GeneSight® Psychotropic
COMBINATORIAL PHARMACOGENOMIC TEST

genesight

Patient, Sample
DOB: 7/22/1984
Order Number: 219
Report Date: 8/5/2020
Clinician: Sample Clinician
Reference: 1456CIP

Questions about report interpretation?
Contact our Medical Information team
855.891.9415
medinfo@assurexhealth.com

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®)	3,8
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 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.
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 and the characteristics of the drug prescribed. Propranolol and oxcarbazepine might be considered off-label when being used for neuropsychiatric disorders. Please consult their respective FDA drug labels for specific guidelines regarding their use.

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ANXIOLYTICS AND HYPNOTICS

USE AS DIRECTED	MODERATE GENE-DRUG INTERACTION		SIGNIFICANT GENE-DRUG INTERACTION	
alprazolam (Xanax®)	**chlordiazepoxide** (Librium®)	1	**diazepam** (Valium®)	1,6
buspirone (BuSpar®)	**clorazepate** (Tranxene®)	1	**propranolol** (Inderal®)	1,6,8
clonazepam (Klonopin®)	**lorazepam** (Ativan®)	1		
eszopiclone (Lunesta®)	**oxazepam** (Serax®)	1		
temazepam (Restoril®)				
zolpidem (Ambien®)				

CLINICAL CONSIDERATIONS

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ANTIPSYCHOTICS

USE AS DIRECTED	MODERATE GENE-DRUG INTERACTION		SIGNIFICANT GENE-DRUG INTERACTION	
asenapine (Saphris®)	**fluphenazine** (Prolixin®)	1	**chlorpromazine** (Thorazine®)	1,6
cariprazine (Vraylar®)	**olanzapine** (Zyprexa®)	1	**aripiprazole** (Abilify®)	1,6,8
lumateperone (Caplyta®)	**quetiapine** (Seroquel®)	1	**brexpiprazole** (Rexulti®)	1,6,8
lurasidone (Latuda®)	**clozapine** (Clozaril®)	1,8	**iloperidone** (Fanapt®)	1,6,8
paliperidone (Invega®)	**haloperidol** (Haldol®)	1,8	**perphenazine** (Trilafon®)	1,6,8
thiothixene (Navane®)			**risperidone** (Risperdal®)	1,6,8
ziprasidone (Geodon®)			**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	MODERATE GENE-DRUG INTERACTION	SIGNIFICANT GENE-DRUG INTERACTION
lamotrigine (Lamictal®)		**carbamazepine** (Tegretol®) 6,8
oxcarbazepine (Trileptal®)		
valproic acid/divalproex (Depakote®)		

NO PROVEN GENETIC MARKERS			
gabapentin (Neurontin®)	10	**topiramate** (Topamax®)	10
lithium (Eskalith®)	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: This medication does not have clinically proven genetic markers that allow it to be categorized.

All psychotropic medications require clinical monitoring.
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 and the characteristics of the drug prescribed. Propranolol and oxcarbazepine might be considered off-label when being used for neuropsychiatric disorders. Please consult their respective FDA drug labels for specific guidelines regarding their use.

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PATIENT GENOTYPES AND PHENOTYPES

PHARMACODYNAMIC GENES

PD

SLC6A4 — **Reduced Response**
S/S

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 decreased likelihood of response to selective serotonin reuptake inhibitors due to the presence of the short form of the gene and may benefit from medications with an alternative mechanism of action.

HTR2A — **Increased Sensitivity**
G/G

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.

HLA-B*1502 — **Lower Risk**
Not Present

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 lower risk of serious dermatologic reactions including toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS) when taking certain mood stabilizers.

HLA-A*3101 — **Higher Risk**
T/T

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 necrolysis (TEN), maculopapular eruptions, and Drug Reaction with Eosinophilia and Systemic Symptoms when taking certain mood stabilizers.

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PATIENT GENOTYPES AND PHENOTYPES

PHARMACOKINETIC GENES (PK)

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.

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GENE-DRUG INTERACTIONS

USE AS DIRECTED

	CYP1A2 Normal	CYP2B6 Normal	CYP2C19 Ultrarapid	CYP2C9 Intermediate	CYP2D6 Poor	CYP3A4 Normal	UGT1A4 Normal	UGT2B15 Intermediate
ANTIDEPRESSANTS								
desvenlafaxine (Pristiq®)			●			○		
levomilnacipran (Fetzima®)			●		●	○		
vilazodone (Viibryd®)			●		●	○		
ANXIOLYTICS AND HYPNOTICS								
alprazolam (Xanax®)						○		
buspirone (BuSpar®)					●	○		
clonazepam (Klonopin®)						○		
eszopiclone (Lunesta®)				●		○		
temazepam (Restoril®)		○		●		○		●
zolpidem (Ambien®)	○		●	●	●	○		
ANTIPSYCHOTICS								
asenapine (Saphris®)	○				●	○	○	
cariprazine (Vraylar®)					●	○		
lumateperone (Caplyta®)						○		
lurasidone (Latuda®)						○		
paliperidone (Invega®)					●	○		
thiothixene (Navane®)	○							
ziprasidone (Geodon®)	○					○		
MOOD STABILIZERS								
lamotrigine (Lamictal®)							○	
oxcarbazepine (Trileptal®)								
valproic acid/divalproex (Depakote®)		○		●			○	

MODERATE GENE-DRUG INTERACTION

	CYP1A2 Normal	CYP2B6 Normal	CYP2C19 Ultrarapid	CYP2C9 Intermediate	CYP2D6 Poor	CYP3A4 Normal	UGT1A4 Normal	UGT2B15 Intermediate
ANTIDEPRESSANTS								
bupropion (Wellbutrin®)		○			●	○		
citalopram (Celexa®)			● *		●	○		
escitalopram (Lexapro®)			● *		●	○		
fluoxetine (Prozac®)			●	●	●	○		
trazodone (Desyrel®)	○				●	○		
venlafaxine (Effexor®)			●	●	● *	○		
ANXIOLYTICS AND HYPNOTICS								
chlordiazepoxide (Librium®)	○					○		●
clorazepate (Tranxene®)	○					○		●
lorazepam (Ativan®)								●
oxazepam (Serax®)								●

● - Variation was found in patient genotype that may impact medication response.
○ - This gene is associated with medication response, but patient genotype is normal.
* - This gene-drug interaction is recognized by the FDA or CPIC.

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GENE-DRUG INTERACTIONS

MODERATE GENE-DRUG INTERACTION

	CYP1A2 Normal	CYP2B6 Normal	CYP2C19 Ultrarapid	CYP2C9 Intermediate	CYP2D6 Poor	CYP3A4 Normal	UGT1A4 Normal	UGT2B15 Intermediate
ANTIPSYCHOTICS								
clozapine (Clozaril®)	○				● *	○	○	
fluphenazine (Prolixin®)	○		●	●	●	○		
haloperidol (Haldol®)	○				●	○	○	
olanzapine (Zyprexa®)	○				●	○	○	
quetiapine (Seroquel®)					●	○		

SIGNIFICANT GENE-DRUG INTERACTION

	CYP1A2 Normal	CYP2B6 Normal	CYP2C19 Ultrarapid	CYP2C9 Intermediate	CYP2D6 Poor	CYP3A4 Normal	UGT1A4 Normal	UGT2B15 Intermediate
ANTIDEPRESSANTS								
amitriptyline (Elavil®)	○		● *	●	● *	○	○	
clomipramine (Anafranil®)	○		● *		● *	○		
desipramine (Norpramin®)					● *			
doxepin (Sinequan®)	○		● *	●	● *	○	○	
duloxetine (Cymbalta®)	○				●			
fluvoxamine (Luvox®)	○				● *			
imipramine (Tofranil®)	○		● *		● *	○		
mirtazapine (Remeron®)	○			●	● *	○		
nortriptyline (Pamelor®)					● *			
paroxetine (Paxil®)					● *	○		
selegiline (Emsam®)	○	○	●			○		
sertraline (Zoloft®)		○	● *		*	○		
vortioxetine (Trintellix®)		○	●	●	● *	○		
ANXIOLYTICS AND HYPNOTICS								
diazepam (Valium®)	○	○	●	●		○		●
propranolol (Inderal®)	○				●			
ANTIPSYCHOTICS								
aripiprazole (Abilify®)					● *	○		
brexpiprazole (Rexulti®)					● *	○		
chlorpromazine (Thorazine®)	○				●	○		
iloperidone (Fanapt®)					● *	○		
perphenazine (Trilafon®)	○		●		● *	○		
risperidone (Risperdal®)					● *	○		
thioridazine (Mellaril®)	○		●		● *	○		
MOOD STABILIZERS								
carbamazepine (Tegretol®)		○				○		

● - Variation was found in patient genotype that may impact medication response.
○ - This gene is associated with medication response, but patient genotype is normal.
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TEST INFORMATION

The buccal swab sample was collected on 8/3/2020 and received in the laboratory on 8/4/2020. Genomic DNA was isolated and the relevant genomic regions were amplified by polymerase chain reaction (PCR). Analysis of CYP2D6 deletion and duplication, HLA-B*1502 and SLC6A4 was completed by electrophoresis of PCR products. Analysis of CYP1A2, CYP2B6, CYP2C19, CYP2C9, CYP2D6, CYP3A4, HTR2A, rs1061235 (indicating presence of the HLA-A*3101 allele or certain HLA-A*33 alleles), UGT1A4 and UGT2B15 was completed by using iPLEX MassARRAY® technology (Agena Bioscience). The following genetic variants may be detected in the assay: CYP1A2 -3860G>A (NG_008431.1:g.28338G>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), -163C>A (NM_000761.4:c.-9-154C>A), 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), 5090C>T (NM_000761.4:c.1291C>T), 5166G>A (NM_000761.4:c.1367G>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), *9 (NM_000767.4:c.516G>T); CYP2C19, *2 (NM_000769.2:c.681G>A), *3 (NM_000769.2:c.636G>A), *4 (NM_000769.2:c.1A>G), *5 (NM_000769.2:c.1297C>T),*6 (NM_000769.2:c.395G>A), *7 (NM_000769.2:c.819+2T>A), *8 (NM_000769.2:c.358T>C), *17 (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; c.100C>T; c.1457G>C), *5 (CYP2D6 Deletion), *6 (NM_000106.5:c.454delT), *7 (NM_000106.5:c.971A>C), *8 (NM_000106.5:c.505G>T; c.886C>T; c.1457G>C), *9 (NM_000106.5:c.841_843delAAG), *10 (NM_000106.5:c.100C>T; c.1457G>C), *11, *12 (NM_000106.5:c.124G>A; c.886C>T; c.1457G>C), *14 (NM_000106.5:c.505G>A; c.886C>T; c.1457G>C), *15, *17 (NM_000106.5:c.320C>T; c.886C>T; c.1457G>C), *41 (NM_000106.5:c.985+39G>A; c.886C>T; c.1457G>C), gene duplication; CYP3A4, *13 (NM_017460.5:c.1247C>T), *15A (NM_017460.5:c.485G>A), *22 (NM_017460.5:c.522-191C>T); HLA-B*1502; rs1061235 (NM_002116.7:c.*66A>T); HTR2A -1438G>A (NM_000621.4:c.-998G>A); SLC6A4 L, S; UGT1A4, *3 (NM_007120.2:c.142T>G); UGT2B15, *2 (NM_001076.3:c.253G>T). The following rare genetic variants have not been observed by the Assurex Health, Inc. laboratory: CYP1A2 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 8/5/2020 by:

Nina King

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@assurexhealth.com for assistance with report interpretation. For all other inquires please contact 866.757.9204 or support@assurexhealth.com.

GeneSight Psychotropic Test Version: 3.0.3