# Antidepressants

## Use as Directed
- desvenlafaxine (Pristiq®)
- levomilnacipran (Fetzima®)
- vilazodone (Viibryd®)

## Moderate Gene-drug Interaction
- trazodone (Desyrel®) 1
- venlafaxine (Effexor®) 1
- fluoxetine (Prozac®) 1.4
- bupropion (Wellbutrin®) 1.6
- citalopram (Celexa®) 3.4
- escitalopram (Lexapro®) 3.4

## Significant Gene-drug Interaction
- selegiline (Emsam®) 2
- mirtazapine (Remeron®) 1.6
- sertraline (Zoloft®) 2.4
- amitriptyline (Elavil®) 1.6,8
- clomipramine (Anafranil®) 1.6,8
- desipramine (Norpramin®) 1.6,8
- doxepin (Sinequan®) 1.6,8
- duloxetine (Cymbalta®) 1.6,8
- imipramine (Tofranil®) 1.6,8
- nortriptyline (Pamelor®) 1.6,8
- vortioxetine (Trintellix®) 1.6,8
- fluvoxamine (Luvox®) 1.4,6,8
- paroxetine (Paxil®) 1.4,6,8

## Clinical Considerations
1. Serum level may be too high, lower doses may be required.
2. Serum level may be too low, higher doses may be required.
3. Difficult to predict dose adjustments due to conflicting variations in metabolism.
4. Genotype may impact drug mechanism of action and result in moderately reduced efficacy.
6. Use of this drug may increase risk of side effects.
8. FDA label identifies a potential gene-drug interaction for this medication.

All psychotropic medications require clinical monitoring. Medications should not be changed based solely on the test results. The results of this test are intended to supplement other clinical information considered by a healthcare provider within the context of a comprehensive medical evaluation.

This report is not intended to imply that the drugs listed are approved for the same indications or that they are comparable in safety or efficacy. The brand name is shown for illustrative purposes only; other brand names may be available. The prescribing physician should review the prescribing information for the drug(s) being considered and make treatment decisions based on the patient’s individual needs, the characteristics of the drug prescribed, and the risk and safety information provided in the drug’s labeling. Propranolol and oxcarbazepine prescribed for neuropsychiatric disorders might be considered off-label. Please consult their respective FDA drug labels for specific guidelines regarding their use.

The GeneSight Psychotropic test interpretations are based on a thorough review of published peer-reviewed literature, internal research, and FDA label information when applicable. The clinical validity and utility of the GeneSight Psychotropic test have been evaluated for patients with major depressive disorder who failed at least one psychotropic medication in multiple clinical studies.
### Anxiolytics and Hypnotics

#### Use as Directed
- alprazolam (Xanax®)
- buspirone (BuSpar®)
- clonazepam (Klonopin®)
- eszopiclone (Lunesta®)
- lemborexant (Dayvigo®)
- suvorexant (Belsomra®)
- temazepam (Restonil®)
- zolpidem (Ambien®)

#### Moderate Gene-drug Interaction
- chlordiazepoxide (Librium®) 1
- clorazepate (Tranxene®) 1
- lorazepam (Ativan®) 1
- oxazepam (Serax®) 1

#### Significant Gene-drug Interaction
- diazepam (Valium®) 1,6
- propranolol (Inderal®) 1,6,8

### Clinical Considerations
1. Serum level may be too high, lower doses may be required.
2. Use of this drug may increase risk of side effects.
3. FDA label identifies a potential gene-drug interaction for this medication.

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All psychotropic medications require clinical monitoring. Medications should not be changed based solely on the test results. The results of this test are intended to supplement other clinical information considered by a healthcare provider within the context of a comprehensive medical evaluation.

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## Antipsychotics

### Use as Directed
- asenapine (Sapris®)
- cariprazine (Vraylar®)
- lumateperone (Caplyta®)
- lurasidone (Lutada®)
- paliperidone (Invega®)
- thiothixene (Navane®)
- ziprasidone (Geodon®)

### Moderate Gene-drug Interaction
- fluphenazine (Prolixin®) 1
- olanzapine (Zyprexa®) 1
- quetiapine (Seroquel®) 1
- clozapine (Clozaril®) 1,8
- haloperidol (Haldol®) 1,8

### Significant Gene-drug Interaction
- chlorpromazine (Thorazine®) 1,6
- aripiprazole (Abilify®) 1,6,8
- brexpiprazole (Rexulti®) 1,6,8
- iloperidone (Fanapt®) 1,6,8
- perphenazine (Trilafon®) 1,6,8
- risperidone (Risperdal®) 1,6,8
- thioridazine (Mellaril®) 1,6,9

## Clinical Considerations
1. Serum level may be too high, lower doses may be required.
6. Use of this drug may increase risk of side effects.
8. FDA label identifies a potential gene-drug interaction for this medication.
9. Per FDA label, this medication is contraindicated for this genotype.

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Mood Stabilizers

**Use as Directed**
- lamotrigine (Lamictal®)
- oxcarbazepine (Trileptal®)
- valproic acid/divalproex (Depakote®)

**Moderate Gene-drug Interaction**

**Significant Gene-drug Interaction**
- carbamazepine (Tegretol®) 6,8

**No Proven Genetic Markers**
- gabapentin (Neurontin®) 10
- lithium (Eskalith®) 10
- topiramate (Topamax®) 10

**Clinical Considerations**

6: Use of this drug may increase risk of side effects.
8: FDA label identifies a potential gene-drug interaction for this medication.
10: While this medication does not have clinically proven genetic markers that allow it to be categorized, it may be an effective choice based on other clinical factors.
## Stimulants

<table>
<thead>
<tr>
<th>Use as Directed</th>
<th>Moderate Gene-drug Interaction</th>
<th>Significant Gene-drug Interaction</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>dexameth phenidate (Focalin®) 4</td>
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<td></td>
<td>methylphenidate (Ritalin®, Concerta®) 4</td>
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</tbody>
</table>

### No Proven Genetic Markers

- **amphetamine salts** (Adderall®) 10
- **dextroamphetamine** (Dexedrine®) 10
- **lisdexamfetamine** (Vyvanse®) 10

## Non-stimulants

<table>
<thead>
<tr>
<th>Use as Directed</th>
<th>Moderate Gene-drug Interaction</th>
<th>Significant Gene-drug Interaction</th>
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<tbody>
<tr>
<td></td>
<td>guanfacine (Intuniv®)</td>
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<td></td>
<td>viloxazine (Qelbree®) 1</td>
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<td>atomoxetine (Strattera®) 1, 5, 8</td>
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</tbody>
</table>

### No Proven Genetic Markers

- **clonidine** (Kapvay®) 10

## Clinical Considerations

1. Serum level may be too high, lower doses may be required.
4. Genotype may impact drug mechanism of action and result in moderately reduced efficacy.
5. CYP2D6 genotype indicates that this patient may experience increased frequency of side effects but also greater symptom improvement in those who find the treatment tolerable.
8. FDA label identifies a potential gene-drug interaction for this medication.
10. While this medication does not have clinically proven genetic markers that allow it to be categorized, it may be an effective choice based on other clinical factors.

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**Patient Genotypes and Phenotypes**

### Pharmacodynamic Genes

**ADRA2A**
- **C/C**
  - Moderately Reduced Response
  - This patient is homozygous for the C allele of the -1291G>C polymorphism in the adrenergic alpha-2A receptor gene. This genotype suggests a moderately reduced response to certain ADHD medications.

**HLA-A*3101**
- **T/T**
  - Higher Risk
  - This patient is homozygous for the T allele of the rs1061235 A>T polymorphism indicating presence of the HLA-A*3101 allele or certain HLA-A*33 alleles. This genotype suggests a higher risk of serious hypersensitivity reactions, including Stevens-Johnson syndrome (SJS), toxic epidermal necrosis (TEN), maculopapular eruptions, and Drug Reaction with Eosinophilia and Systemic Symptoms when taking certain mood stabilizers.

**HLA-B*1502**
- Not Present
  - Normal Risk
  - This patient does not carry the HLA-B*1502 allele or a closely related *15 allele. Absence of HLA-B*1502 and the closely related *15 alleles suggests normal risk of serious dermatologic reactions including toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS) when taking certain mood stabilizers.

**HTR2A**
- **G/G**
  - Increased Sensitivity
  - This individual is homozygous variant for the G allele of the -1438G>A polymorphism for the Serotonin Receptor Type 2A. They carry two copies of the G allele. This genotype has been associated with an increased risk of adverse drug reactions with certain selective serotonin reuptake inhibitors.

**SLC6A4**
- **S/S**
  - Reduced Response
  - This patient is homozygous for the short promoter polymorphism of the serotonin transporter gene. The short promoter allele is reported to decrease expression of the serotonin transporter compared to the homozygous long promoter allele. The patient may have a moderately decreased likelihood of response to selective serotonin reuptake inhibitors due to the presence of the short form of the gene.
Patient Genotypes and Phenotypes

Pharmacokinetic Genes

**CES1A1**
Extensive (Normal) Metabolizer
GLY/GLY
CES1A1 - GLY allele enzyme activity: Normal
CES1A1 - GLY allele enzyme activity: Normal
This genotype is most consistent with the extensive (normal) metabolizer phenotype. This patient is expected to have normal enzyme activity.

**CYP1A2**
Extensive (Normal) Metabolizer
*1/*1
This genotype is most consistent with the extensive (normal) metabolizer phenotype.

**CYP2B6**
Extensive (Normal) Metabolizer
*1/*1
CYP2B6*1 allele enzyme activity: Normal
CYP2B6*1 allele enzyme activity: Normal
This genotype is most consistent with the extensive (normal) metabolizer phenotype.

**CYP2C19**
Ultrarapid Metabolizer
*17/*17
CYP2C19*17 allele enzyme activity: Increased
CYP2C19*17 allele enzyme activity: Increased
This genotype is most consistent with the ultrarapid metabolizer phenotype. This patient may have increased enzyme activity as compared to individuals with the normal phenotype.

**CYP2C9**
Intermediate Metabolizer
*1/*2
CYP2C9*1 allele enzyme activity: Normal
CYP2C9*2 allele enzyme activity: Reduced
This genotype is most consistent with the intermediate metabolizer phenotype. This patient may have reduced enzyme activity as compared to individuals with the normal phenotype.

**CYP2D6**
Poor Metabolizer
*10/*10
CYP2D6*10 allele enzyme activity: Reduced
CYP2D6*10 allele enzyme activity: Reduced
This genotype is most consistent with the poor metabolizer phenotype. This patient may have reduced enzyme activity as compared to individuals with the normal phenotype.

**CYP3A4**
Extensive (Normal) Metabolizer
*1/*1
CYP3A4*1 allele enzyme activity: Normal
CYP3A4*1 allele enzyme activity: Normal
This genotype is most consistent with the extensive (normal) metabolizer phenotype.

**UGT1A4**
Extensive (Normal) Metabolizer
*1/*1
UGT1A4*1 allele enzyme activity: Normal
UGT1A4*1 allele enzyme activity: Normal
This genotype is most consistent with the extensive (normal) metabolizer phenotype. The patient is expected to have normal enzyme activity.

**UGT2B15**
Intermediate Metabolizer
*2/*2
UGT2B15*2 allele enzyme activity: Reduced
UGT2B15*2 allele enzyme activity: Reduced
This genotype is most consistent with the intermediate metabolizer phenotype. This patient may have reduced enzyme activity as compared to individuals with the normal phenotype.
Additional Genotypes
Not Included in Categorizing Medications

Genotypes reported in this section have not been shown to be reliable markers of medication outcomes

COMT
VAL/MET

This patient is heterozygous for the Val158Met polymorphism in the catechol-o-methyltransferase gene. They have one copy of the Met allele and one copy of the Val allele.

A summary of the studies that have assessed the potential effect of COMT genotype on response to psychotropic medications can be found here: https://genesight.com/comt.

To categorize medications on this pharmacogenomic test, a gene must have a variant that has been shown to have a significant impact on medication outcomes, as demonstrated in multiple well-designed studies. Studies assessing the gene in this section have not shown that it is a reliable marker of medication outcomes. Therefore, this gene does not currently meet the criteria for categorizing medications. The patient’s genotype is provided for informational purposes only.
## Gene-drug Interactions

### Use as Directed

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>CES1A1</th>
<th>CYP1A2</th>
<th>CYP2B6</th>
<th>CYP2C19</th>
<th>CYP2C9</th>
<th>CYP2D6</th>
<th>CYP3A4</th>
<th>UGT1A4</th>
<th>UGT2B15</th>
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<td>desvenlafaxine (Pristiq&lt;sup&gt;®&lt;/sup&gt;)</td>
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<td>levomilnacipran (Fetzima&lt;sup&gt;®&lt;/sup&gt;)</td>
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<td>vilazodone (Vibryd&lt;sup&gt;®&lt;/sup&gt;)</td>
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<td>Anxiolytics and hypnotics</td>
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<td>alprazolam (Xanax&lt;sup&gt;®&lt;/sup&gt;)</td>
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<td>buspirone (BuSpar&lt;sup&gt;®&lt;/sup&gt;)</td>
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<td>lemborexant (Dayvigo&lt;sup&gt;®&lt;/sup&gt;)</td>
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<td>suvorexant (Belsomra&lt;sup&gt;®&lt;/sup&gt;)</td>
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<td>zolpidem (Ambien&lt;sup&gt;®&lt;/sup&gt;)</td>
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<td>asenapine (Saphris&lt;sup&gt;®&lt;/sup&gt;)</td>
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<td>cariprazine (Vrylar&lt;sup&gt;®&lt;/sup&gt;)</td>
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<td>lumateperone (Caplyta&lt;sup&gt;®&lt;/sup&gt;)</td>
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<td>paliperidone (Invega&lt;sup&gt;®&lt;/sup&gt;)</td>
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<td>oxcarbazepine (Trileptal&lt;sup&gt;®&lt;/sup&gt;)</td>
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<td>valproic acid/divalproex (Depakote&lt;sup&gt;®&lt;/sup&gt;)</td>
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<td>guanfacine (Intuniv&lt;sup&gt;®&lt;/sup&gt;)</td>
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</tbody>
</table>

- ★ Variation was found in patient genotype that may impact medication metabolism.
- ○ This gene is associated with medication metabolism, but the predicted patient phenotype is normal.
- * This gene-drug interaction is recognized by the FDA or CPIC.
## Gene-drug Interactions

### Moderate Gene-drug Interaction

<table>
<thead>
<tr>
<th></th>
<th>CES1A1 Normal</th>
<th>CYP1A2 Normal</th>
<th>CYP2B6 Normal</th>
<th>CYP2C19 Ultrarapid</th>
<th>CYP2C9 Intermediate</th>
<th>CYP2D6 Poor</th>
<th>CYP3A4 Normal</th>
<th>UGT1A4 Normal</th>
<th>UGT2B15 Intermediate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antidepressants</strong></td>
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<td>bupropion (Wellbutrin®)</td>
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<td>venlafaxine (Effexor®)</td>
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### Significant Gene-drug Interaction

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* Variation was found in patient genotype that may impact medication metabolism.

○ This gene is associated with medication metabolism, but the predicted patient phenotype is normal.

* This gene-drug interaction is recognized by the FDA or CPIC.
## Gene-drug Interactions

### Significant Gene-drug Interaction (Continued)

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### No Proven Genetic Markers

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● Variation was found in patient genotype that may impact medication metabolism.

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○ This gene is associated with medication metabolism, but the predicted patient phenotype is normal.
GeneSight Psychotropic
Pharmacogenomic Test

Test Information

The buccal swab sample was collected on 1/9/2022 and received in the laboratory on 1/10/2022. Genomic DNA is isolated and the relevant genomic regions are amplified by polymerase chain reaction (PCR). Analysis of CYP2D6 deletion and duplication, HLA-B*1502 and SLC6A4 is completed by electrophoresis of PCR products. Analysis of CES1A1, CYP1A2, CYP2B6, CYP2C19, CYP2C9, CYP2D6, CYP3A4, ADRA2A, COMT, HTR2A, rs1061235 (indicating presence of the HLA-A*3101 allele or certain HLA-A*33 alleles), UGT1A4 and UGT2B15 is completed by using iPLEX MassARRAY® technology (Agena Bioscience). The following genetic variants may be detected in the assay: CES1A1 Gly143Glu (NM_001025194.1:c.428G>A); CYP1A2 -3860G>A (NG_008431.1:g.2833G>A), -2467T>delT (NM_000761.4:c.-1635delT), -739T>G (NM_000761.4:c.-10+103T>G), -729C>T (NM_000761.4:c.-10+113C>T), -1636A>(NM_000761.4:c.-9-154A), 125C>G (NM_000761.4:c.125C>G), 558C>A (NM_000761.4:c.558C>A), 2116G>A (NM_000761.4:c.1042G>A), 2473G>A (NM_000761.4:c.1130G>A), 2499A>T (NM_000761.4:c.1156A>T), 3497G>A (NM_000761.4:c.1217G>A), 3533G>A (NM_000761.4:c.1253+1G>A), 5909C>T (NM_000761.4:c.1291C>T), 5166G>A (NM_000761.4:c.1637G>A), 5347C>T (NM_000761.4:c.1548C>T); CYP2B6 *4 (NM_000767.4:c.785A>G), *6 (NM_000767.4:c.516G>T, c.785A>G), *8 (NM_000767.4:c.516G>T, c.681G>A), *9 (NM_000767.4:c.681G>A), 2p (NM_000769.2:c.819+2T>A), *8 (NM_000769.2:c.3587T>C), *7 (NM_000769.2:c.806C>T); CYP2C9 *2 (NM_000771.3:c.430C>T), *3 (NM_000771.3:c.1075A>C), *4 (NM_000771.3:c.1076T>C), *5 (NM_000771.3:c.1080C>G), *6 (NM_000771.3:c.817delA); CYP2D6 *2 (NM_000106.5:c.886C>T, c.1457G>C), *2A (NM_000106.5:c.1584C>G, c.886C>T, c.1457G>C), *3 (NM_000106.5:c.775delA), *4 (NM_000106.5:c.506-1G>A), 100C>T, c.1457G>C), *5 (CYP2D6 Deletion), *6 (NM_000106.5:c.454delT), *7 (NM_000106.5:c.971C>A), *8 (NM_000106.5:c.505G>T, c.886C>T, c.1457G>C), *9 (NM_000106.5:c.841_843delAAAG), *10 (NM_000106.5:c.100C>T, c.1457G>C), *11 (NM_000106.5:c.161-1G>C), *12 (NM_000106.5:c.124G>A, c.886C>T, c.1457G>C), *13 (NM_000106.5:c.505G>A, c.886C>T, c.1457G>C), *14 (NM_000106.5:c.505G>A, c.886C>T, c.1457G>C), *15 (NM_000106.6;c.137dup), *17 (NM_000106.5:c.320C>T, c.886C>T, c.1457G>C), *19 (NM_000106.5:c.935_939delA), *20 (NM_000106.5:c.1291G>C); gene duplication; CYP3A4 *13 (NM_017480.5:c.1427T>G), *15A (NM_017480.5:c.485G>A), *22 (NM_017480.5:c.522-191C>T); ADRA2A -1291G>C (NM_000681.3:c.1252G>C); COMT Val158Met (NM_000731.2:c.322G>A); HLA-B*1502; rs1061235 (NM_0021167.2:c.968A>G); SLC6A4 L, S; UGT1A4 *3 (NM_007120.2:c.142G>T); UGT2B15 *2 (NM_001076.3:c.253G>T). The following rare genetic variants have not been observed by the Assurex Health Inc. Laboratory: CYP2A12 125C>G, 558C>A; CYP2C19*7. *1 is the reference allele and is reported by default if the other tested alleles are not detected.

This test was developed and its performance characteristics determined by Assurex Health. It has not been cleared or approved by the U.S. Food and Drug Administration. These interpretations are based upon data available in scientific literature and prescribing information for the relevant drugs. Interpretations are, in some instances, based on data regarding the pharmacokinetic, pharmacodynamic and pharmacogenomics properties of a drug derived from non-clinical studies (e.g. in vitro studies). Findings from studies performed in a non-clinical setting or clinical studies involving healthy subjects are not necessarily indicative of clinical performance in a particular patient. References used to inform medication categorizations can be found here: https://genesight.com/references.

This report was reviewed and verified on 00/00/0000 by:

Nina E. King, PhD, HCLD(ABB), CC(NRCC), CQ(NYSDOH)

Disclaimer of Liability

The information contained in this report is provided as a service and does not constitute medical advice. At the time of report generation this information is believed to be current and is based upon published research; however, research data evolves and amendments to the prescribing information of the drugs listed will change over time. While this report is believed to be accurate and complete as of the date issued, THE DATA IS PROVIDED “AS IS”, WITHOUT WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION, THE IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE. As medical advice must be tailored to the specific circumstances of each case, the treating healthcare provider has ultimate responsibility for all treatment decisions made with regard to a patient including any made on the basis of a patient’s genotype.

GeneSight Psychotropic is covered by U.S. Patent No. 9,111,028

Genetic testing was completed by a CLIA and CAP accredited laboratory in the United States located at: 6000 Mason-Montgomery Road Mason, OH 45040 Laboratory Director: Nina King, PhD

Customer Service

Please contact 855.891.9415 or medinfo@genesight.com for assistance with report interpretation. For all other inquiries please contact 866.757.9204 or support@genesight.com.

GeneSight Psychotropic Test Version: 4.1