolized by 2D6 include, but are not limited to:

**BETA-BLOCKERS:** Carvedilol, S-metoprolol, Profafenone, Propranolol, Timolol

**CARDIOREACTIVE DRUGS:** Encainide, Flecainide, Lidocaine, Mexiletine, Perhexilene

**ANTIDEPRESSANTS:** Amitryptyline, Clomipramine, Desipramine, Doxepin (E-isomers), Fluoxetine, Fluvoxamine, Imipramine, Maprotiline, Nortriptyline, Paroxetine, Sertraline, Venlafaxine

**ANTIPSYCHOTICS:** Aripiprazole, Haloperidol, Perphenazine, Risperidone, Thioridazine, Zuclopenthixol

**OTHERS:** Codeine, Ondansetron, Phenformin, Tamoxifen, Tramadol

This is not intended to be a comprehensive list of drugs metabolized by CYP2D6. Healthcare providers are encouraged to consult the current literature, the package insert of any medication considered, or contact the drug manufacturer for specific drug information.

### CYP2D6 Information:

Cytochrome P450 enzymes (including 2D6 and 2C19) are involved in the hepatic metabolism of a large percentage of clinically relevant drugs. Of all drugs, 25-30% are metabolized by CYP2D6.

**Methodology:**
DNA analysis of the Cytochrome P450 2D6 gene (OMIM 124030) is performed using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the variants below. Primer extension then generates a biotin-labeled product to
permit flow-sorted detection of both normal and variant sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur.

Alleles Detected:
*1,*2,*3,*4,*5,*6,*7,*8,*9,*10,*11,*15,*29,*35,*41, and gene duplications.
Variant *5 is a gene deletion. Copy number of duplicated alleles is not determined. Duplications are often functional (whole gene) but may be nonfunctional (partial gene). It is not always possible to determine which allele is duplicated.

*1 represents detection of the normal sequence for the variant sites tested. This assay does not detect other variants in the CYP2D6 gene that may affect metabolic activity.

Buccal cells for CYP2D6: This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

References:

Director Review:
Annette K. Taylor, M.S., Ph.D., FACMG
Toni R. Prezant, Ph.D.
Samuel H. Pepkowitz, M.D., FAAP
Joseph B. Kearney, Ph.D., FACMG
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For inquiries, the physician may contact **Branch: 800-222-7566 Lab: 800-282-7300**
## General Comments & Additional Information

### Clinical Info:
ABNORMAL REPORT

### Ordered Items
Cytochrome P450 2D6 Genotyping

### TESTS

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<tr>
<td>2D6 Genotype:</td>
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<td>01</td>
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### Interpretation:

Description of Predicted Metabolic Activity Types:

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