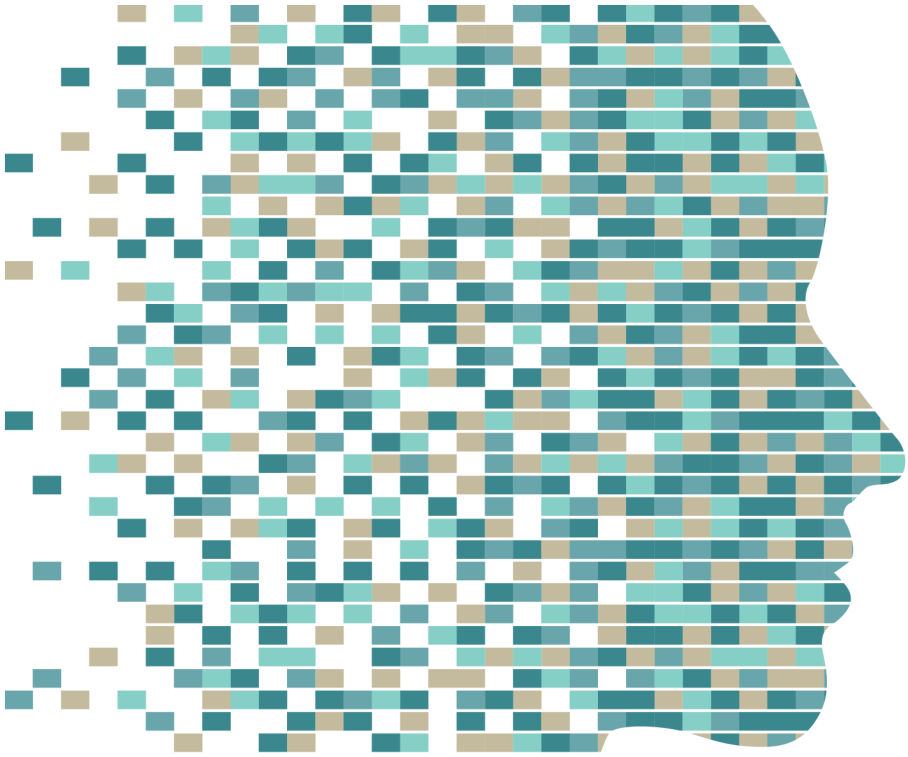

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Pharmacogenetic (PGx) Report

Patient:	**Nora Syke**	Sample ID:	**7524640209**
Patient DOB:	**12/25/1985**	Accession ID:	**250750**
Ordering Clinician:	**Lab Clinician**	Sample Collection Date:	**4/22/2024**
Sample Type:	**Buccal**	Sample Received Date:	**4/24/2024**
Assay Ordered:	**PGx (v3.2)**	Report Date:	**4/24/2024 2:02 PM**

Electronically Signed By
Juel Meya, Quality Assurance

Literature Information Reviewed By David Krause, M.D., Chief Medical Officer

The 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 PGx Reports.

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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	**Increased exposure to certain medications**
CYP1A2	*1B/H7	NM	Normal metabolism is expected
CYP2B6	*1/*1	NM	Normal metabolism is expected
CYP2C19	*2/*3	PM	**Risk of increased (↑) drug levels**
CYP2C9	*1/*3	IM	**Risk of increased (↑) drug levels**
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	**Risk of decreased (↓) drug levels**
UGT2B15	*1/*2	NM	Normal metabolism is expected

Pharmacodynamic Genes (Drug Targets / Mechanisms)

Antidepressant Response

Gene	Result	Result
BDNF	Val/Met	**More pronounced effect to exercise; Possible higher odds of response to SNRIs**
HTR2A	G/G	No known significant clinical impact
MTHFR	C677T: C/T A1298C: A/C	**Reduced MTHFR activity and methylfolate production**
SLC6A4	L(A)/S	**Higher odds of gastrointestinal side effects with SSRIs in individuals of European descent**

Attention-deficit/hyperactivity disorder Response

Gene	Result	Result
ADRA2A	C/C	**Lower 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/C	No known significant clinical impact
MC4R	A/A	**Higher risk of weight gain with certain 2nd generation antipsychotics**

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	**Higher risk of skin reactions with carbamazepine**
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®)	⚠	Monitor for gastrointestinal side effects in individuals of European descent (SLC6A4)	H	**2C19**, ABCB1
		CPIC	Consider alternative or 50% reduction in maintenance dose.		
		DPWG	Up to 65 years old: Max dose is 20 mg/day. 65 years or older: Max dose is 10 mg/day.		
	Escitalopram (Lexapro®)	⚠	Monitor for gastrointestinal side effects in individuals of European descent (SLC6A4)	H	**2C19**, ABCB1
		CPIC	Consider alternative or 50% reduction in maintenance dose.		
		DPWG	Up to 65 years old: Max dose is 10 mg/day. 65 years and older: Max dose is 5 mg/day.		
	Fluoxetine (Prozac®)	⚠	Monitor for gastrointestinal side effects in individuals of European descent (SLC6A4)	L	2D6, **2C9**
	Fluvoxamine (Luvox®)	⚠	Monitor for gastrointestinal side effects in individuals of European descent (SLC6A4)		2D6, 1A2, ABCB1
	Paroxetine (Paxil®)	⚠	Monitor for gastrointestinal side effects in individuals of European descent (SLC6A4)		2D6, ABCB1
	Sertraline (Zoloft®)	⚠	Monitor for gastrointestinal side effects in individuals of European descent (SLC6A4)	H	**2C19**, 2B6, ABCB1
		CPIC	Consider a lower starting dose, slower titration, and 50% lower maintenance dose or select alternative.		
		DPWG	Max dose: 75 mg/day		
SNRIs	**Desvenlafaxine** (Pristiq®)				
	Duloxetine (Cymbalta®)				1A2, 2D6
	Levomilnacipran (Fetzima®)				3A4/5
	Venlafaxine (Effexor®)			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** (Wellbutrin®)				2B6
	Dextromethorphan/Bupropion (Auvelity®)				2B6, 2D6, 3A4/5
	Esketamine (Spravato®)				2B6
	Mirtazapine (Remeron®)				2D6, 3A4/5, 1A2
	Nefazodone				3A4/5
	Trazodone (Desyrel®, Oleptro®)				3A4/5, 2D6
	Vilazodone (Viibryd®)				3A4/5
	Vortioxetine (Trintellix®)				2D6, 3A4/5
TCAs	**Amitriptyline** (Elavil®)	CPIC	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	H	2D6, **2C19**, ABCB1
	Clomipramine (Anafranil®)	CPIC	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	H	2D6, 1A2, **2C19**
	Desipramine (Norpramin®)				2D6
	Doxepin (Sinequan®)	CPIC	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	H	2D6, **2C19**
	Imipramine (Tofranil®)	CPIC	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	H	2D6, **2C19**
	Nortriptyline (Pamelor®)				2D6, ABCB1
	Trimipramine (Surmontil®)	CPIC	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	H	2D6, **2C19**, ABCB1
MAOIs	**Phenelzine** (Nardil®)				
	Selegiline (Eldepryl®, Emsam®)				2B6
	Tranylcypromine (Parnate®)				

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Gene-Drug Associations

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

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

Gene-Drug Associations

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

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Gene-Drug Associations

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

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

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

Gene-Drug Associations

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

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

Gene-Drug Associations

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

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

Gene-Drug Association Footnotes

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

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 **IM** *1/*3 [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 CYP2C9
CYP2C19 **PM** *2/*3 [Low activity]	***Poor 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
UGT1A4 **UM** *1a/*3b [High activity]	***Ultrarapid metabolizer: Risk of decreased serum levels,*** *and possible adverse events associated with increased active metabolites* • **A dose adjustment or alternate therapy may be considered**	⚠	May have altered blood levels with medications metabolized by UGT1A4
ABCG2 **PF** 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. • This genotype is associated with **poor function of ABCG2 and increased serum levels of some medications** • **A dose adjustment or alternate therapy may be considered**	⚠	Increased exposure to medications affected by ABCG2
CYP1A2 **NM** *1B/H7 [Normal activity]	*Variations in the CYP1A2 liver enzyme can result in altered drug metabolism and unexpected drug serum levels* • **This genotype confers normal activity** • 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)		Normal metabolism is expected (other factors may influence metabolism)
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)
CYP2D6 **NM** *1/*1 [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)

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Pharmacokinetic Gene Variations

Gene Results	THERAPEUTIC IMPLICATIONS	GUIDE	CLINICAL IMPACT
UGT2B15 **NM** *1/*2 [Normal activity]	*Variations in the UGT2B15 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 **(rs2032583)** A/A [Normal 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 normal function of ABCB1 and normal drug absorption**		Normal function is expected (other factors may influence drug exposure)
ABCB1 **(rs1045642)** G/G [Normal 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 normal function of ABCB1 and normal drug absorption**		Normal function is expected (other factors may influence drug exposure)
SLCO1B1 **NF** *1/*1 [Normal 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 **normal function of SLCO1B1 and normal hepatic uptake of statins** and other medications		Normal function is expected (other factors may influence drug exposure)

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Pharmacodynamic Gene Variations

Gene Results	THERAPEUTIC IMPLICATIONS	GUIDE	CLINICAL IMPACT
BDNF Val/Met [Altered BDNF secretion]	*Brain-derived Neurotrophic Factor (BDNF) is a protein involved in neuronal development and neural plasticity* • Studies have shown that **Met carriers of European descent** with depression may have a **poorer response to SSRIs and improved response to duloxetine, venlafaxine, and clomipramine;** further studies need to confirm these findings • Exercise has been linked to improvements in cognition and stress response, with Met carriers showing a more pronounced response		Consider **increased levels of physical activity/exercise** if clinically appropriate **SNRIs may be considered** if clinically indicated
MTHFR C677T: C/T A1298C: A/C [~55% 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]		**L-methylfolate** may be considered if clinically indicated
ADRA2A C/C [Decreased response]	*Alpha-2A Adrenergic Receptor (ADRA2A) is a receptor which plays an important role in norepinephrine signaling* • ADRA2A is involved in response to methylphenidate • This genotype is associated with a **reduced response to methylphenidate** for inattentive symptoms of ADHD in children and adolescents as compared to G allele carriers [4]		**Assess alternatives to methylphenidate** for ADHD if clinically appropriate
HLA-A *31:01 Positive [Increased risk of skin reactions]	*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 including Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and maculopapular exanthema (MPE) • **This genotype is associated with increased risk of skin reactions with carbamazepine** [A] [1A]		**Do not initiate carbamazepine**
MC4R A/A [High weight gain risk]	*Melanocortin 4 Receptor (MC4R) is a receptor that plays a central role in the control of food intake* • **Risk of increased weight gain and metabolic changes with certain 2nd generation antipsychotics** [C] [3] **Higher risk:** clozapine; olanzapine **Medium risk:** aripiprazole; brexpiprazole, iloperidone; paliperidone; olanzapine/samidorphan; quetiapine; risperidone **Lower risk:** asenapine; cariprazine; lumateperone; lurasidone; ziprasidone		**Higher risk of weight gain and metabolic changes** with various 2nd generation antipsychotics **Anti-obesity interventions** may be considered if clinically indicated
SLC6A4 L(A)/S [Intermediate activity]	*Serotonin Transporter (SLC6A4) is a synaptic transporter protein responsible for serotonin reuptake* • In individuals of European descent, **greater risk of side effects, particularly gastrointestinal side effects with SSRIs**		**Increased monitoring for adverse effects with SSRIs**

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[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

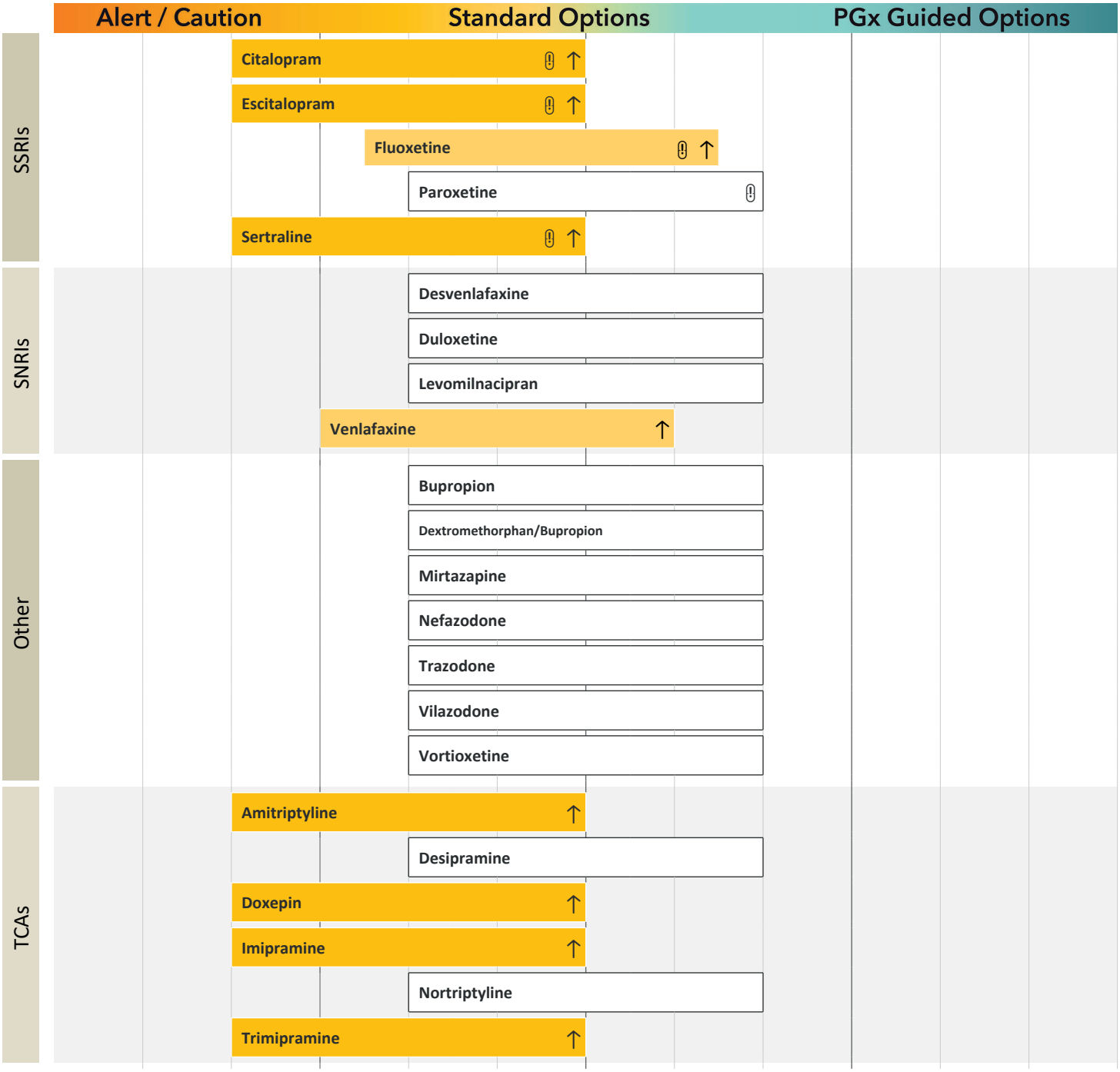
Gene Results	THERAPEUTIC IMPLICATIONS	GUIDE	CLINICAL IMPACT
HTR2A G/G [Normal response]	*Serotonin Receptor 2A (HTR2A) is a serotonin receptor which is a target for several serotonergic drugs* • **This genotype confers normal activity**		No known significant clinical impact
COMT Val/Met [Normal activity]	*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-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
HTR2C C/C [Standard weight gain risk]	*Serotonin Receptor 2C (HTR2C) is a receptor involved in the regulation of satiety* • Some 2nd generation antipsychotics act by blocking this receptor • Patients with the C/C genotype have **standard risk of weight gain** with 2nd generation antipsychotics; C/C is the most common genotype **Higher risk:** clozapine; olanzapine **Medium risk:** aripiprazole; brexpiprazole; iloperidone; olanzapine/samidorphan; paliperidone; quetiapine; risperidone **Lower risk:** asenapine; cariprazine; lumateperone; lurasidone; ziprasidone		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
GRIK1 A/A [Normal activity]	*Glutamate Receptor Kainate 1 (GRIK1) is an excitatory neurotransmitter receptor* • **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

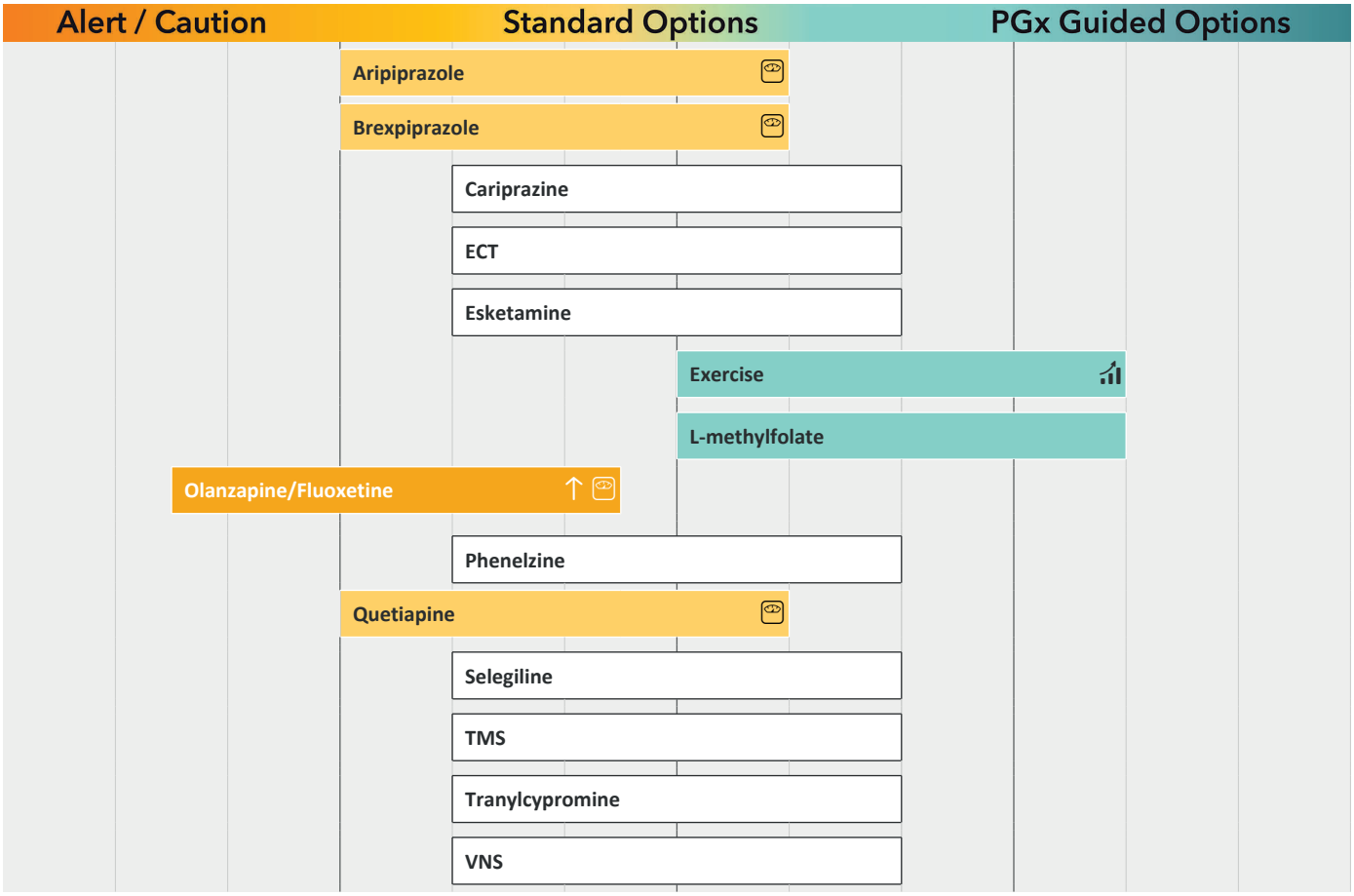
Depression Summary



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.

Depression Augmentation Summary



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 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. The laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA), as qualified to perform high complexity clinical laboratory testing. The dedicated clinical technicians 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 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 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]