OptimalRx Plus Report

Lab ID : **1660060**

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Date of Birth: 1998-01-03
Sex: M
Health Ins. No:
Ext. Ref. No.:

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The OptimalRx Plus 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 and Patients
A complimentary consultation, performed by our expert pharmacists, is included with all OptimalRx Plus Reports. To schedule a consultation, contact us at:

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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/G	DF	**Increased exposure to certain medications**
ABCB1 C3435T	G/A	NF	Normal exposure is expected
ABCG2	G/G	NF	Normal exposure is expected
CYP1A2	*1F/*1F	NM IND	**Normal metabolism but sensitive to induction**
CYP2B6	*1/*1	NM	Normal metabolism is expected
CYP2C19	*1/*2	IM	**Risk of increased (↑) drug levels**
CYP2C9	*27/*27	IND	**Unknown or undefined metabolism**
CYP2D6	*2/*2	NM	Normal metabolism is expected
CYP3A4/5	*1/*1, *3/*3	NA	Normal metabolism is expected
SLCO1B1	*1/*5	DF	**Increased exposure to certain medications**
UGT1A4	*1a/*1a	NM	Normal metabolism is expected
UGT2B15	*2/*2	IM	**Risk of increased (↑) drug levels**

Pharmacodynamic Genes
(Drug Targets / Mechanisms)

Antidepressant Response

Gene	Result	Result
SLC6A4	S/S	**Lower odds of SSRI response and increased side effect risk in those of European descent**
BDNF	Val/Val	**Moderately lower odds of response to SSRIs in East Asians**
HTR2A	G/A	No known significant clinical impact
MTHFR	C677T: T/T A1298C: A/A	**Reduced MTHFR activity and methylfolate production**

Attention-deficit/hyperactivity disorder Response

Gene	Result	Result
ADRA2A	C/G	**Higher odds of response to methylphenidate for inattentive symptoms of ADHD**
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/T	**Lower risk of weight gain with 2nd generation antipsychotics**
MC4R	C/C	No known significant clinical impact

Other

Gene	Result	Result
ANK3	C/C	No known significant clinical impact
CACNA1C	G/G	No known significant clinical impact
GRIK1	C/C	**Possible higher odds of response to topiramate for alcohol use disorder**
HLA-A *31:01	Negative	No known significant clinical impact
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
ANTIDEPRESSANTS					
SSRIs	**Citalopram** (Celexa®)		Lower odds of response and increased side effects in individuals of European descent (SLC6A4) Moderately lower odds of response in East Asians (BDNF)	M	**2C19**, **ABCB1**
		CPIC	Initiate with standard starting dose. Consider a slower titration and lower maintenance dose.		
		DPWG	Up to 65 years old: Max dose is 30 mg/day. 65 years or older: Max dose is 15 mg/day.		
SSRIs	**Escitalopram** (Cipralex®)		Lower odds of response and increased side effects in individuals of European descent (SLC6A4) Moderately lower odds of response in East Asians (BDNF)	M	**2C19**, **ABCB1**
		CPIC	Initiate with standard starting dose. Consider a slower titration and lower maintenance dose.		
		DPWG	Up to 65 years old: Max dose is 15 mg/day. 65 years and older: Max dose is 7.5 mg/day.		
SSRIs	**Fluoxetine** (Prozac®)		Lower odds of response and increased side effects in individuals of European descent (SLC6A4) Moderately lower odds of response in East Asians (BDNF)		2D6, **2C9**
SSRIs	**Fluvoxamine** (Luvox®)		Lower odds of response and increased side effects in individuals of European descent (SLC6A4) Moderately lower odds of response in East Asians (BDNF)	L	2D6, 1A2, **ABCB1**
SSRIs	**Paroxetine** (Paxil®)		Lower odds of response and increased side effects in individuals of European descent (SLC6A4) Moderately lower odds of response in East Asians (BDNF)	L	2D6, **ABCB1**
SSRIs	**Sertraline** (Zoloft®)		Lower odds of response and increased side effects in individuals of European descent (SLC6A4) Moderately lower odds of response in East Asians (BDNF)	M	**2C19**, 2B6, **ABCB1**
		CPIC	Initiate with standard starting dose. Consider a slower titration and lower maintenance dose.		
SNRIs	**Desvenlafaxine** (Pristiq®)				
SNRIs	**Duloxetine** (Cymbalta®)			Reduced Drug Exposure with 1A2 Inducers	1A2, 2D6
SNRIs	**Levomilnacipran** (Fetzima®)				3A4/5
SNRIs	**Venlafaxine XR** (Effexor XR®)			M	2D6, **2C19**, 3A4/5, **ABCB1**

Alert/Caution   PGx Guided Options   Reduced Drug Exposure with 1A2 Inducers   Do Not Initiate

H M L   See Gene-Drug Association footnotes for more information

Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations		Drug Level	Pharmacokinetics
ANTIDEPRESSANTS					
Other	**Bupropion SR/XL** (Wellbutrin SR/XL®)				2B6
Other	**Esketamine** (Spravato®)				2B6
Other	**Mirtazapine** (Remeron®)				2D6, 3A4/5, 1A2
Other	**Trazodone** (Desyrel®)				3A4/5, 2D6
Other	**Vilazodone** (Viibryd®)				3A4/5
Other	**Vortioxetine** (Trintellix®)				2D6, 3A4/5
TCAs	**Amitriptyline** (Elavil®)	CPIC	Initiate with standard starting dose.	M	2D6, **2C19**, **ABCB1**
TCAs	**Clomipramine** (Anafranil®)	CPIC	Initiate with standard starting dose.	M	2D6, 1A2, **2C19**
TCAs	**Desipramine** (Norpramin®)				2D6
TCAs	**Doxepin** (Sinequan®, Silenor®)	CPIC	Initiate with standard starting dose.	M	2D6, **2C19**
TCAs	**Imipramine** (Tofranil®)	CPIC	Initiate with standard starting dose.	M	2D6, **2C19**
TCAs	**Nortriptyline** (Aventyl®)			L	2D6, **ABCB1**
TCAs	**Trimipramine** (Surmontil®)	CPIC	Initiate with standard starting dose.	M	2D6, **2C19**, **ABCB1**
MAOIs	**Phenelzine** (Nardil®)				
MAOIs	**Selegiline** (Eldepryl®)				2B6
MAOIs	**Tranylcypromine** (Parnate®)				

Alert/Caution PGx Guided Options Reduced Drug Exposure with 1A2 Inducers Do Not Initiate

H M L See Gene-Drug Association footnotes for more information

Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations	Drug Level	Pharmacokinetics
	MOOD STABILIZERS/ANTICONVULSANTS			
	Carbamazepine (Tegretol CR®)			3A4/5
	Gabapentin (Neurontin®)			
	Lamotrigine (Lamictal®)			UGT1A4, ABCG2
	Lithium carbonate (Carbolith®)			
	Oxcarbazepine (Trileptal®)			
	Pregabalin (Lyrica®)			
	Topiramate (Topamax®)			ABCB1
	Valproic acid/divalproex (Depakene®, Epival®)			**2C9**
	ANTIPSYCHOTICS			
2nd and 3rd Generation Antipsychotics	**Aripiprazole** (Abilify®)	Lower risk of weight gain (HTR2C)		2D6, 3A4/5, ABCB1
	Asenapine (Saphris®)	Lower risk of weight gain (HTR2C)		1A2, UGT1A4
	Brexpiprazole (Rexulti®)	Lower risk of weight gain (HTR2C)		2D6, 3A4/5
	Cariprazine (Vraylar®)	Lower risk of weight gain (HTR2C)		3A4/5
	Clozapine (Clozaril®)	Lower risk of weight gain (HTR2C)		1A2, 2D6, ABCB1
	Lurasidone (Latuda®)	Lower risk of weight gain (HTR2C)		3A4/5
	Olanzapine (Zyprexa®)	Lower risk of weight gain (HTR2C)		1A2, ABCB1
	Paliperidone (Invega Sustenna®, Invega Trinza®)	Lower risk of weight gain (HTR2C)		
	Quetiapine (Seroquel XR®)	Lower risk of weight gain (HTR2C)		3A4/5
	Risperidone Risperdal®, Perseris®, Risperdal Consta®)	Lower risk of weight gain (HTR2C)		2D6, 3A4/5, ABCB1
	Ziprasidone (Zeldox®)	Lower risk of weight gain (HTR2C)		3A4/5

Alert/Caution | PGx Guided Options | 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
ANTIPSYCHOTICS				
1st Generation Antipsychotics	**Chlorpromazine** (Largactil®)			2D6
	Fluphenazine (Moditen®)			2D6
	Haloperidol (Haldol®)			2D6, 3A4/5
	Loxapine (Loxapac®)			
	Perphenazine (Trilafon®)			1A2, 2D6
	Pimozide (Orap®)			2D6, 3A4/5
	Thiothixene (Navane®)			1A2
	Trifluoperazine (Stelazine®)			1A2, UGT1A4
ANXIOLYTICS				
	Alprazolam (Xanax®)			3A4/5
	Buspirone (Buspar®)			3A4/5
	Chlordiazepoxide (Librium®)		L	3A4/5, **UGT2B15**
	Clonazepam (Rivotril®)			3A4/5
	Diazepam (Valium®)		M	**2C19**, 3A4/5, **UGT2B15**
	Hydroxyzine (Atarax®)			
	Lorazepam (Ativan®)		M	**UGT2B15**
	Oxazepam (Serax®)		M	**UGT2B15**
	Temazepam (Restoril®)		L	**UGT2B15**

Alert/Caution PGx Guided Options Reduced Drug Exposure with 1A2 Inducers Do Not Initiate

H M L See Gene-Drug Association footnotes for more information

Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations	Drug Level	Pharmacokinetics
	ADHD MEDICATIONS			
Dopaminergic Stimulants	**Amphetamine-Dextroamphetamine** (Adderall XR®)			2D6
Dopaminergic Stimulants	**Dextroamphetamine** (Dexedrine®)			2D6
Dopaminergic Stimulants	**Lisdexamfetamine** (Vyvanse®)			2D6
Dopaminergic Stimulants	**Methylphenidate** (Ritalin SR®, Concerta®, Biphentin®, Foquest®)	Higher odds of response (ADRA2A)		
Other	**Atomoxetine** (Strattera®)			2D6
Other	**Clonidine**			
Other	**Guanfacine** (Intuniv XR®)			3A4/5
	SUPPLEMENTS			
	L-methylfolate	May benefit from methylfolate supplementation (MTHFR)		
	SLEEP MODULATORS			
	Eszopiclone (Lunesta®)			3A4/5
	Lemborexant (Dayvigo®)			3A4/5
	Modafinil (Alertec®)			3A4/5, ABCB1
	Zolpidem (Sublinox®)			1A2, 3A4/5

Alert/Caution | PGx Guided Options | 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
	PAIN			
Non-opioid analgesics	**Acetaminophen** (Tylenol®)		L	UGT2B15
Non-opioid analgesics	**Celecoxib** (Celebrex®)			2C9
Non-opioid analgesics	**Diclofenac** (Voltaren SR®, Cambia®)			2C9
Non-opioid analgesics	**Flurbiprofen** (Ansaid®)			2C9
Non-opioid analgesics	**Ibuprofen** (Advil®, Motrin®)			2C9
Non-opioid analgesics	**Ketorolac** (Toradol®)			
Non-opioid analgesics	**Meloxicam** (Mobicox®)			2C9
Non-opioid analgesics	**Naproxen** (Aleve®, Naprosyn®)			2C9
Non-opioid analgesics	**Piroxicam** (Feldene®)			2C9
Opioid analgesics	**Codeine**			2D6, ABCB1
Opioid analgesics	**Fentanyl** (Duragesic®, Fentora®)			3A4/5, ABCB1
Opioid analgesics	**Hydrocodone** (Hycodan®)			2D6, 3A4/5
Opioid analgesics	**Hydromorphone** (Dilaudid®)			
Opioid analgesics	**Methadone** (Metadol®)			2B6, 3A4/5
Opioid analgesics	**Morphine** (MS Contin®, M-Eslon®, Statex®, Kadian®, Doloral®)			ABCB1
Opioid analgesics	**Oxycodone** (Oxycontin®, Oxyneo®, Supeudol®)			2D6, 3A4/5, ABCB1
Opioid analgesics	**Tapentadol** (Nucynta ER®)			
Opioid analgesics	**Tramadol** (Durela®, Zytram XL®, Tridural®, Ralivia®)			2D6, 3A4/5, ABCB1

Alert/Caution   PGx Guided Options   Reduced Drug Exposure with 1A2 Inducers   Do Not Initiate

H M L   See Gene-Drug Association footnotes for more information

Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations		Drug Level	Pharmacokinetics
MISCELLANEOUS					
	Buprenorphine (Butrans®, Probuphine®, Sublocade®)				3A4/5
	Buprenorphine/Naloxone (Suboxone®)				3A4/5
	Naltrexone (Revia®)				
	Phenytoin/Fosphenytoin (Dilantin®, Cerebyx®)			M	**2C19**, **2C9**, ABCB1
STATINS					
	Atorvastatin (Lipitor®)	CPIC	Possible increased myopathy risk especially with 40 mg. Use ≤40 mg as a starting dose and adjust doses based on disease-specific guidelines.	M	3A4/5, **SLCO1B1**, ABCB1, ABCG2
	Fluvastatin (Lescol®)	CPIC	See compound guideline	M	**2C9**, **SLCO1B1**
	Lovastatin (Mevacor®)	CPIC	Possible increased myopathy risk. Use an alternative statin depending on desired potency. If warranted, limit dose to ≤20 mg/day.	M	3A4/5, **SLCO1B1**
	Pravastatin (Pravachol®)	CPIC	Possible increased myopathy risk especially with doses >40 mg/day. Use desired starting dose and adjust doses based on disease-specific guidelines.	M	**SLCO1B1**
	Rosuvastatin (Crestor®)	CPIC	Possible increased myopathy risk especially with doses >20 mg. Use desired starting dose and adjust doses based on disease-specific and specific population guidelines.	M	ABCG2, **SLCO1B1**
	Simvastatin (Zocor®)	CPIC	Increased myopathy risk. Use an alternative statin depending on the desired potency. If warranted, limit dose to <20 mg/day.	M	3A4/5, **SLCO1B1**

Alert/Caution   PGx Guided Options   Reduced Drug Exposure with 1A2 Inducers   Do Not Initiate

H M L   See Gene-Drug Association footnotes for more information

Gene-Drug Association Footnotes

Risk for change in drug exposure: H H Higher Risk   M M Moderate Risk   L L Lower Risk

References for the drug interaction summary are available upon request

Pharmacokinetic Gene Variations

Gene Results	THERAPEUTIC IMPLICATIONS	GUIDE	CLINICAL IMPACT
CYP2C9 **IND** *27/*27 [Indeterminate activity]	*Variations in the CYP2C9 liver enzyme can result in altered drug metabolism and unexpected drug serum levels* • This genotype is considered **indeterminate** according to the most recent CPIC guidelines because it contains at least 1 allele of **unknown function**. • Refer to the CPIC CYP450 specific allele functionality tables for additional information (https://www.pharmgkb.org/page/pgxGeneRef)	⚠	The drug metabolism status for this particular genotype of CYP2C9 is unknown at this time. Consider dose adjustments based on clinical presentation, or use therapeutic drug monitoring.
CYP2C19 **IM** *1/*2 [Intermediate activity]	***Intermediate metabolizer: Risk of elevated serum levels** and drug interactions, or decreased production of active metabolites* • **A dose adjustment or alternate therapy may be considered**	⚠	May have altered blood levels with medications metabolized by CYP2C19
UGT2B15 **IM** *2/*2 [Intermediate Activity]	***Intermediate metabolizer: Risk of elevated serum levels** and drug interactions, or decreased production of active metabolites* • **A dose adjustment or alternate therapy may be considered**	⚠	May have altered blood levels with medications metabolized by UGT2B15
ABCB1 **(rs2032583)** A/G [Decreased function]	*ATP Binding Cassette B1 (ABCB1) encodes for an efflux pump that reduces the intestinal absorption and blood-brain barrier penetration of certain drugs* • This genotype is associated with **increased exposure and side effect burden to several antidepressants**	⚠	Increased exposure to medications affected by ABCB1
SLCO1B1 **DF** *1/*5 [Decreased function]	*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.* • This genotype is associated with **decreased function of SLCO1B1 and increased serum levels of statins** and other medications • **A dose adjustment or alternate therapy may be considered**	⚠	Increased exposure to medications affected by SLCO1B1
CYP1A2 **NM IND** *1F/*1F [Normal activity but sensitive to induction]	***Normal metabolizer (Induction Sensitive):** This genotype confers **normal activity, except in the presence of inducers.** In the presence of inducers, there is a risk of **decreased serum levels, and a risk of possible adverse events** associated with active metabolites* • CYP1A2 *1F is highly induced by certain substances including **tobacco/marijuana smoke, excessive coffee consumption or other medications;** if the patient uses these substances, a higher dose of CYP1A2 substrates may be considered • **A dose adjustment or alternate therapy may be considered in the presence of inducers**	⚠	May have altered blood levels with medications metabolized by CYP1A2 in the presence of inducers
CYP2B6 **NM** *1/*1 [Normal activity]	*Variations in the CYP2B6 liver enzyme can result in altered drug metabolism and unexpected drug serum levels* • **This genotype confers normal activity**		Normal metabolism is expected (other factors may influence metabolism)

⚠ Alert/Caution   PGx Guided Options

Pharmacokinetic Gene Variations

Gene Results	THERAPEUTIC IMPLICATIONS	GUIDE	CLINICAL IMPACT
CYP2D6 **NM** *2/*2 [Normal activity]	*Variations in the CYP2D6 liver enzyme can result in altered drug metabolism and unexpected drug serum levels* • **This genotype confers normal activity**		Normal metabolism is expected (other factors may influence metabolism)
CYP3A4 ***1/*1** **CYP3A5** ***3/*3** [Normal activity]	*Variations in the CYP3A4/5 liver enzymes can result in altered drug metabolism and unexpected drug serum levels* • 3A5 non-expresser • CYP3A activity is determined by the sum activity of the CYP3A family of genes; in adults the most influential are 3A4 and 3A5 • **This genotype confers normal activity**		Normal metabolism is expected (other factors may influence metabolism)
UGT1A4 **NM** *1a/*1a [Normal activity]	*Variations in the UGT1A4 liver enzyme can result in altered drug metabolism and unexpected drug serum levels* • **This genotype confers normal activity**		Normal metabolism is expected (other factors may influence metabolism)
ABCB1 **(rs1045642)** G/A [Normal function]	*ATP Binding Cassette B1 (ABCB1) encodes for an efflux pump that affects the intestinal absorption and blood-brain barrier penetration of certain drugs* • This genotype is associated with decreased function of ABCB1, but does not consistently impact drug exposure in heterozygotes. Increased exposure for aripiprazole, clozapine, olanzapine, risperidone has been observed.		Normal function is expected (other factors may influence drug exposure)
ABCG2 **NF** G/G [Normal 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.* • This genotype is associated with **normal function of ABCG2 and normal absorption/excretion** of medications sensitive to ABCG2		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
SLC6A4 S/S [Low Activity]	*Serotonin Transporter (SLC6A4) is a synaptic transporter protein responsible for serotonin reuptake* • Associated with a **lower likelihood of remission or response with SSRIs** in individuals of European descent with depression [C] [3/4] • **Increased side effect risk with SSRIs** • Potential for increased cortisol release in response to stress	Alert/Caution	**Assess alternatives to SSRIs** in individuals with depression **SNRIs** or other **non-SSRI antidepressants** may be considered if clinically indicated
MTHFR C677T: T/T A1298C: A/A [~70% reduction]	*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* • Risk for reduced MTHFR enzyme activity and reduced methylfolate production • **L-methylfolate supplementation** 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. • L-methylfolate may be an effective monotherapy for patients with major depressive disorder and MTHFR polymorphisms [B/C] [3]	PGx Guided Options	**L-methylfolate** may be considered if clinically indicated
ADRA2A C/G [Improved response]	*Alpha-2A Adrenergic Receptor (ADRA2A) is a receptor which plays an important role in norepinephrine signaling* • **Improved response to methylphenidate** for inattentive symptoms of ADHD in children and adolescents as compared to those with the C/C genotype [4]	PGx Guided Options	**Methylphenidate** may be considered for ADHD if clinically indicated
HTR2C C/T [Lower weight gain risk]	*Serotonin Receptor 2C (HTR2C) is a receptor involved in the regulation of satiety* • The T allele confers a **lower risk of weight gain** with 2nd generation antipsychotics as compared to the C/C genotype [C] [3]	PGx Guided Options	**Lower weight gain risk** with 2nd generation antipsychotics
GRIK1 C/C [Improved response]	*Glutamate Receptor Kainate 1 (GRIK1) is an excitatory neurotransmitter receptor* • An initial study showed that individuals of European descent with the C/C genotype may be more likely to respond to topiramate for alcohol use disorder as compared to A allele carriers. However, recent studies have shown contradictory findings; other genetic and clinical factors may also influence response to topiramate. [3]	PGx Guided Options	**Topiramate** may be considered to reduce heavy drinking if clinically indicated
BDNF Val/Val [Normal activity]	*Brain-derived Neurotrophic Factor (BDNF)* is a protein involved in neuronal development and neural plasticity • This genotype confers normal activity • Studies have shown that **Val/Val individuals of East Asian descent** with depression may have a **moderately lower odds of response to SSRIs** compared to Met carriers	Alert/Caution	**Assess alternatives to SSRIs** in East Asians if clinically appropriate
HTR2A G/A [Normal response]	*Serotonin Receptor 2A (HTR2A) is a serotonin receptor which is a target for several serotonergic drugs* • **This genotype confers normal activity**		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

Pharmacodynamic Gene Variations

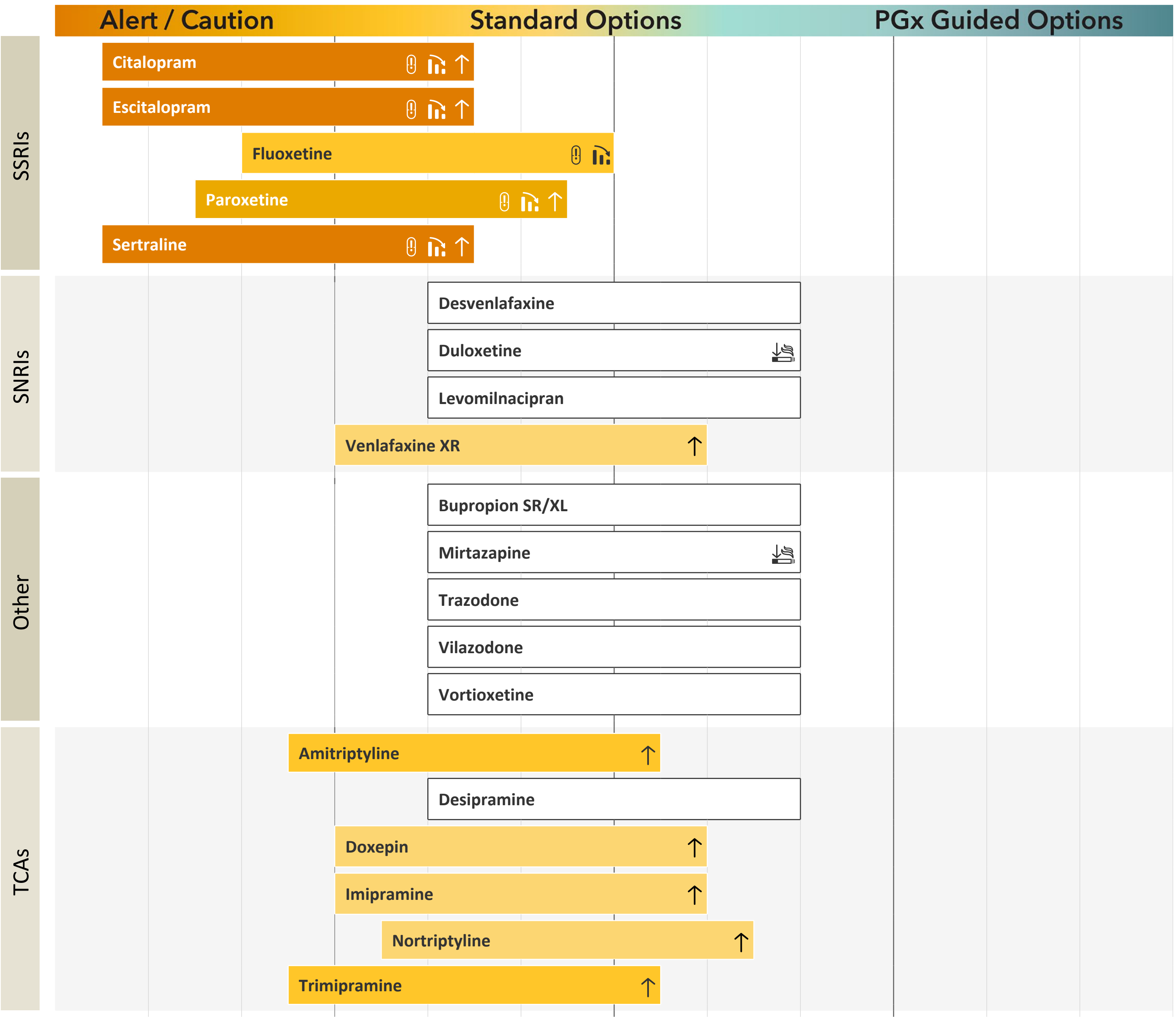
Gene Results	THERAPEUTIC IMPLICATIONS	GUIDE	CLINICAL IMPACT
COMT Val/Met [Normal activity]	*Catechol-O-Methyltransferase (COMT) is an enzyme responsible for breakdown of dopamine in the frontal cortex of the brain* • COMT is involved in response to stimulants • **This genotype confers normal activity**		No known significant clinical impact
HLA-A *31:01 Negative [Normal]	*Major histocompatibility complex, class I, A (HLA-A) is part of a cluster of genes known as the Human Leukocyte Antigen complex* • Certain variants greatly increase risk of drug induced skin reactions • **This genotype is associated with normal risk of skin reactions with carbamazepine**		Normal risk of skin reactions with carbamazepine
HLA-B *15:02 Negative [Normal]	*Major histocompatibility complex, class I, B (HLA-B) is part of a cluster of genes known as the Human Leukocyte Antigen complex* • Certain variants greatly increase risk of drug induced skin reactions • **This genotype is associated with normal risk of skin reactions with carbamazepine, oxcarbazepine, phenytoin, fosphenytoin and lamotrigine**		Normal risk of skin reactions with carbamazepine, oxcarbazepine, phenytoin, fosphenytoin, and lamotrigine
DRD2 C/C [Normal activity]	*Dopamine Receptor D2 (DRD2) is a receptor activated by dopamine in the brain* • DRD2 is involved in response to antipsychotics • **This genotype confers normal activity**		No known significant clinical impact
MC4R C/C [Normal activity]	*Melanocortin 4 Receptor (MC4R) is a receptor that plays a central role in the control of food intake* • MC4R is involved in antipsychotic-induced weight gain • **This genotype confers normal activity and average risk of weight gain**		No known significant clinical impact
ANK3 C/C [Normal activity]	*Sodium Channel (ANK3) is a protein that plays a role in sodium ion channel function and is involved in excitatory signaling in the brain* • **This genotype confers normal activity**		No known significant clinical impact
CACNA1C G/G [Normal activity]	*Calcium Channel (CACNA1C) is a subunit of L-type voltage gated calcium channels which are involved in excitatory signaling in the brain* • **This genotype confers normal activity**		No known significant clinical impact
OPRM1 A/A [Normal activity]	*µ-Opioid Receptor (OPRM1) is an opioid receptor which is affected by endogenous and exogenous opioids* • OPRM1 is involved in response to opioids • **This genotype confers normal activity**		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



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 in the supplemental diagnoses report.

Depression Augmentation Summary

Alert / Caution	Standard Options	PGx Guided Options
	Aripiprazole	
	Brexpiprazole	
	Cariprazine	
	ECT	
	Esketamine	
	Exercise	
	L-methylfolate	L-methylfolate
	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

The performance characteristics of this test were validated by Dynacare. This test has not been cleared or approved by the Therapeutic Products Directorate of Health Canada. The Dynacare laboratory is ISO 15189 accredited by the Standards Council of Canada for "Medical Laboratories - Requirements for Quality and Competence". The testing is performed 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 OptimalRx Plus 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 OptimalRx Plus 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.

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Literature References

Summaries of references are available upon request. Please contact Dynacare at DynacareGenetics@dynacare.ca for a comprehensive literature summary. Literature information was reviewed by David Krause, M.D., Chief Medical Officer for Genomind, Inc.