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## Genomind Pharmacogenetic Report

Patient:	<b>Nora Syke</b>	Sample ID:	<b>7524640209</b>
Patient DOB:	<b>12/25/1985</b>	Accession ID:	<b>250750</b>
Ordering Clinician:	<b>Genomind Clinician</b>	Sample Collection Date:	<b>4/22/2023</b>
Sample Type:	<b>Buccal</b>	Sample Received Date:	<b>4/24/2023</b>
Assay Ordered:	<b>Genomind PGx (v3.2)</b>	Report Date:	<b>4/24/2023 2:02 PM</b>

### Electronically Signed By

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### Literature Information Reviewed By

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The Genomind PGx Report is intended to provide genetic information to healthcare professionals which may aid in the prescribing of medications for individuals with mental illness and associated comorbidities.\*

### Personalized Consultation Available for Clinicians

A complimentary consultation, performed by our expert psychopharmacologists, is included with all Genomind PGx Reports. Consultations can be scheduled directly from the [Genomind Precision Health Platform](#).

### CONTACT INFORMATION

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\*Disclaimer: This report is designed to be adjunctive to a complete patient assessment, including but not limited to proper diagnosis, clinical history, assessment of concomitant co-morbidities and medications, family history, and other factors. Prescribers should be familiar with the approved indications, warnings, precautions, and other sections of the drug manufacturer's prescribing information, as well as relevant clinical practice guidelines. Prescribers should not rely solely on this report in making prescribing decisions. The understanding of the relationship between specific genes and pharmacokinetics or pharmacodynamics changes periodically, and this report will not be updated to reflect new findings. For more information on gene-drug associations, please reference PharmGKB, CPIC, PharmVar or the FDA Table of Pharmacogenetic Associations or Pharmacogenomic Biomarkers.



## Gene Results Overview

Pharmacokinetic Genes (Drug Metabolism / Drug Absorption)	Gene	Genotype	Phenotype	Impact
	ABCB1	A/A	NF	Normal exposure is expected
	ABCB1 C3435T	G/G	NF	Normal exposure is expected
	ABCG2	T/T	PF	<b>Increased exposure to certain medications</b>
	CYP1A2	*1B/H7	NM	Normal metabolism is expected
	CYP2B6	*1/*1	NM	Normal metabolism is expected
	CYP2C19	*2/*3	PM	<b>Risk of increased (↑) drug levels</b>
	CYP2C9	*1/*3	IM	<b>Risk of increased (↑) drug levels</b>
	CYP2D6	*1/*1	NM	Normal metabolism is expected
	CYP3A4/5	*1/*1, *3/*3	NA	Normal metabolism is expected
	SLCO1B1	*1/*1	NF	Normal exposure is expected
	UGT1A4	*1a/*3b	UM	<b>Risk of decreased (↓) drug levels</b>
	UGT2B15	*1/*2	NM	Normal metabolism is expected

Pharmacodynamic Genes (Drug Targets / Mechanisms)	Antidepressant Response		
	Gene	Result	Result
	BDNF	Val/Met	<b>More pronounced effect to exercise; Possible higher odds of response to SNRIs</b>
	HTR2A	G/G	No known significant clinical impact
	MTHFR	C677T: C/T A1298C: A/C	<b>Reduced MTHFR activity and methylfolate production</b>
	SLC6A4	L(A)/S	<b>Higher odds of gastrointestinal side effects with SSRIs in individuals of European descent</b>
	Attention-deficit/hyperactivity disorder Response		
	Gene	Result	Result
	ADRA2A	C/C	<b>Lower odds of response to methylphenidate for inattentive symptoms of ADHD</b>
	COMT	Val/Met	No known significant clinical impact
	Antipsychotic Response and Tolerability		
	Gene	Result	Result
	DRD2	C/C	No known significant clinical impact
HTR2C	C/C	No known significant clinical impact	
MC4R	A/A	<b>Higher risk of weight gain with certain 2nd generation antipsychotics</b>	
Other			
Gene	Result	Result	
ANK3	C/C	No known significant clinical impact	
CACNA1C	G/G	No known significant clinical impact	
GRIK1	A/A	No known significant clinical impact	
HLA-A *31:01	Positive	<b>Higher risk of skin reactions with carbamazepine</b>	
HLA-B *15:02	Negative	No known significant clinical impact	
OPRM1	A/A	No known significant clinical impact	

## Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations	Drug Level	Pharmacokinetics	
<b>ANTIDEPRESSANTS</b>					
SSRIs	<b>Citalopram</b> (Celexa®)	Monitor for gastrointestinal side effects in individuals of European descent (SLC6A4)			
		<a href="#">CPIC</a> Consider alternative or 50% reduction in maintenance dose.		<u>2C19</u> , ABCB1	
	<a href="#">DPWG</a> Up to 65 years old: Max dose is 20 mg/day. 65 years or older: Max dose is 10 mg/day.				
	<b>Escitalopram</b> (Lexapro®)	Monitor for gastrointestinal side effects in individuals of European descent (SLC6A4)			
		<a href="#">CPIC</a> Consider alternative or 50% reduction in maintenance dose.		<u>2C19</u> , ABCB1	
	<a href="#">DPWG</a> Up to 65 years old: Max dose is 10 mg/day. 65 years and older: Max dose is 5 mg/day.				
<b>Fluoxetine</b> (Prozac®)	Monitor for gastrointestinal side effects in individuals of European descent (SLC6A4)			2D6, <u>2C9</u>	
<b>Fluvoxamine</b> (Luvox®)	Monitor for gastrointestinal side effects in individuals of European descent (SLC6A4)			2D6, 1A2, ABCB1	
<b>Paroxetine</b> (Paxil®)	Monitor for gastrointestinal side effects in individuals of European descent (SLC6A4)			2D6, ABCB1	
<b>Sertraline</b> (Zoloft®)	Monitor for gastrointestinal side effects in individuals of European descent (SLC6A4)				
	<a href="#">CPIC</a> Consider a lower starting dose, slower titration, and 50% lower maintenance dose or select alternative.		<u>2C19</u> , 2B6, ABCB1		
<a href="#">DPWG</a> Max dose: 75 mg/day					
SNRIs	<b>Desvenlafaxine</b> (Pristiq®)				
	<b>Duloxetine</b> (Cymbalta®)			1A2, 2D6	
	<b>Levomilnacipran</b> (Fetzima®)			3A4/5	
	<b>Venlafaxine</b> (Effexor®)			2D6, <u>2C19</u> , 3A4/5, ABCB1	



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Reduced Drug Exposure with 1A2 Inducers



Do Not Initiate



See Gene-Drug Association footnotes for more information



## Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations	Drug Level	Pharmacokinetics
<b>ANTIDEPRESSANTS</b>				
Other	<b>Bupropion</b> (Wellbutrin®)			2B6
	<b>Dextromethorphan/Bupropion</b> (Auvelity®)			2B6, 2D6, 3A4/5
	<b>Esketamine</b> (Spravato®)			2B6
	<b>Mirtazapine</b> (Remeron®)			2D6, 3A4/5, 1A2
	<b>Nefazodone</b>			3A4/5
	<b>Trazodone</b> (Desyrel®, Olepro®)			3A4/5, 2D6
	<b>Vilazodone</b> (Viibryd®)			3A4/5
	<b>Vortioxetine</b> (Trintellix®)			2D6, 3A4/5
TCAs	<b>Amitriptyline</b> (Elavil®)	<a href="#">CPIC</a>	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	2D6, <b>2C19</b> , ABCB1
	<b>Clomipramine</b> (Anafranil®)	<a href="#">CPIC</a>	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	2D6, 1A2, <b>2C19</b>
	<b>Desipramine</b> (Norpramin®)			2D6
	<b>Doxepin</b> (Sinequan®)	<a href="#">CPIC</a>	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	2D6, <b>2C19</b>
	<b>Imipramine</b> (Tofranil®)	<a href="#">CPIC</a>	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	2D6, <b>2C19</b>
	<b>Nortriptyline</b> (Pamelor®)			2D6, ABCB1
	<b>Trimipramine</b> (Surmontil®)	<a href="#">CPIC</a>	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	2D6, <b>2C19</b> , ABCB1
MAOIs	<b>Phenelzine</b> (Nardil®)			
	<b>Selegiline</b> (Eldepryl®, Emsam®)			2B6
	<b>Tranlycypromine</b> (Parnate®)			



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See Gene-Drug Association footnotes for more information



## Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations	Drug Level	Pharmacokinetics
<b>MOOD STABILIZERS/ANTICONVULSANTS</b>				
	<b>Carbamazepine</b> (Equetro®, Tegretol®)	Do not initiate therapy: Higher risk of drug induced skin reactions (HLA-A *31:01) <a href="#">CPIC</a>		3A4/5
	<b>Gabapentin</b> (Neurontin®)			
	<b>Lamotrigine</b> (Lamictal®)		[1]	<u>UGT1A4</u> , <u>ABCG2</u>
	<b>Lithium</b> (Lithobid®, Eskalith®)			
	<b>Oxcarbazepine</b> (Trileptal®, Oxtellar®)			
	<b>Pregabalin</b> (Lyrica®)			
	<b>Topiramate</b> (Topamax®)			ABCB1
	<b>Valproate</b> (Depakote®, Depakene®)			<u>2C9</u>



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See Gene-Drug Association footnotes for more information

## Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations	Drug Level	Pharmacokinetics
<b>ANTIPSYCHOTICS</b>				
2nd Generation Antipsychotics	<b>Aripiprazole</b> (Abilify®)	Higher risk of weight gain (MC4R)		2D6, 3A4/5, ABCB1
	<b>Asenapine</b> (Saphris®)			1A2, <b>UGT1A4</b>
	<b>Brexiprazole</b> (Rexulti®)	Higher risk of weight gain (MC4R)		2D6, 3A4/5
	<b>Cariprazine</b> (Vraylar®)			3A4/5
	<b>Clozapine</b> (Clozaril®)	Higher risk of weight gain (MC4R)		1A2, 2D6, ABCB1
	<b>Iloperidone</b> (Fanapt®)	Higher risk of weight gain (MC4R)		2D6, 3A4/5
	<b>Lumateperone</b> (Caplyta®)			3A4/5
	<b>Lurasidone</b> (Latuda®)			3A4/5
	<b>Olanzapine</b> (Zyprexa®)	Higher risk of weight gain (MC4R)		1A2, ABCB1
	<b>Olanzapine/Samidorphan</b> (Lybalvi®)	Higher risk of weight gain (MC4R)		1A2, 3A4/5, ABCB1
	<b>Paliperidone</b> (Invega®)	Higher risk of weight gain (MC4R)		
	<b>Pimavanserin</b> (Nuplazid®)			3A4/5
	<b>Quetiapine</b> (Seroquel®)	Higher risk of weight gain (MC4R)		3A4/5
	<b>Risperidone</b> (Risperdal®)	Higher risk of weight gain (MC4R)		2D6, 3A4/5, ABCB1
<b>Ziprasidone</b> (Geodon®)			3A4/5	



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See Gene-Drug Association footnotes for more information

## Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations	Drug Level	Pharmacokinetics
<b>ANTIPSYCHOTICS</b>				
1st Generation Antipsychotics	<b>Chlorpromazine</b> (Thorazine®)			2D6
	<b>Fluphenazine</b> (Prolixin®)			2D6
	<b>Haloperidol</b> (Haldol®)			2D6, 3A4/5
	<b>Loxapine</b> (Adasuve®, Loxitane®)			
	<b>Perphenazine</b> (Trilafon®)			1A2, 2D6
	<b>Pimozide</b> (Orap®)			2D6, 3A4/5
	<b>Thioridazine</b> (Mellaril®)			2D6
	<b>Thiothixene</b> (Navane®)			1A2
	<b>Trifluoperazine</b> (Stelazine®)			↓ 1A2, <b>UGT1A4</b>
<b>ANXIOLYTICS</b>				
	<b>Alprazolam</b> (Xanax®)			3A4/5
	<b>Buspirone</b> (Buspar®)			3A4/5
	<b>Chlordiazepoxide</b> (Librium®)			3A4/5, UGT2B15
	<b>Clonazepam</b> (Klonopin®)			3A4/5
	<b>Diazepam</b> (Valium®)		↑	<b>2C19</b> , 3A4/5, UGT2B15
	<b>Hydroxyzine</b> (Vistaril®)			
	<b>Lorazepam</b> (Ativan®)			UGT2B15
	<b>Oxazepam</b> (Serax®)			UGT2B15
	<b>Temazepam</b> (Restoril®)			UGT2B15



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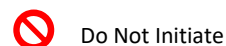
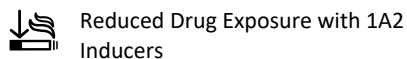
Do Not Initiate



See Gene-Drug Association footnotes for more information

## Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations	Drug Level	Pharmacokinetics
<b>ADHD MEDICATIONS</b>				
Dopaminergic Stimulants	<b>Amphetamine-Dextroamphetamine</b> (Adderall®, Evekeo®)			2D6
	<b>Dexmethylphenidate</b> (Focalin®)	Moderately lower odds of response (ADRA2A)		
	<b>Dextroamphetamine</b> (Dexedrine®)			2D6
	<b>Lisdexamfetamine</b> (Vyvanse®)			2D6
	<b>Methylphenidate</b> (Ritalin®, Concerta®)	Moderately lower odds of response (ADRA2A)		
Other	<b>Atomoxetine</b> (Strattera®)			2D6
	<b>Clonidine</b> (Kapvay®)			
	<b>Guanfacine</b> (Intuniv®)			3A4/5
	<b>Viloxazine</b> (Qelbree®)			2D6
<b>SUPPLEMENTS</b>				
	<b>L-methylfolate</b> (Deplin®)	May benefit from methylfolate supplementation (MTHFR)		
<b>SLEEP MODULATORS</b>				
	<b>Armodafinil</b> (Nuvigil®)			3A4/5, ABCB1
	<b>Daridorexant</b> (Quviviq®)			3A4/5
	<b>Eszopiclone</b> (Lunesta®)			3A4/5
	<b>Lemborexant</b> (Dayvigo®)			3A4/5
	<b>Modafinil</b> (Provigil®)			3A4/5, ABCB1
	<b>Ramelteon</b> (Rozerem®)		M	1A2, <b>2C19</b> , 3A4/5
	<b>Suvorexant</b> (Belsomra®)			3A4/5
	<b>Zaleplon</b> (Sonata®)			3A4/5
	<b>Zolpidem</b> (Ambien®)			1A2, 3A4/5



See Gene-Drug Association footnotes for more information



## Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations	Drug Level	Pharmacokinetics
<b>PAIN</b>				
Non-opioid analgesics	<b>Acetaminophen</b> (Tylenol®)			UGT2B15
	<b>Celecoxib</b> (Celebrex®)	<a href="#">CPIC</a> Initiate with lowest standard starting dose and titrate with caution.		<b>2C9</b>
	<b>Diclofenac</b> (Voltaren®, Cataflam®)			<b>2C9</b>
	<b>Flurbiprofen</b> (Ansaid®)	<a href="#">CPIC</a> Initiate with lowest standard starting dose and titrate with caution.		<b>2C9</b>
	<b>Ibuprofen</b> (Advil®, Motrin®)	<a href="#">CPIC</a> Initiate with lowest standard starting dose and titrate with caution.		<b>2C9</b>
	<b>Ketorolac</b> (Toradol®)			
	<b>Meloxicam</b> (Mobic®)	<a href="#">CPIC</a> Initiate 50% of the lowest standard starting dose and titrate dose to clinical effect or 50% of max dose.		<b>2C9</b>
	<b>Naproxen</b> (Aleve®, Naprosyn®)			<b>2C9</b>
	<b>Piroxicam</b> (Feldene®)	<a href="#">CPIC</a> Choose alternative not significantly impacted by CYP2C9.		<b>2C9</b>
Opioid analgesics	<b>Alfentanil</b> (Alfenta®)			3A4/5
	<b>Codeine</b>			2D6, ABCB1
	<b>Fentanyl</b> (Duragesic®)			3A4/5, ABCB1
	<b>Hydrocodone</b>			2D6, 3A4/5
	<b>Hydromorphone</b> (Dilaudid®)			
	<b>Methadone</b> (Methadose®)			2B6, 3A4/5
	<b>Morphine</b> (MS Contin®)			ABCB1
	<b>Oxycodone</b> (Oxycontin®)			2D6, 3A4/5, ABCB1
	<b>Oxymorphone</b>			
	<b>Tapentadol</b> (Nucynta®)			
<b>Tramadol</b> (Ultram®)			2D6, 3A4/5, ABCB1	



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Do Not Initiate



See Gene-Drug Association footnotes for more information

## Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations	Drug Level	Pharmacokinetics
<b>MISCELLANEOUS</b>				
	<b>Buprenorphine</b> (Butrans®)			3A4/5
	<b>Buprenorphine/Naloxone</b> (Suboxone®)			3A4/5
	<b>Cannabidiol (CBD)</b> (Epidiolex®)			3A4/5, <b>2C19</b>
	<b>Deutetrabenazine</b> (Austedo®)			2D6
	<b>Dextromethorphan/Quinidine</b> (Nuedexta®)			2D6, 3A4/5, 2B6
	<b>Naltrexone</b> (Vivitrol®)			
	<b>Phenytoin/Fosphenytoin</b> (Dilantin®, Cerebyx®)	<a href="#">CPIC</a> Use standard starting or loading dose. For subsequent doses, use around 25% less than standard maintenance dose.		<b>2C19, 2C9</b> , ABCB1
	<b>Valbenazine</b> (Ingrezza®)			3A4/5, 2D6
<b>STATINS</b>				
	<b>Atorvastatin</b> (Lipitor®)			3A4/5, SLCO1B1, ABCB1, <b>ABCG2</b>
	<b>Fluvastatin</b> (Lescol®)	<a href="#">CPIC</a> Use ≤ 40 mg/day as a starting dose and adjust doses based on disease-specific guidelines.		<b>2C9</b> , SLCO1B1
	<b>Lovastatin</b> (Mevacor®)			3A4/5, SLCO1B1
	<b>Pitavastatin</b> (Livalo®)			SLCO1B1
	<b>Pravastatin</b> (Pravachol®)			SLCO1B1
	<b>Rosuvastatin</b> (Crestor®)	<a href="#">CPIC</a> Use ≤ 20 mg as a starting dose and adjust doses based on disease-specific and specific population guidelines.		<b>ABCG2</b> , SLCO1B1
	<b>Simvastatin</b> (Zocor®)			3A4/5, SLCO1B1



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See Gene-Drug Association footnotes for more information

### Gene-Drug Association Footnotes

[1] Multiple competing CYP450 genotypes may impact this drug. Refer to Genomind's Precision Medicine Software for a more complete evaluation of this gene-drug interaction

Risk for change in drug exposure:



Higher Risk



Moderate Risk



Lower Risk

References for the drug interaction summary are available upon request

## Pharmacokinetic Gene Variations

Gene Results	THERAPEUTIC IMPLICATIONS	GUIDE	CLINICAL IMPACT
<b>CYP2C9 IM</b>  *1/*3 [Intermediate activity]	<b>Intermediate metabolizer: Risk of elevated serum levels and drug interactions, or decreased production of active metabolites</b> <ul style="list-style-type: none"> <li>A dose adjustment or alternate therapy may be considered</li> </ul>		May have altered blood levels with medications metabolized by CYP2C9
<b>CYP2C19 PM</b>  *2/*3 [Low activity]	<b>Poor metabolizer: Risk of elevated serum levels and drug interactions, or decreased production of active metabolites</b> <ul style="list-style-type: none"> <li>A dose adjustment or alternate therapy may be considered</li> </ul>		May have altered blood levels with medications metabolized by CYP2C19
<b>UGT1A4 UM</b>  *1a/*3b [High activity]	<b>Ultrarapid metabolizer: Risk of decreased serum levels, and possible adverse events associated with increased active metabolites</b> <ul style="list-style-type: none"> <li>A dose adjustment or alternate therapy may be considered</li> </ul>		May have altered blood levels with medications metabolized by UGT1A4
<b>ABCG2 PF</b>  T/T [Poor function]	ATP Binding Cassette G2 (ABCG2) codes for an efflux pump that normally regulates intestinal absorption and biliary excretion of some drugs. Variability in this efflux pump can impact the serum levels of several medications. <ul style="list-style-type: none"> <li>This genotype is associated with <b>poor function of ABCG2 and increased serum levels of some medications</b></li> <li>A dose adjustment or alternate therapy may be considered</li> </ul>		Increased exposure to medications affected by ABCG2
<b>CYP1A2 NM</b>  *1B/H7 [Normal activity]	Variations in the CYP1A2 liver enzyme can result in altered drug metabolism and unexpected drug serum levels <ul style="list-style-type: none"> <li><b>This genotype confers normal activity</b></li> <li>Each of the CYP1A2 variants detected in this patient sample is well characterized, although this specific combination of alleles has not been formally named. We have adopted a modified (*)star allele naming system that identifies all the variants detected for this gene. (Adapted from Soyama et al 2005. PMID: 15770072; Gunes et al 2009. PMID: 19450128)</li> </ul>		Normal metabolism is expected (other factors may influence metabolism)
<b>CYP2B6 NM</b>  *1/*1 [Normal activity]	Variations in the CYP2B6 liver enzyme can result in altered drug metabolism and unexpected drug serum levels <ul style="list-style-type: none"> <li><b>This genotype confers normal activity</b></li> </ul>		Normal metabolism is expected (other factors may influence metabolism)
<b>CYP2D6 NM</b>  *1/*1 [Normal activity]	Variations in the CYP2D6 liver enzyme can result in altered drug metabolism and unexpected drug serum levels <ul style="list-style-type: none"> <li><b>This genotype confers normal activity</b></li> </ul>		Normal metabolism is expected (other factors may influence metabolism)
<b>CYP3A4 *1/*1</b> <b>CYP3A5 *3/*3</b>  [Normal activity]	Variations in the CYP3A4/5 liver enzymes can result in altered drug metabolism and unexpected drug serum levels <ul style="list-style-type: none"> <li>3A5 non-expresser</li> <li>CYP3A activity is determined by the sum activity of the CYP3A family of genes; in adults the most influential are 3A4 and 3A5</li> <li><b>This genotype confers normal activity</b></li> </ul>		Normal metabolism is expected (other factors may influence metabolism)



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## Pharmacokinetic Gene Variations

Gene Results	THERAPEUTIC IMPLICATIONS	GUIDE	CLINICAL IMPACT
<b>UGT2B15</b> <b>NM</b>  *1/*2 [Normal activity]	<i>Variations in the UGT2B15 liver enzyme can result in altered drug metabolism and unexpected drug serum levels</i> <ul style="list-style-type: none"> <li><b>This genotype confers normal activity</b></li> </ul>		Normal metabolism is expected (other factors may influence metabolism)
<b>ABCB1</b> <b>(rs2032583)</b>  A/A [Normal function]	<i>ATP Binding Cassette B1 (ABCB1) encodes for an efflux pump that reduces the intestinal absorption and blood-brain barrier penetration of certain drugs</i> <ul style="list-style-type: none"> <li><b>This genotype is associated with normal function of ABCB1 and normal drug absorption</b></li> </ul>		Normal function is expected (other factors may influence drug exposure)
<b>ABCB1</b> <b>(rs1045642)</b>  G/G [Normal function]	<i>ATP Binding Cassette B1 (ABCB1) encodes for an efflux pump that reduces the intestinal absorption and blood-brain barrier penetration of certain drugs</i> <ul style="list-style-type: none"> <li><b>This genotype is associated with normal function of ABCB1 and normal drug absorption</b></li> </ul>		Normal function is expected (other factors may influence drug exposure)
<b>SLCO1B1</b> <b>NF</b>  *1/*1 [Normal function]	<i>Solute Carrier Organic Anion Transporter 1B1 (SLCO1B1) codes for a transporter that normally facilitates hepatic uptake of several drugs. Variability in the function of this transporter can alter systemic concentrations of statins and other medications.</i> <ul style="list-style-type: none"> <li>This genotype is associated with <b>normal function of SLCO1B1 and normal hepatic uptake of statins</b> and other medications</li> </ul>		Normal function is expected (other factors may influence drug exposure)



Alert/Caution



PGx Guided Options

## Pharmacodynamic Gene Variations

Gene Results	THERAPEUTIC IMPLICATIONS	GUIDE	CLINICAL IMPACT
<b>BDNF</b> Val/Met [Altered BDNF secretion]	<p><i>Brain-derived Neurotrophic Factor (BDNF) is a protein involved in neuronal development and neural plasticity</i></p> <ul style="list-style-type: none"> <li>Studies have shown that <b>Met carriers of European descent</b> with depression may have a <b>poorer response to SSRIs and improved response to duloxetine, venlafaxine, and clomipramine</b>; further studies need to confirm these findings</li> <li>Exercise has been linked to improvements in cognition and stress response, with Met carriers showing a more pronounced response</li> </ul>		Consider <b>increased levels of physical activity/exercise</b> if clinically appropriate  <b>SNRIs may be considered</b> if clinically indicated
<b>MTHFR</b> C677T: C/T A1298C: A/C [~55% reduction]	<p><i>Methylenetetrahydrofolate Reductase (MTHFR) is an enzyme responsible for the conversion of folic acid to methylfolate, which is a cofactor needed for serotonin, norepinephrine and dopamine synthesis</i></p> <ul style="list-style-type: none"> <li>Risk for reduced MTHFR enzyme activity and reduced methylfolate production</li> <li><b>L-methylfolate supplementation</b> of SSRIs and SNRIs may result in greater symptom reduction compared to SSRIs/SNRIs alone in major depressive disorder. BMI greater than or equal to 30 and/or high C-reactive protein (CRP) have been associated with greater response to adjunctive L-methylfolate in SSRI-resistant depression.</li> <li>L-methylfolate may be an effective monotherapy for patients with major depressive disorder and MTHFR polymorphisms <a href="#">[B/C]</a> <a href="#">[3]</a></li> </ul>		<b>L-methylfolate</b> may be considered if clinically indicated
<b>ADRA2A</b> C/C [Decreased response]	<p><i>Alpha-2A Adrenergic Receptor (ADRA2A) is a receptor which plays an important role in norepinephrine signaling</i></p> <ul style="list-style-type: none"> <li>ADRA2A is involved in response to methylphenidate</li> <li>This genotype is associated with a <b>reduced response to methylphenidate</b> for inattentive symptoms of ADHD in children and adolescents as compared to G allele carriers <a href="#">[4]</a></li> </ul>		<b>Assess alternatives to methylphenidate</b> for ADHD if clinically appropriate
<b>HLA-A *31:01</b> Positive [Increased risk of skin reactions]	<p><i>Major histocompatibility complex, class I, A (HLA-A) is part of a cluster of genes known as the Human Leukocyte Antigen complex</i></p> <ul style="list-style-type: none"> <li>Certain variants greatly increase risk of drug induced skin reactions including Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and maculopapular exanthema (MPE)</li> <li><b>This genotype is associated with increased risk of skin reactions with carbamazepine</b> <a href="#">[A]</a> <a href="#">[1A]</a></li> </ul>		<b>Do not initiate carbamazepine</b>
<b>MC4R</b> A/A [High weight gain risk]	<p><i>Melanocortin 4 Receptor (MC4R) is a receptor that plays a central role in the control of food intake</i></p> <ul style="list-style-type: none"> <li><b>Risk of increased weight gain and metabolic changes with certain 2nd generation antipsychotics</b> <a href="#">[C]</a> <a href="#">[3]</a></li> </ul> <p><b>Higher risk:</b> clozapine; olanzapine  <b>Medium risk:</b> aripiprazole; brexpiprazole, iloperidone; paliperidone; olanzapine/samidorphan; quetiapine; risperidone  <b>Lower risk:</b> asenapine; cariprazine; lumateperone; lurasidone; ziprasidone</p>	  	<b>Higher risk of weight gain and metabolic changes</b> with various 2nd generation antipsychotics  <b>Anti-obesity interventions</b> may be considered if clinically indicated
<b>SLC6A4</b> L(A)/S [Intermediate activity]	<p><i>Serotonin Transporter (SLC6A4) is a synaptic transporter protein responsible for serotonin reuptake</i></p> <ul style="list-style-type: none"> <li>In individuals of European descent, <b>greater risk of side effects, particularly gastrointestinal side effects with SSRIs</b></li> </ul>		<b>Increased monitoring for adverse effects with SSRIs</b>



Alert/Caution



PGx Guided Options

[A] [A/B] [B] [B/C] [C] [C/D] [D] CPIC® level of evidence  
<https://cpicpgx.org/prioritization/#leveldef>

[1A] [1B] [2A] [2B] [3] [4] PharmGKB level of evidence  
<https://www.pharmgkb.org/page/clinAnnLevels>

## Pharmacodynamic Gene Variations

Gene Results	THERAPEUTIC IMPLICATIONS	GUIDE	CLINICAL IMPACT
<b>HTR2A</b> G/G [Normal response]	<i>Serotonin Receptor 2A (HTR2A) is a serotonin receptor which is a target for several serotonergic drugs</i> <ul style="list-style-type: none"> <li><b>This genotype confers normal activity</b></li> </ul>		No known significant clinical impact
<b>COMT</b> Val/Met [Normal activity]	<i>Catechol-O-Methyltransferase (COMT) is an enzyme responsible for breakdown of dopamine in the frontal cortex of the brain</i> <ul style="list-style-type: none"> <li>COMT is involved in response to stimulants</li> <li><b>This genotype confers normal activity</b></li> </ul>		No known significant clinical impact
<b>HLA-B *15:02</b> Negative [Normal]	<i>Major histocompatibility complex, class I, B (HLA-B) is part of a cluster of genes known as the Human Leukocyte Antigen complex</i> <ul style="list-style-type: none"> <li>Certain variants greatly increase risk of drug induced skin reactions</li> <li><b>This genotype is associated with normal risk of skin reactions with carbamazepine, oxcarbazepine, phenytoin, fosphenytoin and lamotrigine</b></li> </ul>		Normal risk of skin reactions with carbamazepine, oxcarbazepine, phenytoin, fosphenytoin, and lamotrigine
<b>DRD2</b> C/C [Normal activity]	<i>Dopamine Receptor D2 (DRD2) is a receptor activated by dopamine in the brain</i> <ul style="list-style-type: none"> <li>DRD2 is involved in response to antipsychotics</li> <li><b>This genotype confers normal activity</b></li> </ul>		No known significant clinical impact
<b>HTR2C</b> C/C [Standard weight gain risk]	<i>Serotonin Receptor 2C (HTR2C) is a receptor involved in the regulation of satiety</i> <ul style="list-style-type: none"> <li>Some 2nd generation antipsychotics act by blocking this receptor</li> <li>Patients with the C/C genotype have <b>standard risk of weight gain</b> with 2nd generation antipsychotics; C/C is the most common genotype</li> </ul> <p> <b>Higher risk:</b> clozapine; olanzapine  <b>Medium risk:</b> aripiprazole; brexpiprazole; iloperidone; olanzapine/samidorphan; paliperidone; quetiapine; risperidone  <b>Lower risk:</b> asenapine; cariprazine; lumateperone; lurasidone; ziprasidone                     </p>		No known significant clinical impact
<b>ANK3</b> C/C [Normal activity]	<i>Sodium Channel (ANK3) is a protein that plays a role in sodium ion channel function and is involved in excitatory signaling in the brain</i> <ul style="list-style-type: none"> <li><b>This genotype confers normal activity</b></li> </ul>		No known significant clinical impact
<b>CACNA1C</b> G/G [Normal activity]	<i>Calcium Channel (CACNA1C) is a subunit of L-type voltage gated calcium channels which are involved in excitatory signaling in the brain</i> <ul style="list-style-type: none"> <li><b>This genotype confers normal activity</b></li> </ul>		No known significant clinical impact
<b>OPRM1</b> A/A [Normal activity]	<i>μ-Opioid Receptor (OPRM1) is an opioid receptor which is affected by endogenous and exogenous opioids</i> <ul style="list-style-type: none"> <li>OPRM1 is involved in response to opioids</li> <li><b>This genotype confers normal activity</b></li> </ul>		No known significant clinical impact
<b>GRIK1</b> A/A [Normal activity]	<i>Glutamate Receptor Kainate 1 (GRIK1) is an excitatory neurotransmitter receptor</i> <ul style="list-style-type: none"> <li><b>This genotype confers normal activity</b></li> </ul>		No known significant clinical impact



Alert/Caution



PGx Guided Options

[A] [A/B] [B] [B/C] [C] [C/D] [D] CPIC® level of evidence  
<https://cpicpgx.org/prioritization/#leveldef>

[1A] [1B] [2A] [2B] [3] [4] PharmGKB level of evidence  
<https://www.pharmgkb.org/page/clinAnnLevels>



# Depression Summary

	Alert / Caution	Standard Options	PGx Guided Options
SSRIs	Citalopram	ⓘ ↑	
	Escitalopram	ⓘ ↑	
	Fluoxetine	ⓘ ↑	
	Paroxetine	ⓘ	
	Sertraline	ⓘ ↑	
SNRIs		Desvenlafaxine	
		Duloxetine	
		Levomilnacipran	
		Venlafaxine	↑
Other		Bupropion	
		Dextromethorphan/Bupropion	
		Mirtazapine	
		Nefazodone	
		Trazodone	
		Vilazodone	
		Vortioxetine	
TCAs	Amitriptyline	↑	
		Desipramine	
	Doxepin	↑	
	Imipramine	↑	
		Nortriptyline	
		Trimipramine	↑

- Do Not Initiate
- Decreased Efficacy
- Side Effects Risk
- Drug Exposure
- Decreased Sensitivity
- Increased Efficacy
- Weight Gain
- Reduced Drug Exposure with 1A2 Inducers

Diagnosis specific summaries are available for the diagnoses of depression, anxiety & related disorders, bipolar disorder, schizophrenia, pain management and ADHD. The provided pages in this report are the closest fit for this individual's diagnosis, as provided to us. All summaries, however, are available to you on the [Genomind Precision Health Platform](#).



# Depression Augmentation Summary

Alert / Caution		Standard Options		PGx Guided Options	
		Aripiprazole			
		Brexpiprazole			
		Cariprazine			
		ECT			
		Esketamine			
				Exercise	
				L-methylfolate	
		Olanzapine/Fluoxetine			
		Phenelzine			
		Quetiapine			
		Selegiline			
		TMS			
		Tranylcypromine			
		VNS			

- Do Not Initiate
- Decreased Efficacy
- Side Effects Risk
- Drug Exposure
- Decreased Sensitivity
- Increased Efficacy
- Weight Gain
- Reduced Drug Exposure with 1A2 Inducers





## Test Methodology/Literature References

### Test Methodology

This test was developed and performance characteristics were validated in the Genomind clinical laboratory. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). This test is used for clinical purposes and should not be regarded as investigational or for research use. Genomind's laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA), as qualified to perform high complexity clinical laboratory testing. Genomind performed the testing using standard and custom TaqMan reagents for all variants. The test results are intended to be used as prognostic and not diagnostic and are not intended as the sole means for patient management decisions.

*Test Methodology Limitations:* Factors influencing the amount and quality of DNA extracted include but are not limited to the amount of buccal cells extracted, patient oral hygiene, collection technique, and the presence of dietary or microbial sources of nucleic acids and nucleases. DNA quality and quantity are subject to matrix dependent influences. PCR inhibitors, extraneous DNA and nucleic acid degrading enzymes are all factors which may affect the evaluation of assay results. Some single nucleotide polymorphism (SNP) assays are problematic due to multiple base repeats and other sequence aberrations, which may hinder proper amplification and analysis. DNA purity can influence the assay. SLC6A4 contains many polymorphisms, and the assay was developed and validated according to the current available scientific information. For pharmacogenetic tests like the Genomind Pharmacogenetic Report, undetected genetic and/or non-genetic factors such as drug-drug interactions may impact the phenotype. In liver transplant recipients, certain genotypes of the donor liver may not be the same as those of the recipient. In these cases, it may be necessary to account for both the donor and recipient genotypes when evaluating drug metabolism genes. However, studies to date have been inconclusive as to the relative influence of the donor and recipient genotypes. The Genomind Pharmacogenetic Report is based on a current understanding of the clinical relevance of the variant identified, penetrance, phenotype predictions, and recurrence risks.

Variants tested include ABCB1 C3435T rs1045642; ABCB1 rs2032583; ABCG2 rs2231142, ADRA2A rs1800544; ANK3 rs10994336; BDNF rs6265; CACNA1C rs1006737; COMT rs4680; CYP1A2 \*1B, \*1C, \*1D, \*1E, \*1F, \*1K and \*11; CYP2B6 \*4, \*5, \*6 and \*9; CYP2C19 \*2, \*3, \*4, \*5, \*6, \*7, \*8, \*9, \*10, \*17, and \*35; CYP2C9 \*2, \*3, \*4, \*5, \*6, \*8, \*11, \*13, and \*27; CYP2D6 \*2, \*3, \*4, gene deletion (\*5), gene duplication, \*6, \*7, \*8, \*9, \*10, \*11, \*12, \*14, \*15, \*17, \*29 and \*41; CYP3A4 \*22; CYP3A5 \*3, \*6, \*7; DRD2 rs1799732; GRIK1 rs2832407; HLA-B\*15:02 presence and HLA-A\*31:01 presence detected by qPCR; HTR2A rs7997012; HTR2C rs3813929; MC4R rs489693; MTHFR rs1801131 and rs1801133; OPRM1 rs1799971; SLC6A4 rs25531 and rs63749047; SLCO1B1\*5, UGT2B15 rs1902023; and UGT1A4 rs2011425. Other known variants that are not listed are not detected and will not be included in the test report.

Version 3.2 [4/24/2023]

### Literature References

Summaries of references are available upon request of Genomind's comprehensive literature summary [April 2023 (V3.2)].

<https://genomind.com/providers/genomind-pgx-literature-review/>