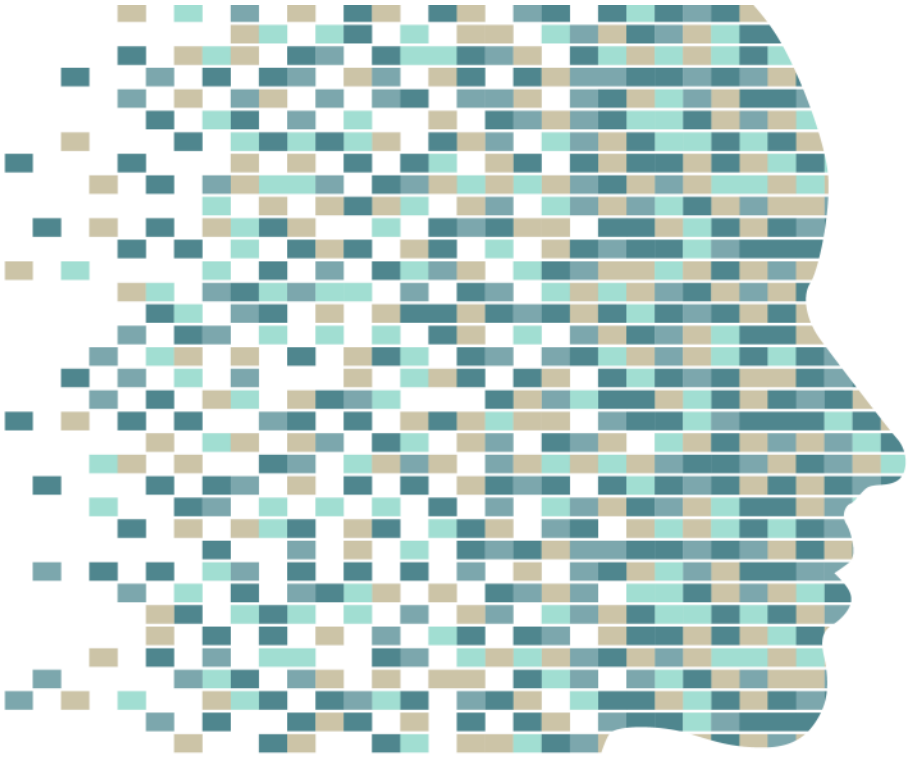

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Genomind Pharmacogenetic Report

Patient:	**Bob Sample**	Sample ID:	**0000096272**
Patient DOB:	**12/25/1985**	Accession ID:	**10101010**
Ordering Clinician:	**Joe Clinician**	Sample Collection Date:	**9/10/2018**
Sample Type:	**Buccal**	Sample Received Date:	**9/14/2018**
Assay Ordered:	**Genomind PGx (v3.2)**	Report Date:	**9/17/2018 10:17 AM**

Electronically Signed By
David Robbins, PhD, DABCC, MT (AAB), Lab Director for Genomind, Inc.

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

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.

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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	N/A	**Increased exposure to certain medications**
ABCB1 C3435T	G/G	PGP EM	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/*1	NM	Normal metabolism is expected
CYP2C9	*1/*3	IM	**Risk of increased (↑) drug levels**
CYP2D6	*4/*4	PM	**Risk of increased (↑) drug levels**
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/*1	NM	Normal metabolism is expected

Pharmacodynamic Genes (Drug Targets / Mechanisms)

Antidepressant Response

Gene	Result	Impact
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	S/S	**Lower odds of SSRI response and increased side effect risk in those of European descent**

Attention-deficit/hyperactivity disorder Response

Gene	Result	Impact
ADRA2A	C/G	**Higher odds of response to methylphenidate for inattentive symptoms of ADHD**
COMT	Val/Val	**Higher odds of response to stimulants for inattentive symptoms of ADHD**

Antipsychotic Response and Tolerability

Gene	Result	Impact
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	Impact
ANK3	C/C	No known significant clinical impact
CACNA1C	G/A	No known significant clinical impact
GRIK1	A/A	No known significant clinical impact
HLA-A *31:01	Negative	No known significant clinical impact
HLA-B *15:02	Positive	**Higher risk of skin reactions with carbamazepine, oxcarbazepine, lamotrigine, phenytoin**
OPRM1	A/A	No known significant clinical impact

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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)	L	2C19, **ABCB1**
	Escitalopram (Lexapro®)	⚠	Lower odds of response and increased side effects in individuals of European descent (SLC6A4)	L	2C19, **ABCB1**
	Fluoxetine (Prozac®)	⚠	Lower odds of response and increased side effects in individuals of European descent (SLC6A4)	M	**2D6**, **2C9**
	Fluvoxamine (Luvox®)	⚠ CPIC	Lower odds of response and increased side effects in individuals of European descent (SLC6A4) Consider 25-50% reduction of standard starting dose and slower titration or consider alternative.	H	**2D6**, 1A2, **ABCB1**
	Paroxetine (Paxil®)	⚠ CPIC	Lower odds of response and increased side effects in individuals of European descent (SLC6A4) Consider a 50% reduction in standard starting dose, slower titration, and 50% lower maintenance dose.	H	**2D6**, **ABCB1**
	Sertraline (Zoloft®)	⚠	Lower odds of response and increased side effects in individuals of European descent (SLC6A4)	L	2C19, 2B6, **ABCB1**
SNRIs	**Desvenlafaxine** (Pristiq®)				
	Duloxetine (Cymbalta®)			M	1A2, **2D6**
	Levomilnacipran (Fetzima®)				3A4/5
	Venlafaxine (Effexor®)	DPWG	Avoid use. If unable to avoid, reduce the dose and increase monitoring or check plasma levels.	H	**2D6**, 2C19, 3A4/5, **ABCB1**
Other	**Bupropion** (Wellbutrin®)				2B6
	Dextromethorphan/Bupropion (Auvelity®)	FDA	Recommended dosage: One tablet once daily in the morning	H	2B6, **2D6**, 3A4/5
	Esketamine (Spravato®)				2B6
	Mirtazapine (Remeron®)			M	**2D6**, 3A4/5, 1A2
	Nefazodone				3A4/5
	Trazodone (Desyrel®, Oleptro®)			M	3A4/5, **2D6**
	Vilazodone (Viibryd®)				3A4/5
	Vortioxetine (Trintellix®)	FDA	Max dose: 10 mg/day.	H	**2D6**, 3A4/5
TCAs	**Amitriptyline** (Elavil®)	CPIC	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	H	**2D6**, 2C19, **ABCB1**

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

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Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations		Drug Level	Pharmacokinetics
	ANTIDEPRESSANTS				
TCAs	**Amoxapine** (Asendin®)			H	**2D6**
TCAs	**Clomipramine** (Anafranil®)	CPIC	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	H	**2D6**, 1A2, 2C19
TCAs	**Desipramine** (Norpramin®)	CPIC	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	H	**2D6**
TCAs	**Doxepin** (Sinequan®)	CPIC	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	H	**2D6**, 2C19
TCAs	**Imipramine** (Tofranil®)	CPIC	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	H	**2D6**, 2C19
TCAs	**Nortriptyline** (Pamelor®)	CPIC	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	H	**2D6**, **ABCB1**
TCAs	**Protriptyline** (Vivactil®)			H	**2D6**
TCAs	**Trimipramine** (Surmontil®)	CPIC	Avoid use. If use warranted, consider 50% reduction of standard starting dose.	H	**2D6**, 2C19, **ABCB1**
MAOIs	**Phenelzine** (Nardil®)				
MAOIs	**Selegiline** (Eldepryl®, Emsam®)				2B6
MAOIs	**Tranylcypromine** (Parnate®)				
	MOOD STABILIZERS/ANTICONVULSANTS				
	Carbamazepine (Equetro®, Tegretol®)	CPIC	Do not initiate therapy: Higher risk of drug induced skin reactions (HLA-B)		3A4/5
	Gabapentin (Neurontin®)				
	Lamotrigine (Lamictal®)	DPWG	Do not initiate therapy: Higher risk of drug induced skin reactions (HLA-B)	M	**UGT1A4**, ABCG2
	Lithium (Lithobid®, Eskalith®)				
	Oxcarbazepine (Trileptal®, Oxtellar®)	CPIC	Do not initiate therapy: Higher risk of drug induced skin reactions (HLA-B)		
	Pregabalin (Lyrica®)				
	Topiramate (Topamax®)				ABCB1
	Valproate (Depakote®, Depakene®)			L	**2C9**

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Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations	Drug Level	Pharmacokinetics
	ANTIPSYCHOTICS			
2nd Generation Antipsychotics	**Aripiprazole** (Abilify®)	⚠ Higher risk of weight gain (MC4R) FDA Use 50% of standard dose. DPWG Max dose: 10mg/day or 300 mg/month	H	**2D6**, 3A4/5, ABCB1
	Asenapine (Saphris®)		L	1A2, **UGT1A4**
	Brexpiprazole (Rexulti®)	⚠ Higher risk of weight gain (MC4R) FDA Use 50% of standard dose.	H	**2D6**, 3A4/5
	Cariprazine (Vraylar®)			3A4/5
	Clozapine (Clozaril®)	⚠ Higher risk of weight gain (MC4R)	M	1A2, **2D6**, ABCB1
	Iloperidone (Fanapt®)	⚠ Higher risk of weight gain (MC4R) FDA Use 50% of standard dose.	H	**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) DPWG Use 67% of the standard dose. If side effects occur, reduce the dose further to 50% of standard dose.	H	**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®)		H	**2D6**
	Fluphenazine (Prolixin®)		H	**2D6**
	Haloperidol (Haldol®)	DPWG Use 60% of standard dose.	H	**2D6**, 3A4/5
	Loxapine (Adasuve®, Loxitane®)			
	Perphenazine (Trilafon®)		H	1A2, **2D6**
	Pimozide (Orap®)	DPWG 12 years and older: Max dose is 10 mg/day. Younger than 12 years: No more than 0.05 mg/kg/day to a max of 2 mg/day.	H	**2D6**, 3A4/5
	Thioridazine (Mellaril®)	FDA Contraindicated	H	**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®)			2C19, 3A4/5, UGT2B15
	Hydroxyzine (Vistaril®)			
	Lorazepam (Ativan®)			UGT2B15
	Oxazepam (Serax®)			UGT2B15
	Temazepam (Restoril®)			UGT2B15

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Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations	Drug Level	Pharmacokinetics
	ADHD MEDICATIONS			
Dopaminergic Stimulants	**Amphetamine-Dextroamphetamine** (Adderall®, Evekeo®)	Higher odds of response (COMT) FDA: Consider lower starting dose or use alternative.	M	2D6
Dopaminergic Stimulants	**Dexmethylphenidate** (Focalin®)	Higher odds of response (ADRA2A,COMT)		
Dopaminergic Stimulants	**Dextroamphetamine** (Dexedrine®)	Higher odds of response (COMT)	M	2D6
Dopaminergic Stimulants	**Lisdexamfetamine** (Vyvanse®)	Higher odds of response (COMT)	M	2D6
Dopaminergic Stimulants	**Methylphenidate** (Ritalin®, Concerta®)	Higher odds of response (ADRA2A,COMT)		
Other	**Atomoxetine** (Strattera®)	CPIC: Pediatric dosing: Initiate 0.5 mg/kg/day and if no response after 2 weeks, consider checking blood level. Adult dosing: See link.	H	2D6
Other	**Clonidine** (Kapvay®)			
Other	**Guanfacine** (Intuniv®)			3A4/5
Other	**Viloxazine** (Qelbree®)		M	2D6
	SUPPLEMENTS			
	L-methylfolate (Deplin®)	May benefit from methylfolate supplementation (MTHFR)		

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Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations		Drug Level	Pharmacokinetics
	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®)				1A2, 2C19, 3A4/5
	Suvorexant (Belsomra®)				3A4/5
	Zaleplon (Sonata®)				3A4/5
	Zolpidem (Ambien®)				1A2, 3A4/5
	PAIN				
Non-opioid analgesics	**Acetaminophen** (Tylenol®)				UGT2B15
Non-opioid analgesics	**Celecoxib** (Celebrex®)	CPIC	Initiate with lowest standard starting dose and titrate with caution.	M	**2C9**
Non-opioid analgesics	**Diclofenac** (Voltaren®, Cataflam®)			L	**2C9**
Non-opioid analgesics	**Flurbiprofen** (Ansaid®)	CPIC	Initiate with lowest standard starting dose and titrate with caution.	M	**2C9**
Non-opioid analgesics	**Ibuprofen** (Advil®, Motrin®)	CPIC	Initiate with lowest standard starting dose and titrate with caution.	M	**2C9**
Non-opioid analgesics	**Ketorolac** (Toradol®)				
Non-opioid analgesics	**Meloxicam** (Mobic®)	CPIC	Initiate 50% of the lowest standard starting dose and titrate dose to clinical effect or 50% of max dose.	M	**2C9**
Non-opioid analgesics	**Naproxen** (Aleve®, Naprosyn®)			L	**2C9**
Non-opioid analgesics	**Piroxicam** (Feldene®)	CPIC	Choose alternative not significantly impacted by CYP2C9.	M	**2C9**

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Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations		Drug Level	Pharmacokinetics
	PAIN				
Opioid analgesics	**Alfentanil** (Alfenta®)				3A4/5
	Codeine	CPIC	Prodrug: Avoid use. Greatly reduced formation of morphine (active metabolite) leading to diminished analgesia.	H	**2D6**, ABCB1
	Fentanyl (Duragesic®)				3A4/5, ABCB1
	Hydrocodone	CPIC	Prodrug: Decreased metabolism to hydromorphone (active metabolite). Use label recommended dose. If no response, consider a non-codeine or non-tramadol opioid.	H	**2D6**, 3A4/5
	Hydromorphone (Dilaudid®)				
	Methadone (Methadose®)				2B6, 3A4/5
	Morphine (MS Contin®)				ABCB1
	Oxycodone (Oxycontin®)	CPIC	No dose recommendation.	H	**2D6**, 3A4/5, ABCB1
	Oxymorphone				
	Tapentadol (Nucynta®)				
	Tramadol (Ultram®)	CPIC	Prodrug: Avoid use. Greatly reduced formation of active metabolite leading to diminished analgesia.	H	**2D6**, 3A4/5, ABCB1
	MISCELLANEOUS				
	Buprenorphine (Butrans®)				3A4/5
	Buprenorphine/Naloxone (Suboxone®)				3A4/5
	Cannabidiol (CBD) (Epidiolex®)				3A4/5, 2C19
	Deutetrabenazine (Austedo®)	FDA	Max daily dose: 36 mg; Max single dose: 18 mg	H	**2D6**
	Dextromethorphan/Quinidine (Nuedexta®)			H	**2D6**, 3A4/5, 2B6
	Naltrexone (Vivitrol®)				
	Phenytoin/Fosphenytoin (Dilantin®, Cerebyx®)	CPIC	Do not initiate therapy: Higher risk of drug induced skin reactions (HLA-B)	M	2C19, **2C9**, ABCB1
	Valbenazine (Ingrezza®)	FDA	Max dose: 40 mg/day	M	3A4/5, **2D6**

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Gene-Drug Associations

Class	Medication	Pharmacogenetic Associations	Drug Level	Pharmacokinetics
	STATINS			
	Atorvastatin (Lipitor®)			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®)			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

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

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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
CYP2D6 **PM** *4/*4 Duplication [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 CYP2D6
UGT1A4 **UM** *1a/*3b [Increased 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
ABCB1 **(rs2032583)** A/G [Increased absorption/ penetration]	*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
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)
CYP2C19 **NM** *1/*1 [Normal activity]	*Variations in the CYP2C19 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)

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Pharmacokinetic Gene Variations

Gene Results	Therapeutic Implications	Guide	Clinical Impact
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)
UGT2B15 **NM** *1/*1 [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 **(rs1045642)** G/G [Normal activity]	***ATP Binding Cassette B1 (ABCB1)*** *encodes for P-glycoprotein (P-gp). P-gp is a drug efflux pump that reduces the intestinal absorption and blood-brain barrier penetration of certain drugs* • **This genotype is associated with normal activity of P-gp**		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)
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)

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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] • **Increased side effect risk with SSRIs** • Potential for increased cortisol release in response to stress	⚠	**Assess alternatives to SSRIs** in individuals with depression **SNRIs** or other **non-SSRI antidepressants** may be considered if clinically indicated
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
COMT Val/Val [High activity]	*Catechol-O-Methyltransferase (COMT) is an enzyme responsible for breakdown of dopamine in the frontal cortex of the brain* • Risk for increased COMT enzyme activity, and a parallel **decrease in frontal cortex dopamine** and working memory • **Dopaminergic stimulants may lead to greater improvements in executive function** as compared to Met allele carriers • Electroconvulsive therapy (ECT) has been associated with improved response in Val/Val patients with treatment-resistant depression. Transcranial magnetic stimulation (TMS) has been demonstrated to increase dopamine in the prefrontal cortex, but data evaluating the effect of COMT on TMS response has been limited.	💡	**Dopamine enhancing agents** 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]	💡	**Methylphenidate** may be considered for ADHD if clinically indicated

⚠ 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

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Pharmacodynamic Gene Variations

Gene Results	Therapeutic Implications	Guide	Clinical Impact
HLA-B *15:02 Positive [Increased risk of skin reactions]	*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 severe drug induced skin reactions, including Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) • **This genotype is associated with increased risk of skin reactions with carbamazepine, oxcarbazepine, phenytoin, fosphenytoin and lamotrigine** [A] [1A] • Based on clinical data or similar drug structure, phenobarbital and eslicarbazepine may also be associated with increased risk of skin reactions in patients with this genotype		**Do not initiate carbamazepine, oxcarbazepine, phenytoin, fosphenytoin or lamotrigine; caution with eslicarbazepine or phenobarbital**
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
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
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
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

 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

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Pharmacodynamic Gene Variations

Gene Results	Therapeutic Implications	Guide	Clinical Impact
CACNA1C G/A [Altered neuronal signaling]	*Calcium Channel (CACNA1C) is a subunit of L-type voltage gated calcium channels, which are involved in excitatory signaling in the brain* • Altered calcium signaling may be clinically associated with impairment of mood or cognition		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

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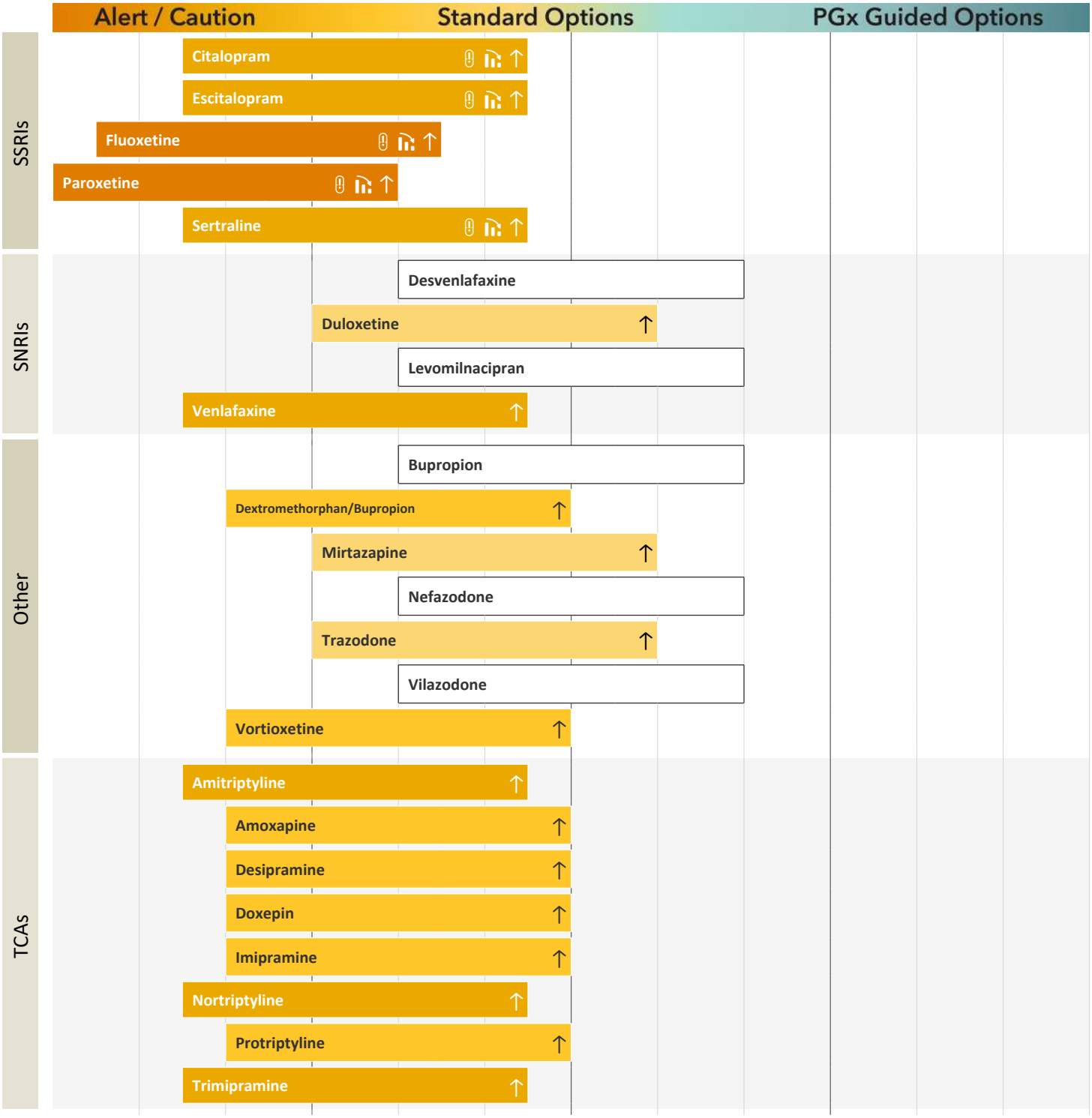
Depression Summary



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 on the Genomind Precision Health Platform.

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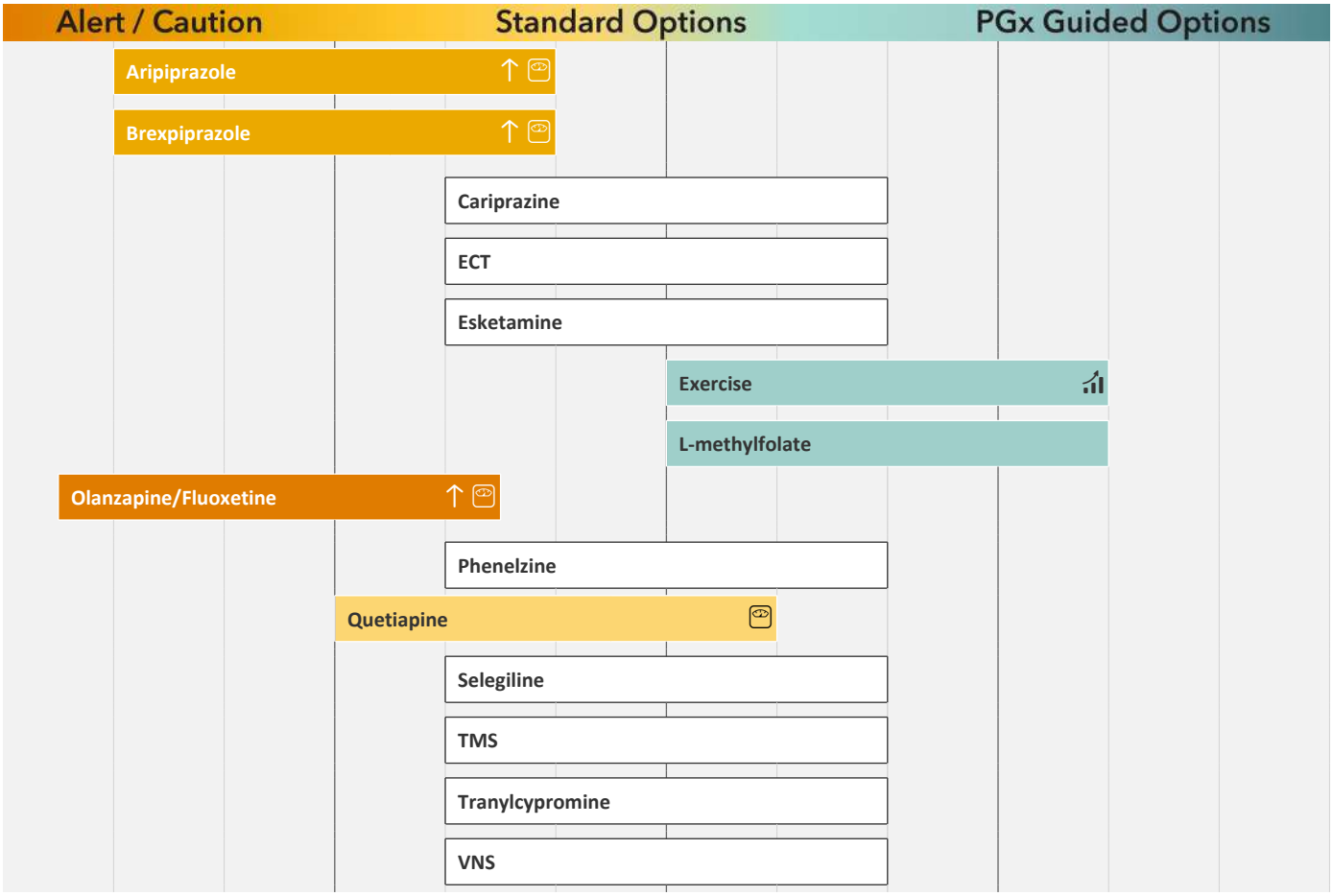
Depression Augmentation Summary



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

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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 [02/02/2023]

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/

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