GENOMIND®

PROFESSIONAL PGx™

PERSONAL. PROVEN. PRECISE.

Patient:	**Example Patient**	Sample ID:	**1000001111**
Patient DOB:	**07/31/1973**	Accession ID:	**91111**
Ordering Clinician:	**Example Clinician**	Sample Collection Date:	**04/01/2019**
Sample Type:	**Buccal**	Sample Received Date:	**04/02/2019**
Assay Ordered:	**Genomind Professional PGx 3.0**	Report Date:	**04/05/2019 10:17 AM**

Electronically Signed By
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Genomind Professional PGx is intended to assist health care professionals in the selection of safe and appropriate pharmaceuticals and other treatment modalities for patients with mental illness and other brain disorders. 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.

Personalized Consultation Available for Clinicians

A complimentary consultation, performed by our expert psychopharmacologists, is included with all Genomind® Professional PGx™ tests.

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*Diagnosis specific summaries are available for the diagnoses of depression, anxiety & related disorders, bipolar disorder, pain management and ADHD. The provided pages in this report are the closest fit for this individual's diagnosis, as provided to us. All 5 summaries, however, are available to you in the Summary Diagnoses Pages.

Disclaimer: The following report provides a summary of the pharmacokinetic and pharmacodynamic impact certain genes can have on particular drugs. This report is intended to serve as a guide for health care professionals to compare different medication options based on an individual patient's genetics. This report is not intended to recommend a particular course of treatment or medication for a patient. Prescribing health care professionals must use their independent medical judgment and are solely responsible for determining the most appropriate medication for their patients. The clinician must consider other relevant clinical factors in determining which is the most appropriate medication. The test results in this report are intended to be prognostic and not diagnostic. The understanding of the relationship between genetics and pharmacokinetics and pharmacodynamics changes periodically; this report will not be updated to reflect new information. A White Paper summarizing individual gene-drug associations, strength of evidence and effect size is available upon request.

I. PHARMACODYNAMIC GENE VARIATIONS

GENE RESULT	THERAPEUTIC IMPLICATIONS	GUIDE	CLINICAL IMPACT
SLC6A4 S/S [Low Activity]	***Serotonin Transporter (SLC6A4)*** *is a synaptic transporter protein responsible for serotonin reuptake* • SSRIs act by blocking this transporter to produce a therapeutic response • In Caucasians, **lower likelihood of remission and increased side effect risk with SSRIs** • Potential for increased cortisol release in response to stress	⚠	**Assess alternatives to SSRIs** in Caucasians **Therapeutic options: 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 *Caucasian ancestry*** may have a **poorer response to SSRIs**, and **improved response to SNRIs or TCAs**. Further studies need to confirm these findings • Studies show that **Met carriers of *Asian ancestry*** may have an **improved response to SSRIs** • **Exercise** has been linked to improvements in cognition and stress response, with **Met carriers showing a more pronounced response**	💡	**Therapeutic options:** increased levels of **physical activity/exercise** if clinically appropriate **Ethnicity dependent antidepressant response**
MTHFR C677T: C/T A1298C: A/C [Low to intermediate activity]	***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 • L-methylfolate may be an effective monotherapy for patients with major depressive disorder	💡	**Therapeutic options: L-methylfolate** may be used 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 Val/Met or Met/Met patients • Brain stimulation therapies such as electroconvulsive therapy **(ECT)** and transcranial magnetic stimulation **(TMS)** have been demonstrated to increase dopamine in the prefrontal cortex or are associated with improved response in Val/Val patients • Studies have shown that Val/Val patients used **higher doses of opioids to achieve analgesia**	⚠ 💡	**Monitor opioid dose response** **Therapeutic options: 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 stimulants (mostly methylphenidate studies)** for symptoms of attention deficit/hyperactivity disorder in children and adolescents as compared to those with the C/C genotype	💡	**Therapeutic options: methylphenidate** may be considered for attention deficit/hyperactivity disorder if clinically indicated

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I. PHARMACODYNAMIC GENE VARIATIONS

GENE RESULT	THERAPEUTIC IMPLICATIONS	GUIDE	CLINICAL IMPACT
HLA-B *15:02 Detected [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, and fosphenytoin** • Based on clinical data or similar drug structure, lamotrigine, phenobarbital, and eslicarbazepine may also be associated with increased risk of skin reactions in patients with this genotype • https://cpicpgx.org/guidelines/guideline-for-carbamazepine-and-hla-b/ • https://cpicpgx.org/guidelines/guideline-for-phenytoin-and-cyp2c9-and-hla-b		**Do not initiate carbamazepine, oxcarbazepine, phenytoin or fosphenytoin. Caution with lamotrigine, 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 2nd generation antipsychotics** **Higher risk:** clozapine; olanzapine **Medium risk:** aripiprazole; brexpiprazole, iloperidone; paliperidone; quetiapine; risperidone **Lower risk:** asenapine; cariprazine; lurasidone; ziprasidone	 	**Higher risk of weight gain and metabolic changes** with various 2nd generation antipsychotics **Anti-obesity interventions** may be used 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 Not Detected [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
5HT2C C/C [Standard weight gain risk]	***Serotonin Receptor 2C (5HT2C)*** *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; paliperidone; quetiapine; risperidone **Lower risk:** asenapine; cariprazine; lurasidone; ziprasidone		**Assess weight gain risk** with various second generation antipsychotics
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

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I. PHARMACODYNAMIC GENE VARIATIONS

GENE RESULT	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 • **A single A allele confers only modest changes to measurable physiological parameters**		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* • GRIK1 is involved in response to topiramate for alcohol abuse • Patients of European descent with the A allele may be **less likely to respond to topiramate for alcohol use disorder**; future studies, however, are needed to confirm these findings		No known significant clinical impact

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II. PHARMACOKINETIC GENE VARIATIONS

GENE RESULT	THERAPEUTIC IMPLICATIONS	GUIDE	CLINICAL IMPACT
CYP2C9 **IM** *1/*3 [Intermediate activity]	***Intermediate metabolizer:*** *Risk of* ***elevated serum levels*** *& drug interactions, or decreased production of active metabolites* • **A dose adjustment or alternate therapy may be considered**	⚠	Be advised that there may be altered exposure to medications metabolized by CYP2C9
CYP2D6 **PM** *4/*4 [Low activity]	***Poor metabolizer:*** *Risk of* ***elevated serum levels*** *& drug interactions, or decreased production of active metabolites* • **A dose adjustment or alternate therapy may be considered**	⚠	Be advised that there may be altered exposure to medications metabolized by CYP2D6
UGT1A4 **UM** *1a/*3b [Increased activity]	***Ultrarapid metabolizer:*** *Risk of* ***decreased serum levels****. Possible adverse events associated with increased active metabolites* • **A dose adjustment or alternate therapy may be considered**	⚠	Be advised that there may be altered exposure to medications metabolized by UGT1A4
ABCB1 **(rs2032583)** A/G [Increased absorption/ penetration]	***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 **increased exposure and side effect burden to several antidepressants** • Studies have shown, however, that people with this variant **responded to lower doses**, had higher remission rates, or decreased time to response for citalopram, escitalopram, paroxetine, venlafaxine, amitriptyline, nortriptyline, or trimipramine	⚠	Be advised that there may be increased exposure to medications affected by ABCB1
CYP1A2 **EM** *1F/*1F [Normal activity but sensitive to induction]	***Extensive metabolizer (Induction Sensitive):*** *This genotype confers* ***normal activity, except in the presence of inducers.*** *In the presence of inducers, risk of* ***decreased serum levels. Also 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 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**	⚠	Be advised that there may be altered exposure to medications metabolized by CYP1A2 in the presence of inducers
CYP2B6 **EM** *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 **EM** *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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II. PHARMACOKINETIC GENE VARIATIONS

GENE RESULT	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 **EM** *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 exposure is expected (other factors may influence drug exposure)

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III. GENE DRUG INTERACTION SUMMARY

CLASS	MEDICATION	PHARMACODYNAMIC ASSOCIATIONS	PHARMACODYNAMIC GENE	DRUG EXPOSURE	PHARMACOKINETIC GENE
	ANTIDEPRESSANTS				
SSRIs	**Citalopram** (Celexa®)	Lower odds of remission or response and increased side effects in Caucasians Higher odds of remission or response in Asians	SLC6A4,BDNF	↑	2C19, P-gp
SSRIs	**Escitalopram** (Lexapro®)	Lower odds of remission or response and increased side effects in Caucasians Higher odds of remission or response in Asians	SLC6A4,BDNF	↑	2C19, P-gp
SSRIs	**Fluoxetine** (Prozac®)	Lower odds of remission or response and increased side effects in Caucasians Higher odds of remission or response in Asians	SLC6A4,BDNF	↑	2D6, 2C9
SSRIs	**Fluvoxamine** (Luvox®)	Lower odds of remission or response and increased side effects in Caucasians Higher odds of remission or response in Asians	SLC6A4,BDNF	↑	2D6, 1A2, P-gp
SSRIs	**Paroxetine** (Paxil®)	Lower odds of remission or response and increased side effects in Caucasians Higher odds of remission or response in Asians	SLC6A4,BDNF	↑	2D6, P-gp
SSRIs	**Sertraline** (Zoloft®)	Lower odds of remission or response and increased side effects in Caucasians Higher odds of remission or response in Asians	SLC6A4,BDNF		2C19, 2B6
SNRIs	**Desvenlafaxine** (Pristiq®)				
SNRIs	**Duloxetine** (Cymbalta®)	Possible higher odds of remission or response in Caucasians	BDNF	↑	1A2, 2D6
SNRIs	**Levomilnacipran** (Fetzima®)				3A4/5
SNRIs	**Venlafaxine[1]** (Effexor®)	Possible higher odds of remission or response in Caucasians	BDNF	↑	2D6, 2C19, 3A4/5, P-gp
Other	**Bupropion[1]** (Wellbutrin®)				2B6
Other	**Esketamine** (Spravato®)				2B6, 3A4/5
Other	**Mirtazapine** (Remeron®)			↑	2D6, 3A4/5, 1A2
Other	**Nefazodone**				3A4/5
Other	**Trazodone** (Desyrel®, Oleptro®)			↑	3A4/5, 2D6
Other	**Vilazodone** (Viibryd®)				3A4/5
Other	**Vortioxetine** (Trintellix®)			↑	2D6, 3A4/5

Alert/Caution | PGx Guided Options | Reduced Drug Exposure with 1A2 Inducers | ↑↓ Drug Exposure

[1] See Gene Drug Interaction Summary footnotes for more information

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CLASS	MEDICATION	PHARMACODYNAMIC ASSOCIATIONS	PHARMACODYNAMIC GENE	DRUG EXPOSURE	PHARMACOKINETIC GENE
	ANTIDEPRESSANTS				
TCAs	**Amitriptyline** (Elavil®)			↑	2D6, 2C19, P-gp
TCAs	**Amoxapine** (Asendin®)			↑	2D6
TCAs	**Clomipramine** (Anafranil®)	Possible higher odds of remission or response in Caucasians	BDNF	↑	2D6, 2C19, 1A2
TCAs	**Desipramine** (Norpramin®)			↑	2D6
TCAs	**Doxepin** (Sinequan®)			↑	2D6, 2C19
TCAs	**Imipramine** (Tofranil®)			↑	2D6, 2C19
TCAs	**Nortriptyline** (Pamelor®)			↑	2D6, P-gp
TCAs	**Protriptyline** (Vivactil®)			↑	2D6
TCAs	**Trimipramine** (Surmontil®)			↑	2D6, 2C19, P-gp
MAOIs	**Phenelzine** (Nardil®)				
MAOIs	**Selegiline** (Eldepryl®, Emsam®)				2B6
MAOIs	**Tranylcypromine** (Parnate®)				
	MOOD STABILIZERS/ANTICONVULSANTS				
	Carbamazepine (Equetro®, Tegretol®)	Do not initiate therapy: Higher risk of drug induced skin reactions	HLA-B		3A4/5
	Gabapentin (Neurontin®)				
	Lamotrigine (Lamictal®)	Possible higher risk of drug induced skin reactions	HLA-B	↓	UGT1A4
	Lithium (Lithobid®, Eskalith®)				
	Oxcarbazepine (Trileptal®, Oxtellar®)	Do not initiate therapy: Higher risk of drug induced skin reactions	HLA-B		
	Pregabalin (Lyrica®)				
	Topiramate (Topamax®)				
	Valproate (Depakote®, Depakene®)			↑	2C9

Alert/Caution | PGx Guided Options | Reduced Drug Exposure with 1A2 Inducers | ↑↓ Drug Exposure

[1] See Gene Drug Interaction Summary footnotes for more information

III. GENE DRUG INTERACTION SUMMARY

CLASS	MEDICATION	PHARMACODYNAMIC ASSOCIATIONS	PHARMACODYNAMIC GENE	DRUG EXPOSURE	PHARMACOKINETIC GENE
	ANTIPSYCHOTICS				
2nd Generation Antipsychotics	**Aripiprazole** (Abilify®)	Higher risk of weight gain	MC4R	↑	2D6, 3A4/5, P-gp
	Asenapine (Saphris®)			↓	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, 3A4/5, P-gp
	Iloperidone (Fanapt®)	Higher risk of weight gain	MC4R	↑	2D6, 3A4/5
	Lurasidone (Latuda®)				3A4/5
	Olanzapine (Zyprexa®)	Higher risk of weight gain	MC4R	Reduced Drug Exposure with 1A2 Inducers	1A2, P-gp
	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, P-gp
	Ziprasidone (Geodon®)				

Alert/Caution | PGx Guided Options | Reduced Drug Exposure with 1A2 Inducers | ↑↓ Drug Exposure

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CLASS	MEDICATION	PHARMACODYNAMIC ASSOCIATIONS	PHARMACODYNAMIC GENE	DRUG EXPOSURE	PHARMACOKINETIC GENE
	ANTIPSYCHOTICS				
1st Generation Antipsychotics	**Chlorpromazine** (Thorazine®)			↑	2D6
	Fluphenazine (Prolixin®)			↑	2D6
	Haloperidol (Haldol®)			↑	2D6, 3A4/5
	Loxapine (Adasuve®, Loxitane®)			🚬↓	3A4/5, 1A2
	Perphenazine (Trilafon®)			↑	2D6
	Pimozide (Orap®)			↑	2D6, 3A4/5
	Thioridazine (Mellaril®)			↑	2D6
	Thiothixene (Navane®)			🚬↓	1A2
	Trifluoperazine (Stelazine®)			↓	1A2, UGT1A4
	ANXIOLYTICS				
	Alprazolam (Xanax®)				3A4/5
	Buspirone (Buspar®)				3A4/5
	Chlordiazepoxide (Librium®)				3A4/5, UGT2B15
	Clonazepam (Klonopin®)				3A4/5
	Clorazepate (Tranxene®)				UGT2B15
	Diazepam (Valium®)				2C19, 3A4/5, UGT2B15
	Hydroxyzine (Vistaril®)				
	Lorazepam (Ativan®)				UGT2B15
	Oxazepam (Serax®)				UGT2B15
	Temazepam (Restoril®)				UGT2B15

Alert/Caution PGx Guided Options Reduced Drug Exposure with 1A2 Inducers ↑↓ Drug Exposure

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CLASS	MEDICATION	PHARMACODYNAMIC ASSOCIATIONS	PHARMACODYNAMIC GENE	DRUG EXPOSURE	PHARMACOKINETIC GENE
	ADHD MEDICATIONS				
Dopaminergic Stimulants	**Amphetamine-Dextroamphetamine** (Adderall®, Evekeo®)	Higher odds of response	COMT	↑	2D6
	Dexmethylphenidate (Focalin®)	Higher odds of response	ADRA2A,COMT		
	Dextroamphetamine (Dexedrine®, Procentra®, Zenzedi®)	Higher odds of response	COMT	↑	2D6
	Lisdexamfetamine (Vyvanse®)	Higher odds of response	COMT	↑	2D6
	Methamphetamine (Desoxyn®)	Higher odds of response	COMT	↑	2D6
	Methylphenidate (Ritalin®, Concerta®, Daytrana®, Metadate®)	Higher odds of response	ADRA2A,COMT		
Other	**Atomoxetine** (Strattera®)			↑	2D6
	Clonidine (Kapvay®)			↑	2D6
	Guanfacine (Intuniv®)				3A4/5
	SUPPLEMENTS				
	L-methylfolate (Deplin®)	May benefit from methylfolate supplementation	MTHFR		
	SLEEP MODULATORS				
	Armodafinil (Nuvigil®)				3A4/5
	Eszopiclone (Lunesta®)				3A4/5
	Modafinil (Provigil®)				3A4/5
	Ramelteon (Rozerem®)			Reduced with 1A2 Inducers	1A2
	Suvorexant (Belsomra®)				3A4/5, 2C19
	Zaleplon (Sonata®)				3A4/5
	Zolpidem (Ambien®)				3A4/5

Alert/Caution | PGx Guided Options | Reduced Drug Exposure with 1A2 Inducers | ↑↓ Drug Exposure

[1] See Gene Drug Interaction Summary footnotes for more information

III. GENE DRUG INTERACTION SUMMARY

CLASS	MEDICATION	PHARMACODYNAMIC ASSOCIATIONS	PHARMACODYNAMIC GENE	DRUG EXPOSURE	PHARMACOKINETIC GENE
PAIN					
Non-opioid analgesics	**Acetaminophen** (Tylenol®)				
	Celecoxib (Celebrex®)			↑	2C9
	Diclofenac (Voltaren®, Cataflam®)			↑	2C9
	Flurbiprofen (Ansaid®)			↑	2C9
	Ibuprofen (Advil®, Motrin®)			↑	2C9
	Ketorolac (Toradol®)				
	Meloxicam (Mobic®)			↑	2C9
	Naproxen (Aleve®, Naprosyn®)			↑	1A2, 2C9
	Piroxicam (Feldene®)			↑	2C9
Opioid analgesics	**Alfentanil** (Alfenta®)	Decreased sensitivity	COMT		3A4/5
	Codeine[1]	Decreased sensitivity	COMT	↑	2D6, P-gp
	Fentanyl (Duragesic®)	Decreased sensitivity	COMT		3A4/5, P-gp
	Hydrocodone[1] (Vicodin®, Norco®, Lorcet®)	Decreased sensitivity	COMT	↑	2D6, 3A4/5
	Hydromorphone (Dilaudid®)	Decreased sensitivity	COMT		
	Meperidine (Demerol®)	Decreased sensitivity	COMT		2B6, 3A4/5
	Methadone (Dolophine®, Methadose®)	Decreased sensitivity	COMT		3A4/5, 2B6
	Morphine (MS Contin®, Kadian®)	Decreased sensitivity	COMT		P-gp
	Oxycodone (Oxycontin®)	Decreased sensitivity	COMT	↑	2D6, 3A4/5, P-gp
	Oxymorphone (Opana®)	Decreased sensitivity	COMT		
	Tapentadol (Nucynta®)	Decreased sensitivity	COMT		
	Tramadol[1] (Ultram®)	Decreased sensitivity	COMT	↑	2D6, 3A4/5, P-gp

Alert/Caution PGx Guided Options Reduced Drug Exposure with 1A2 Inducers ↑↓ Drug Exposure

[1] See Gene Drug Interaction Summary footnotes for more information

III. GENE DRUG INTERACTION SUMMARY

CLASS	MEDICATION	PHARMACODYNAMIC ASSOCIATIONS	PHARMACODYNAMIC GENE	DRUG EXPOSURE	PHARMACOKINETIC GENE
MISCELLANEOUS					
	Dextromethorphan/Quinidine (Nuedexta®)			↑	2D6, 3A4/5
	Baclofen (Lioresal®)				
	Buprenorphine/Naloxone (Suboxone®)				3A4/5
	Buprenorphine (Butrans®)	⚠ Decreased sensitivity	COMT		3A4/5
	Cannibidiol (CBD) (Epidiolex®)				3A4/5, 2C19
	Carisoprodol (Soma®)				2C19
	Cyclobenzaprine (Flexeril®)			🚬	1A2
Rx	**Deutetrabenazine** (Austedo®)			↑	2D6
	Metaxalone (Skelaxin®)				
	Methocarbamol (Robaxin®)				
	Naltrexone (Revia®, Vivitrol®)				
Rx 📋	**Phenytoin/Fosphenytoin** (Dilantin®, Cerebyx®)	⚠ Do not initiate therapy: Higher risk of drug induced skin reactions	HLA-B	↑	2C19, 2C9
	Tizanidine (Zanaflex®)			🚬	1A2
Rx	**Valbenazine** (Ingrezza®)			↑	3A4/5, 2D6

⚠ Alert/Caution PGx Guided Options 🚬 Reduced Drug Exposure with 1A2 Inducers ↑↓ Drug Exposure

Rx 📋 [1] See Gene Drug Interaction Summary footnotes for more information

GENE DRUG INTERACTION SUMMARY FOOTNOTES

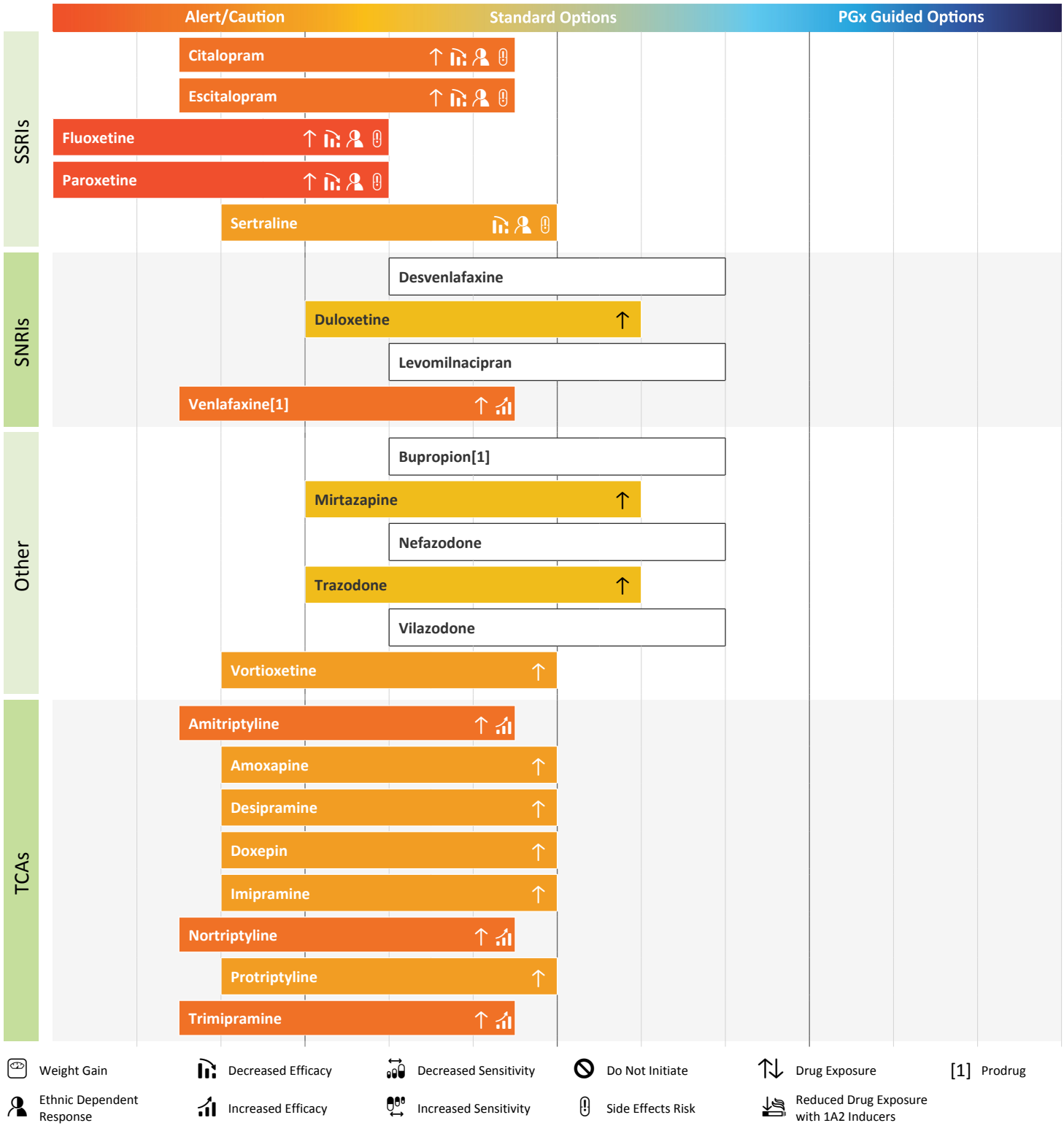
[1] Prodrug or highly active metabolite - requiring activation by the liver; CYP450 IMs/PMs may experience lower efficacy due to reduced conversion to the active metabolite and higher levels of the parent drug; CYP450 UMs may experience increased conversion of the parent drug, and higher levels of the active metabolite

Rx Medication has FDA biomarker guidance available
- https://www.fda.gov/downloads/Drugs/ScienceResearch/UCM578588.pdf

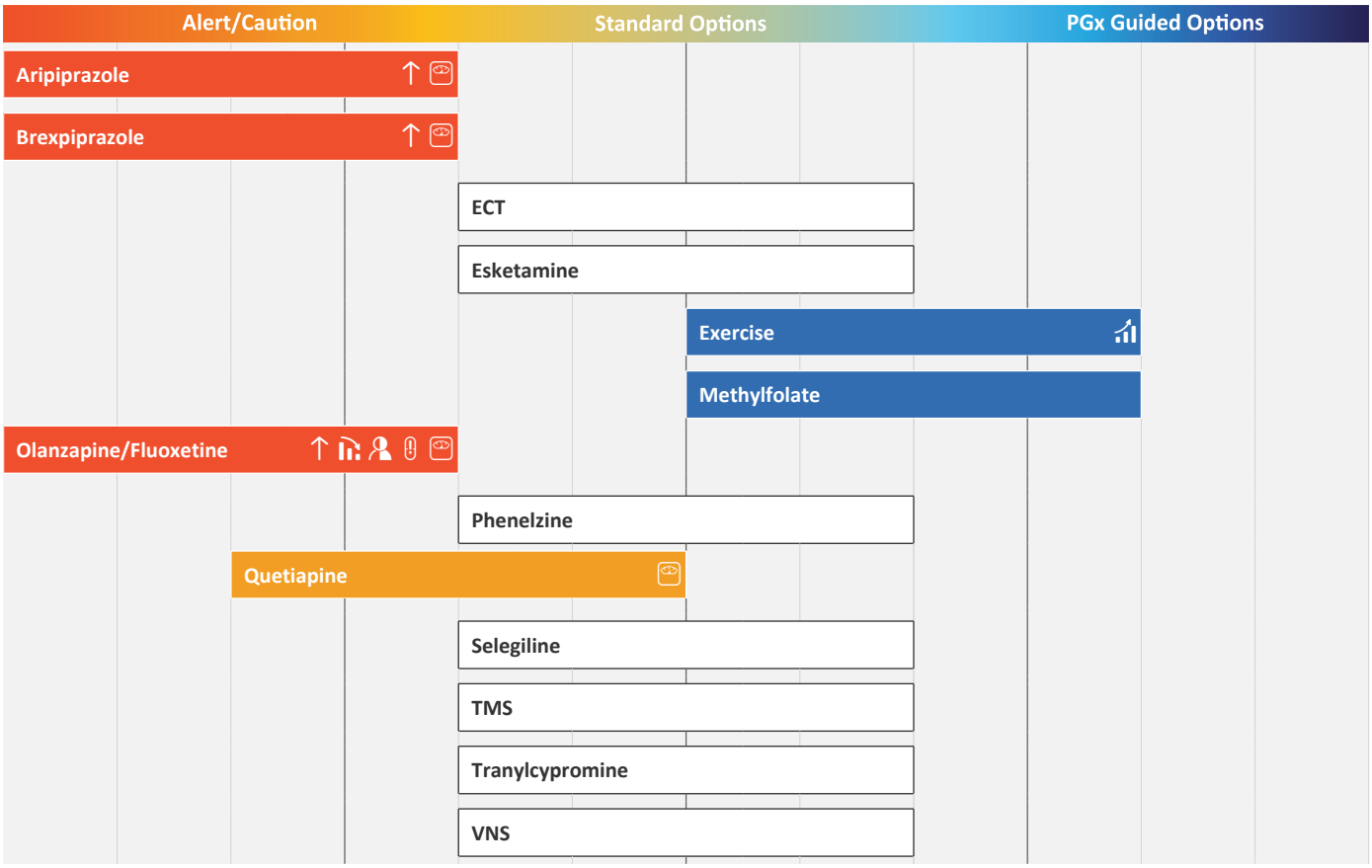
📋 Medication has CPIC® or DPWG biomarker guidance available
- https://cpicpgx.org/guidelines/
- https://www.pharmgkb.org/page/dpwg

*References for the drug interaction summary are available upon request

IV. DEPRESSION SUMMARY



IV. DEPRESSION AUGMENTATION SUMMARY



Weight Gain
Decreased Efficacy
Decreased Sensitivity
Do Not Initiate
Drug Exposure
[1] Prodrug
Ethnic Dependent Response
Increased Efficacy
Increased Sensitivity
Side Effects Risk
Reduced Drug Exposure with 1A2 Inducers

V. TEST METHODOLOGY/LITERATURE REFERENCE

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. This 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 pharmacogenetics tests like Genomind Professional PGx Express, undetected genetic and/or non-genetic factors such as drug-drug interactions may impact the phenotype. The Genomind Professional PGx Express report is based on a current understanding of the clinical relevance of the variant identified, penetrance, phenotype predictions, and recurrence risks.

Variants tested include 5HT2C rs3813929; ABCB1 C3435T rs1045642; ABCB1 rs2032583; ADRA2A rs1800544; ANK3 rs10994336; BDNF rs6265; CACNA1C rs1006737; COMT rs4680; CYP1A2 *1B, *1C, *1D, *1E, *1F, *1K and *11; CYP2B6 *4, *5, and *6; 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 with reflex testing for presence of HLA-B*15:13 for all positive samples and Sanger sequencing for all double positive samples; HLA-A*31:01 rs1061235; HTR2A rs7997012; MC4R rs489693; MTHFR rs1801131 and rs1801133; OPRM1 rs1799971; SLC6A4 rs25531 and rs63749047; 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 3.0 [05/20/2019]

LITERATURE REFERENCES

THE LITERATURE INFORMATION UPON WHICH THIS REPORT RELIES WAS AGGREGATED AND REVIEWED BY GENOMIND, INC. SUMMARIES OF THESE NUMBERED REFERENCES BELOW ARE AVAILABLE UPON REQUEST OF GENOMIND'S COMPREHENSIVE LITERATURE SUMMARY [V2019-05].

Gene	References
5HT2C	10-24
ADRA2A	25-33
ANK3	34-57
BDNF	58-78
CACNA1C	34, 37-39, 42, 47-55, 79-97
COMT	28, 98-131
DRD2	132-138
GRIK1	139-143
HLA-A *31:01	145-149
HLA-B *15:02	146-147, 150-157
HTR2A	71, 158-164
MC4R	21, 23, 165-172

Gene	References
MTHFR	173-185
OPRM1	186-197
SLC6A4	163, 198-214
ABCB1	215-233
UGT1A4	235-238
UGT2B15	238-241
CYP1A2	20, 164, 247-250, 252, 258-281, 286-288
CYP2B6	247-252, 273, 284, 288-305
CYP2C9	247-257, 261, 288, 306-312
CYP2C19	15, 242, 244, 247-252, 254-255, 273, 284, 288, 306, 311-323
CYP2D6	15, 20, 244-245, 247-252, 254-255, 258, 261, 273-274, 288, 306, 311-314, 322, 324-344
CYP3A4/5	15, 20, 247-252, 258, 261, 273-274, 282-285

VI. PATIENT'S GENOMIND RX METATYPE™ CARD

Your Genomind Rx MetaType™ wallet card includes information on six liver enzymes that are responsible for the metabolism of most drugs, and identifies your unique enzyme profile (your genotype). It is intended for use by your current, additional or future healthcare providers. This genetic information is mentioned in the FDA prescribing information of many drugs, and may provide useful prescribing recommendations. The websites on the back of the card provide more information.

GENOMIND® PROFESSIONAL PGx™

Rx MetaType™ Card

Example Patient

#1000001111

Gene	Genotype	Phenotype	Clinical Meaning*
CYP1A2	*1F/*1F	Extensive	Normal Metabolism, but ↑ metabolism in smokers
CYP2B6	*1/*1	Extensive	Normal Metabolism
CYP2C19	*1/*1	Extensive	Normal Metabolism
CYP2C9	*1/*3	Intermediate	↓ Metabolism of some drugs
CYP2D6	*4/*4	Poor	↓ Metabolism of some drugs
CYP3A4/5	*1/*1, *3/*3	Normal	Normal Metabolism

GENOMIND® PROFESSIONAL PGx™

Issued Date: 04/05/2019

FOR USE BY HEALTHCARE PROFESSIONALS ONLY

Most medicines are metabolized by liver enzymes. Like blood types, you have a specific genetic profile which can affect the rate of metabolism, and may influence the dose of medicines prescribed for you. You may wish to inform your healthcare provider(s) about your metabolism status, shown on the reverse. More information about specific gene/drug interactions can be found at:

https://drug-interactions.medicine.iu.edu/Clinical-Table.aspx
https://www.pharmgkb.org/guidelines
https://www.fda.gov/downloads/Drugs/ScienceResearch/UCM578588.pdf

***Do not discontinue or change the dose of any medicine without the advice of your healthcare provider. In addition to genetics, other factors may influence your metabolizer status.**

GENOMIND® PROFESSIONAL PGx™

Rx MetaType™ Card

Example Patient

#1000001111

Gene	Genotype	Phenotype	Clinical Meaning*
CYP1A2	*1F/*1F	Extensive	Normal Metabolism, but ↑ metabolism in smokers
CYP2B6	*1/*1	Extensive	Normal Metabolism
CYP2C19	*1/*1	Extensive	Normal Metabolism
CYP2C9	*1/*3	Intermediate	↓ Metabolism of some drugs
CYP2D6	*4/*4	Poor	↓ Metabolism of some drugs
CYP3A4/5	*1/*1, *3/*3	Normal	Normal Metabolism

GENOMIND® PROFESSIONAL PGx™

Issued Date: 04/05/2019

FOR USE BY HEALTHCARE PROFESSIONALS ONLY

Most medicines are metabolized by liver enzymes. Like blood types, you have a specific genetic profile which can affect the rate of metabolism, and may influence the dose of medicines prescribed for you. You may wish to inform your healthcare provider(s) about your metabolism status, shown on the reverse. More information about specific gene/drug interactions can be found at:

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