

Patient, Sample

DOB: 7/22/1984
Order Number: 9904
Report Date: 6/22/2016
Clinician: Sample Clinician
Reference: 1456CIP

Questions? Call 855.891.9415 or email medinfo@assurexhealth.com

ANTIDEPRESSANTS

USE AS DIRECTED	MODERATE GENE-DRUG INTERACTION	SIGNIFICANT GENE-DRUG INTERACTION
<p>desvenlafaxine (Pristiq®) levomilnacipran (Fetzima®) vilazodone (Viibryd®)</p>	<p>trazodone (DesyreI®) 1 venlafaxine (Effexor®) 1 selegiline (Emsam®) 2 fluoxetine (Prozac®) 1,4 citalopram (Celexa®) 3,4 escitalopram (Lexapro®) 3,4 sertraline (Zoloft®) 3,4</p>	<p>bupropion (Wellbutrin®) 1,6 mirtazapine (Remeron®) 1,6 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</p>

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 might be considered off-label when being used for neuropsychiatric disorders. Please consult the FDA drug label for specific guidelines regarding its use.

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ANXIOLYTICS AND HYPNOTICS

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

CLINICAL CONSIDERATIONS

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ANTIPSYCHOTICS

USE AS DIRECTED
asenapine (Saphris®)
lurasidone (Latuda®)
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

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- 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®)

MODERATE GENE-DRUG INTERACTION

valproic acid/divalproex (Depakote®) 1

SIGNIFICANT GENE-DRUG INTERACTION

oxcarbazepine (Trileptal®) 6,8
carbamazepine (Tegretol®) 6,8,9

NO PROVEN GENETIC MARKERS

gabapentin (Neurontin®)	10	topiramate (Topamax®)	10
lithium (Eskalith®)	10		

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.
- 10: This medication does not have clinically proven genetic markers that allow it to be categorized.

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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.

HLA-B*1502 **Higher Risk**
Present

This patient carries either the HLA-B*1502 allele or a closely related *15 allele. Presence of HLA-B*1502 or some of the closely related *15 alleles suggests higher risk of serious dermatologic reactions including toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS) when taking certain mood stabilizers.

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-A*3101 **Higher Risk**
A/T

This patient is heterozygous for the A allele and 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 **Intermediate Metabolizer**
*1/*6

CYP2B6*1 allele enzyme activity: Normal
CYP2B6*6 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.

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.

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.

CYP2D6 **Poor Metabolizer**
*4/*4 (Duplication)

CYP2D6*4 allele enzyme activity: None
CYP2D6*4 allele enzyme activity: None

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.

A duplication of the gene CYP2D6 has been detected in this patient. While current genotyping techniques allow for the detection of this duplication, in the case of heterozygosity, such techniques do not allow for the identification of the allele that has been duplicated. This duplication, depending on the allele duplicated, can result in increased expression of CYP2D6.

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	CYP2B6	CYP2C19	CYP2C9	CYP3A4	CYP2D6	UGT1A4	UGT2B15
ANTIDEPRESSANTS								
desvenlafaxine (Pristiq®)			●		○			
levomilnacipran (Fetzima®)			●		○	●		
vilazodone (Viibryd®)			●		○	●		
ANXIOLYTICS AND HYPNOTICS								
alprazolam (Xanax®)					○			
bupirone (BuSpar®)					○	●		
clonazepam (Klonopin®)					○			
eszopiclone (Lunesta®)				●	○			
temazepam (Restoril®)		●		●	○			●
zolpidem (Ambien®)	○		●	●	○	●		
ANTIPSYCHOTICS								
asenapine (Saphris®)	○				○	●	○	
lurasidone (Latuda®)					○			
paliperidone (Invega®)					○	●		
thiothixene (Navane®)	○							
ziprasidone (Geodon®)	○				○			
MOOD STABILIZERS								
lamotrigine (Lamictal®)							○	

MODERATE GENE-DRUG INTERACTION								
	CYP1A2	CYP2B6	CYP2C19	CYP2C9	CYP3A4	CYP2D6	UGT1A4	UGT2B15
ANTIDEPRESSANTS								
citalopram (Celexa®)			●		○	●		
escitalopram (Lexapro®)			●		○	●		
fluoxetine (Prozac®)			●	●	○	●		
selegiline (Emsam®)	○	●	●		○			
sertraline (Zoloft®)		●	●	●	○	●		
trazodone (Desyrel®)	○				○	●		
venlafaxine (Effexor®)			●	●	○	●		
ANXIOLYTICS AND HYPNOTICS								
chlordiazepoxide (Librium®)	○				○			●
clorazepate (Tranxene®)	○				○			●
diazepam (Valium®)	○	●	●	●	○			●
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.

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GENE-DRUG INTERACTIONS

MODERATE GENE-DRUG INTERACTION								
	CYP1A2	CYP2B6	CYP2C19	CYP2C9	CYP3A4	CYP2D6	UGT1A4	UGT2B15
ANTIPSYCHOTICS								
clozapine (Clozaril®)	○				○	●	○	
fluphenazine (Prolixin®)	○		●	●	○	●		
haloperidol (Haldol®)	○				○	●	○	
olanzapine (Zyprexa®)	○				○	●	○	
quetiapine (Seroquel®)					○	●		
MOOD STABILIZERS								
valproic acid/divalproex (Depakote®)		●		●			○	

SIGNIFICANT GENE-DRUG INTERACTION								
	CYP1A2	CYP2B6	CYP2C19	CYP2C9	CYP3A4	CYP2D6	UGT1A4	UGT2B15
ANTIDEPRESSANTS								
amitriptyline (Elavil®)	○		●	●	○	●	○	
bupropion (Wellbutrin®)		●			○	●		
clomipramine (Anafranil®)	○		●		○	●		
desipramine (Norpramin®)						●		
doxepin (Sinequan®)	○		●	●	○	●	○	
duloxetine (Cymbalta®)	○					●		
fluvoxamine (Luvox®)	○					●		
imipramine (Tofranil®)	○		●		○	●		
mirtazapine (Remeron®)	○			●	○	●		
nortriptyline (Pamelor®)						●		
paroxetine (Paxil®)					○	●		
vortioxetine (Trintellix®)		●	●	●	○	●		
ANXIOLYTICS AND HYPNOTICS								
propranolol (Inderal®)	○					●		
ANTIPSYCHOTICS								
aripiprazole (Abilify®)					○	●		
brexpiprazole (Rexulti®)					○	●		
chlorpromazine (Thorazine®)	○				○	●		
iloperidone (Fanapt®)					○	●		
perphenazine (Trilafon®)	○		●		○	●		
risperidone (Risperdal®)					○	●		
thioridazine (Mellaril®)	○		●		○	●		
MOOD STABILIZERS								
carbamazepine (Tegretol®)		●			○			
oxcarbazepine (Trileptal®)								

● - 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 6/20/2016 and received in the laboratory on 6/21/2016. 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 *1, *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 *1, *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 *1, *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 *1, *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 *1, *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 *1, *3 (NM_007120.2:c.142T>G); UGT2B15 *1, *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.

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.

This report was reviewed and verified on 6/22/2016 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

Customer Service

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

GeneSight Psychotropic Test Version: 3.0