PHARMACOGENOMIC REPORT

Biron

Psychiatry and ADHD

YOUR RESULTS ARE CONFIDENTIAL. As per the Genetic Non-Discrimination Act (S-201), no person, company or institution, including insurers and employers, can force you to share this report.

DO NOT MAKE ANY CHANGES TO YOUR CURRENT MEDICATION(S) WITHOUT TALKING TO YOUR DOCTOR FIRST. While genetics is important, other factors also contribute to how you react to medications. The final choice of medication used will be based on your health care provider's professional judgement and may be different than what is recommended in this report. This test does not determine your risk of any health problem. It only evaluates select portions of your DNA that help predict how you may react to the medications covered.

ADMINISTRATIVE DATA

Patient Name
First Last Name

Gender: Male
Date of birth: 1000-01-01
Phone Number:
Email: N/A

Ordering Clinician
Dr Grey

Patient Address
N/A

Sample ID: TEST19012314
Sample Type: saliva

Date ordered: 2023-11-10
Date of sample reception: 2023-11-10
Date of report: 2023-11-10

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VARIANT(S) OF VERY IMPORTANT PHARMACOGENES (VIPS)

CYP1A2 IND, CYP2C9 IM, CYP2D6 UM, POR IA, UGT1A1 IM, UGT2B7 variable, UGT2B15 IM.

Very Important Pharmacogenes (VIPs) - visit pharmgkb.org/vips for more information.
Abbreviations - NM: Normal Metaboliser, IM: Intermediate Metaboliser, PM: Poor Metaboliser, RM: Rapid Metaboliser, UM: Ultrarapid Metaboliser, Ind: Inducible Metaboliser, NA: Normal Activity, IA: Intermediate Activity, PA: Poor Activity.

CAUTIONARY INFORMATION - MEDICATIONS TO AVOID OR USE WITH CAUTION

Medication	Identified risk	Recommendation
Codeine	Potential of serious toxicity due to increased formation of morphine (CYP2D6 UM).	Avoid using codeine.[1]
Tramadol Ultram®	Potential of serious toxicity due to increased formation of active metabolite (CYP2D6 UM).	Avoid using tramadol; if an alternative is not possible, consider reducing the dose by 60% and be alert to side effects.[1]

PGx RECOMMENDATIONS - PSYCHIATRY

↑ Dose increase may be required.

↓ Dose reduction may be required.

~ Exposure is difficult to predict, insufficient data to calculate dose adjustments.

✓ All of the tested variants associate with an increased likelihood of a better response, compared to non-carriers.

! > 50% of tested variants are associated with an increased likelihood of a poorer response and/or adverse drug reactions, compared to non-carriers.

✗ Medication not recommended by peer-reviewed guidelines.

Genetic Associations Identified			
Medications	Exposure	Efficacy	Adverse Drug Reactions
Antidepressants			
Selective serotonin reuptake inhibitors (SSRIs)			
Citalopram (Celexa®)	CYP2C19 NM, CYP3A4 NM, ABCB1 - Initiate with recommended dose; a low dose may be adequate.	3/6 variants: increased likelihood of a poorer response (FKBP5, HTR2A, BDNF).	0/3 variants: no increased risk of gastrointestinal or SSRI-induced sexual side effects.
Escitalopram (Cipralex®)	CYP2C19 NM, CYP3A4 NM, ABCB1 - Initiate with recommended dose; a low dose may be adequate.	3/6 variants: increased likelihood of a poorer response (FKBP5, HTR2A, BDNF).	0/3 variants: no increased risk of gastrointestinal or SSRI-induced sexual side effects.
Fluoxetine (Prozac®)	CYP2D6 UM - Initiate with recommended dose but monitor more closely for response; may require a higher dose.	3/6 variants: increased likelihood of a poorer response (FKBP5, HTR2A, BDNF).	no marker available
Sertraline (Zoloft®)	CYP2B6 NM, CYP2C19 NM, ABCB1 - Initiate with recommended dose; a low dose may be adequate.	2/5 variants: increased likelihood of a poorer response (BDNF, FKBP5).	0/3 variants: no increased risk of gastrointestinal or SSRI-induced sexual side effects.
Fluvoxamine (Luvox®)	↑ CYP2D6 UM - Initiate with recommended starting dose but may require a higher dose. If patient does not respond to recommended maintenance dosing, consider an alternative drug not predominantly metabolized by CYP2D6.	3/6 variants: increased likelihood of a poorer response (FKBP5, HTR2A, BDNF).	no marker available
Paroxetine (Paxil®)	✗ CYP2D6 UM - Consider an alternative drug not predominantly metabolized by CYP2D6 due to potential lack of efficacy.[2]	3/6 variants: increased likelihood of a poorer response (FKBP5, HTR2A, BDNF).	no marker available
Serotonin–norepinephrine reuptake inhibitors (SNRIs)			
Desvenlafaxine (Pristiq®)	UGT1A1 IM, UGT2B15 IM - Initiate with recommended dose; a low dose may be adequate.	1/2 variants: increased likelihood of a poorer response (FKBP5).	no marker available
Levomilnacipran (Fetzima®)	CYP3A4 NM, ABCB1 - Initiate with recommended dose; a low dose may be adequate.	1/2 variants: increased likelihood of a poorer response (FKBP5).	no marker available
Duloxetine (Cymbalta®)	↑ CYP1A2 Ind, CYP2D6 UM - Initiate therapy with recommended starting dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	1/3 variants: increased likelihood of a poorer response (FKBP5).	no marker available
Venlafaxine (Effexor XR®)	↑ CYP2D6 UM - Consider a dose increase up to 150% of the standard dose. If dose adjustment does not result in efficacy, consider an alternative drug not predominantly metabolized by CYP2D6.[3]	! 3/4 variants: increased likelihood of a poorer response (COMT, FKBP5, SLC6A2).	no marker available
Other antidepressants			

Genetic Associations Identified

Medications	Exposure	Efficacy	Adverse Drug Reactions
Esketamine (Spravato®)	POR - Initiate therapy with recommended starting dose; a low dose may be adequate.	0/1 variant: no increased likelihood of a poorer response.	0/1 variant: no increased risk of emergent hypertension.
Ketamine (Ketalar®)	POR - Initiate therapy with recommended starting dose; a low dose may be adequate.	0/1 variant: no increased likelihood of a poorer response.	0/1 variant: no increased risk of emergent hypertension.
Trazodone (Desyrel®)	CYP3A4 NM - Normal exposure	no marker available	no marker available
Vilazodone (Viibryd®)	CYP3A4 NM, ABCB1 - Initiate with recommended dose; a low dose may be adequate.	no marker available	no marker available
Bupropion (Wellbutrin®)	POR - Initiate with recommended dose; a low dose may be adequate.	! 1/1 variant: increased likelihood of a poorer response for treatment of depressive symptoms (HTR2A).	no marker available
Mirtazapine (Remeron®)	↑ CYP1A2 Ind, CYP2D6 UM - Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	! 2/2 variants: increased likelihood of a poorer response (FKBP5, TPH2).	no marker available
Vortioxetine (Trintellix®)	✕ CYP2D6 UM - Consider an alternative drug not predominantly metabolized by CYP2D6 due to potential lack of efficacy. If vortioxetine use is warranted, initiate with standard starting dose and titrate to maintenance dose based on efficacy and side effects; increasing the target dose by 50% or more may be needed for efficacy.[2]	no marker available	no marker available
Tricyclic antidepressants (TCAs)			
Amitriptyline (Elavil®)	✕ CYP2D6 UM - Avoid tricyclic use due to potential lack of efficacy, or consider titrating to a higher target dose.[4]	! 1/1 variant: increased likelihood of a poorer response (TPH2)	no marker available
Clomipramine (Anafranil®)	✕ CYP2D6 UM - Avoid tricyclic use due to potential lack of efficacy, or consider titrating to a higher target dose.[4]	! 1/1 variant: increased likelihood of a poorer response (TPH2)	no marker available
Desipramine (Norpramin®)	✕ CYP2D6 UM - Avoid tricyclic use due to potential lack of efficacy. If a tricyclic is warranted, consider titrating to a higher dose.[4]	! 1/1 variant: increased likelihood of a poorer response (TPH2)	no marker available
Doxepin (Sinequan®)	✕ CYP2D6 UM - Avoid tricyclic use due to potential lack of efficacy, or consider titrating to a higher target dose.[4]	! 1/1 variant: increased likelihood of a poorer response (TPH2)	no marker available
Imipramine (Tofranil®)	✕ CYP2D6 UM - Avoid tricyclic use due to potential lack of efficacy, or consider titrating to a higher target dose.[4]	! 1/1 variant: increased likelihood of a poorer response (TPH2)	no marker available
Nortriptyline (Aventyl®)	✕ CYP2D6 UM - Avoid tricyclic use due to potential lack of efficacy. If a tricyclic is warranted, consider titrating to a higher dose.[4]	! 1/1 variant: increased likelihood of a poorer response (TPH2)	no marker available
Trimipramine (Surmontil®)	✕ CYP2D6 UM - Avoid tricyclic use due to potential lack of efficacy, or consider titrating to a higher target dose.[4]	! 1/1 variant: increased likelihood of a poorer response (TPH2)	no marker available
Monoamine oxidase inhibitors (MAOs)			
Phenelzine (Nardil®)	no marker available	no marker available	no marker available
Tranylcypromine	no marker available	no marker available	no marker available

Genetic Associations Identified			
Medications	Exposure	Efficacy	Adverse Drug Reactions
(Parnate®)			
Moclobemide (Manerix®)	↑ CYP2D6 UM - Initiate with recommended dose but may require a higher dose.[5]	no marker available	no marker available
Antipsychotics			
1st generation antipsychotics			
Chlorpromazine (Largactil®)	↑ CYP2D6 UM, CYP1A2 Ind - Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	no marker available	no marker available
Fluphenazine (Moditen®)	↑ CYP2D6 UM - Initiate therapy with recommended starting dose but may require a higher dose.	no marker available	no marker available
Haloperidol (Haldol®)	↑ CYP2D6 UM - A higher maintenance dose may be required based on response and tolerance, or consider an alternative drug not predominantly metabolized by CYP2D6, such as flupentixol, fluphenazine, quetiapine, olanzapine or clozapine.[3]	no marker available	0/1 variant: no increased risk of extrapyramidal side effects.
Loxapine (Loxapac®)	↑ CYP1A2 Ind - Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	no marker available	no marker available
Perphenazine (Trilafon®)	↑ CYP2D6 UM - Initiate with recommended dose but may require a higher dose.	no marker available	no marker available
Pimozide (Orap®)	↑ CYP2D6 UM - Initiate with recommended dose but may require a higher dose.	no marker available	no marker available
Trifluoperazine (Stelazine®)	↑ CYP1A2 Ind - Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	no marker available	no marker available
Zuclopenthixol (Clopixol®)	↑ CYP2D6 UM - Consider increasing the standard dose by 50% based on response and tolerance, or using an alternative drug not predominantly metabolized by CYP2D6, such as flupentixol, fluphenazine, quetiapine, olanzapine or clozapine.[3]	no marker available	no marker available
2nd generation antipsychotics			
Cariprazine (Vraylar®)	CYP3A4 NM - Normal exposure	no marker available	no marker available
Lurasidone (Latuda®)	CYP3A4 NM - Normal exposure	no marker available	no marker available
Paliperidone (Invega®)	CYP3A4 NM, ABCB1 - Initiate with recommended dose; a low dose may be adequate.	no marker available	no marker available
Ziprasidone (Zeldox®)	CYP3A4 NM - Normal exposure	no marker available	no marker available
Asenapine (Saphris®)	↑ CYP1A2 Ind, UGT1A4 NM - Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	no marker available	no marker available

Genetic Associations Identified

Medications	Exposure	Efficacy	Adverse Drug Reactions
Brexpiprazole (Rexulti®)	↑ CYP2D6 UM, CYP3A4 NM - Initiate with recommended dose but may require a higher dose.	no marker available	no marker available
Clozapine (Clozaril®)	↑ CYP1A2 Ind, CYP2D6 UM - Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	no marker available	2/6 variants: increased risk of antipsychotic-induced weight gain (MC4R, INSIG2).
Olanzapine (Zyprexa®)	↑ CYP1A2 Ind - Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	no marker available	2/6 variants: increased risk of antipsychotic-induced weight gain (MC4R, INSIG2).
Quetiapine (Seroquel®)	CYP3A4 NM, ABCB1 - Initiate with recommended dose; a low dose may be adequate.	no marker available	! 2/2 variants: increased risk of antipsychotic-induced weight gain (MC4Ra, MC4Rb).
Aripiprazole (Abilify®)	↑ CYP2D6 UM - Initiate with recommended dose but may require a higher dose.	! 1/1 variant: increased likelihood of a poorer response (ANKK1).	no marker available
Risperidone (Risperdal®)	✗ CYP2D6 UM - Consider using an alternative drug, or titrate according to the following maximum doses. Oral: 12mg/day (≥ 15yrs, ≥ 51kg) or 6mg/day (< 15yrs, < 51kg). Intramuscular: 75mg per 2 weeks.[3]	! 1/1 variant: increased likelihood of a poorer response (ANKK1).	2/6 variants: increased risk of antipsychotic-induced weight gain (MC4R, INSIG2).
Anxiolytics			
Alprazolam (Xanax®)	CYP3A4 NM, CYP3A5 NM - Normal exposure	no marker available	no marker available
Buspirone (Buspar®)	CYP3A4 NM - Normal exposure	no marker available	no marker available
Chlordiazepoxide (Librium®)	CYP3A4 NM, UGT2B15 IM - Initiate with recommended dose; a low dose may be adequate.	no marker available	no marker available
Clobazam (Frisium®)	CYP2C19 NM - Normal exposure	no marker available	no marker available
Clonazepam (Rivotril®)	CYP3A4 NM - Normal exposure	no marker available	no marker available
Clorazepate (Tranxene®)	CYP3A4 NM, UGT2B15 IM - Initiate with recommended dose; a low dose may be adequate.	no marker available	no marker available
Diazepam (Valium®)	CYP3A4 NM, UGT2B15 IM, CYP2C19 NM - Normal exposure	no marker available	no marker available
Flurazepam (Dalmane®)	CYP3A4 NM - Normal exposure	no marker available	no marker available
Hydroxyzine (Atarax®)	CYP3A4 NM, CYP3A5 PM - Normal exposure	no marker available	no marker available
Lorazepam (Ativan®)	UGT2B15 IM - Initiate with recommended dose; a low dose may be adequate.	no marker available	no marker available
Midazolam (Versed®)	CYP3A4 NM, CYP3A5 PM, CYP2C19 NM - Normal exposure	no marker available	no marker available
Nitrazepam (Mogadon®)	CYP3A4 NM - Normal exposure	no marker available	no marker available
Oxazepam (Serax®)	UGT2B15 IM - Initiate with recommended dose; a low dose may be adequate.	no marker available	no marker available
Temazepam (Restoril®)	UGT2B15 IM - Initiate with recommended dose; a low dose may be adequate.	no marker available	no marker available
Bromazepam (Lectopam®)	↑ CYP1A2 Ind - Initiate with recommended dose but may require a	no marker available	no marker available

Genetic Associations Identified

Medications	Exposure	Efficacy	Adverse Drug Reactions
	higher dose, especially with CYP1A2 inducers, such as smoke.		
Beta blocker			
Propranolol	↑ CYP1A2 Ind, CYP2D6 UM - Initiate therapy with recommended starting dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	no marker available	no marker available
Central alpha-adrenergic agonists			
Guanfacine (Intuniv XR®)	CYP3A4 NM - Normal exposure	no marker available	no marker available
Clonidine (Catapres®)	↑ CYP2D6 UM - Initiate therapy with recommended starting dose but may require a higher dose.	! 1/1 variant: increased likelihood of a poorer response (GNB3).	no marker available
Mood Stabilizers			
Gabapentin (Neurontin®)	Normal exposure	no marker available	no marker available
Levetiracetam (Keppra®)	Normal exposure	no marker available	no marker available
Pregabalin (Lyrica®)	no marker available	no marker available	no marker available
Carbamazepine (Tegretol®)	↑ UGT2B7 UM - Initiate with recommended dose but may require a higher dose.	no marker available	HLA-A*31:01 negative, HLA-B*15:02 negative - Normal risks of cutaneous adverse reactions.
Oxcarbazepine (Trileptal®)	↑ UGT2B7 UM - Initiate with recommended dose but may require a higher dose.	no marker available	HLA-B*15:02 negative - Normal risks of cutaneous adverse reactions.
Lamotrigine (Lamictal®)	↓ UGT2B7 PM - Consider using a lower dose.	no marker available	HLA-B*15:02 negative - Normal risks of cutaneous adverse reactions.
Phenytoin (Dilantin®)	↓ CYP2C9 IM - Initiate with recommended starting dose but consider using 25% less than the typical maintenance dose based on response and tolerance.[6]	no marker available	HLA-B*15:02 negative - normal risks of cutaneaous adverse reactions.
Lithium (Carbolith®)	no marker available	! 1/1 variant: increased likelihood of a poorer response (CACNG2); 2/2 variants: increased likelihood of relapse after successful lithium therapy (lncRNA) - for bipolar disorder.	no marker available
Topiramate (Topamax®)	no marker available	! 1/1 variant: increased likelihood of a poorer response for treatment of alcohol-related disorders (GRIK1).	no marker available
Valproic acid, Divalproex (Depakene®, Epival®)	CYP2A6 NM, CYP2C9 IM - Normal exposure	no marker available	! 1/1 variant: increased likelihood of weight gain (ANKK1).
Norepinephrine Reuptake Inhibitor			
Atomoxetine (Strattera®)	↑ CYP2D6 UM - Children: Initiate with a dose of 0.5mg/kg/day and increase gradually to 1.2mg/kg/day after 3 days. If no clinical response and in the absence of adverse events after 2 weeks, consider a dose increase or consider an alternative drug not predominantly metabolized by CYP2D6. Adults: Initiate with a dose of 40mg/day and increase gradually to	no marker available	no marker available

Genetic Associations Identified			
Medications	Exposure	Efficacy	Adverse Drug Reactions
	80mg/day after 3 days. If no clinical response and in the absence of adverse events after 2 weeks, consider increasing dose to 100mg/day. If no clinical response observed after 2 weeks, consider a dose increase or consider an alternative drug not predominantly metabolized by CYP2D6.[3,7]		
Psychostimulants			
Amphetamine / Dextroamphetamine (Adderall XR®)	↑ CYP2D6 UM - Initiate therapy with recommended starting dose but may require a higher dose.	no marker available	no marker available
Dextroamphetamine (Dexedrine®)	↑ CYP2D6 UM - Initiate therapy with recommended starting dose but may require a higher dose.	no marker available	no marker available
Lisdexamfetamine (Vyvanse®)	↑ CYP2D6 UM - Initiate therapy with recommended starting dose but may require a higher dose.	no marker available	no marker available
Methylphenidate (Ritalin®, Concerta®, Biphentin®, Foquest®)	CES1 NM - Normal exposure	! 3/5 variants: increased likelihood of a poorer response (ADRA2A, COMT Val/Val, SLC6A2).	no marker available
Sedative-Hypnotics			
Diphenydramine (Benadryl®)	no marker available	no marker available	no marker available
Eszopiclone (Lunesta®)	CYP3A4 NM - Normal exposure	no marker available	no marker available
Lemborexant (Dayvigo®)	CYP3A4 NM, CYP3A5 PM - Normal exposure	no marker available	no marker available
Melatonin	no marker available	no marker available	no marker available
Phenobarbital (Phenobarb®)	CYP2C9 IM - Initiate therapy with recommended starting dose; a low dose may be adequate.	no marker available	no marker available
Triazolam (Halcion®)	CYP3A4 NM - Normal exposure	no marker available	no marker available
Zolpidem (Sublinox®)	CYP3A4 NM, CYP2C9 IM - Normal exposure	no marker available	no marker available
Zopiclone (Imovane®)	CYP3A4 NM - Normal exposure	no marker available	no marker available
Wakefulness-promoting agents			
Modafinil (Alertec®)	CYP3A4 NM - Normal exposure	no marker available	no marker available
Sodium oxybate (Xyrem®)	no marker available	no marker available	no marker available
Solriamfetol (Sunosi®)	no marker available	no marker available	no marker available
Pitolisant (Wakix®)	↑ CYP2D6 UM - Initiate therapy with recommended starting dose but may require a higher dose.	no marker available	no marker available

PGx RECOMMENDATIONS - COMPLEMENTARY TREATMENTS

Dose increase may be required.

Dose reduction may be required.

Exposure is difficult to predict, insufficient data to calculate dose adjustments.

All of the tested variants associate with an increased likelihood of a better response, compared to non-carriers.

> 50% of tested variants are associated with an increased likelihood of a poorer response and/or adverse drug reactions, compared to non-carriers.

Medication not recommended by peer-reviewed guidelines.

Genetic Associations Identified			
Medications	Exposure	Efficacy	Adverse Drug Reactions
Antiemetics			
Dimenhydrinate (Gravol®)	no marker available	no marker available	no marker available
Granisetron (Kytril®)	CYP3A4 NM, CYP3A5 PM - Normal exposure	no marker available	no marker available
Palonosetron (Aloxi®)	CYP2D6 UM - Initiate with recommended dose but may require a higher dose.	no marker available	no marker available
Ondansetron (Zofran®)	CYP2D6 UM - Consider an alternative drug not predominantly metabolized by CYP2D6 (i.e. granisetron) due to decreased response.[8]	no marker available	no marker available
Proton pump inhibitors (PPI)			
Esomeprazole (Nexium®)	no marker available	no marker available	no marker available
Dexlansoprazole (Dexilant®)	CYP2C19 NM - Initiate therapy with standard dose but consider increasing the dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.[9]	no marker available	no marker available
Lansoprazole (Prevacid®)	CYP2C19 NM - Initiate therapy with standard dose but consider increasing the dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.[9]	no marker available	no marker available
Omeprazole (Losec®)	CYP2C19 NM - Initiate therapy with standard dose but consider increasing the dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.[9]	no marker available	no marker available
Pantoprazole (Pantoloc®)	CYP2C19 NM - Initiate therapy with standard dose but consider increasing the dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.[9]	no marker available	no marker available

PGx ASSOCIATIONS - EXPOSURE

METABOLISM

The level of activity of the enzymes listed below influence your exposure to active metabolite(s).

	CYP450	POR	CES	UGT
Variants detected / tested	3/8	1/1	0/1	3/4

Enzymes	Phenotype (PM IM NM RM UM)	Genotype	Details
CYTOCHROME P450 (CYP450)			
CYP3A5		*3/*3	**Poor metabolizer (PM)** Low CYP3A5 activity is the most common phenotype and has been used to establish standard doses.
CYP2C9		*1/*3	**Intermediate metabolizer (IM)** Reduced CYP2C9 activity compared to normal metabolizers.
CYP2A6		*1/*1	**Normal metabolizer (NM)** Normal CYP2A6 activity.
CYP2B6		*1/*1	**Normal metabolizer (NM)** Normal CYP2B6 activity.
CYP2C19		*1/*1	**Normal metabolizer (NM)** Normal CYP2C19 activity.
CYP3A4		*1/*1	**Normal metabolizer (NM)** Normal CYP3A4 activity.
CYP1A2		*1F/*1F	**Inducible metabolizer (Ind)** Increased CYP1A2 activity compared to normal metabolizers if the patient is exposed to CYP1A2 inducers, such as smoke.

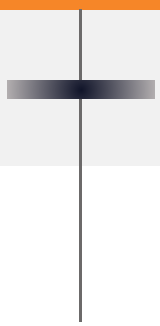
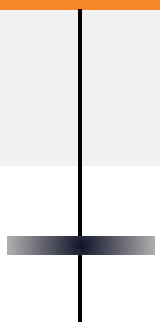
Enzymes	Phenotype	Genotype	Details
	PM IM **NM** RM UM		
CYP2D6		*1/*2xN	**Ultrarapid metabolizer (UM)** Increased CYP2D6 activity compared to normal metabolizers.
CARBOXYLESTERASE-1 (CES1) AND CYTOCHROME P450 OXIDOREDUCTASE (POR)			
POR		A/G	**Intermediate activity (IA)** Reduced POR activity compared to normal phenotypes (POR participates in CYP2B6 activation).
CES1		C/C	**Normal metabolizer (NM)** Normal CES1 activity.
UDP-GLUCURONOSYLTRANSFERASES (UGT)			
UGT1A1		*1/*28	**Intermediate metabolizer (IM)** Reduced UGT1A1 activity compared to normal metabolizers.
UGT2B15		*1/*2	**Intermediate metabolizer (IM)** Reduced UGT2B15 activity compared to normal metabolizers.
UGT1A4		*1/*1	**Normal metabolizer (NM)** Normal UGT1A4 activity.
UGT2B7		*2/*2	**Variable metabolizer activity** The function of the *2 allele of UGT2B7 is substrate-dependent. Thus, compared to normal metabolizers, UGT2B7 activity can be increased or reduced depending on the medication substrate.

PGx ASSOCIATIONS - EXPOSURE

DISTRIBUTION

The level of activity of the efflux pumps listed below influence your exposure to medications at the site of action (e.g., central nervous system).

	ABCB1	ABCG2
Variant(s) detected / tested	1/1	0/1

Efflux Pump	Phenotype (Poor activity / Intermediate activity / **Normal activity**)	Genotype	Details
EFFLUX PUMPS (P-GLYCOPROTEIN, MULTIDRUG RESISTANCE PROTEIN)			
ABCB1		ACC/GCT or ACT/GCC	**Poor activity (PA)** Reduced efflux pump activity may result in higher substrate concentrations, increasing the likelihood of response but also increasing the risk of adverse drug reactions.
ABCG2		G/G	**Normal activity (NA)** Normal efflux pump activity may result in normal or lower concentrations of substrates at the site of action.

PGx ASSOCIATIONS - EFFICACY

	The variants listed below have been associated with a higher likelihood of a poorer response to medications, compared to non-carriers.
	Poorer response more likely
Variant(s) detected / tested	15/23

Poorer response more likely

Gene	Reference SNP cluster ID	Variant detected	Associated medication(s)
ADRA2A	rs1800544	yes	methylphenidate
ANKK1	rs1800497	yes	aripiprazole, risperidone
BDNF	rs6265	yes	citalopram, escitalopram, sertraline, fluoxetine, fluvoxamine, paroxetine
CACNG2	rs2283967	yes	lithium
COMT	rs4680	yes	venlafaxine (AA), methylphenidate (GG)
FKBP5	rs4713916	yes	citalopram, desvenlafaxine, duloxetine, escitalopram, levomilnacipran, sertraline, fluoxetine, fluvoxamine, mirtazapine, paroxetine, venlafaxine
GNB3	rs5443	yes	clonidine
GRIK1	rs2832407	yes	topiramate
HTR2A	rs2770296	yes	bupropion
HTR2A	rs6311	yes	citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine
lncRNA	rs74795342	yes	lithium
lncRNA	rs75222709	yes	lithium
SLC6A2	rs2242446	yes	venlafaxine
SLC6A2	rs28386840	yes	methylphenidate
TPH2	rs1487278	yes	amitriptyline, clomipramine, desipramine, doxepin, imipramine, mirtazapine, nortriptyline, trimipramine
ANKK1	rs1800497	no	bupropion
BDNF	rs6265	no	esketamine, ketamine
DRD3	rs963468	no	duloxetine

Gene	Reference SNP cluster ID	Variant detected	Associated medication(s)
GRIK4	rs1954787	no	citalopram, desvenlafaxine, duloxetine, escitalopram, fluoxetine, fluvoxamine, levomilnacipran, paroxetine, sertraline, venlafaxine
HTR7	rs7905446	no	citalopram, escitalopram, sertraline, fluoxetine, fluvoxamine, paroxetine
SLC6A2	rs5569	no	methylphenidate
SLC6A4	5-HTTLPR	no	citalopram, escitalopram, sertraline, fluoxetine, fluvoxamine, paroxetine
TH	rs2070762	no	methylphenidate

PGx ASSOCIATIONS - ADVERSE DRUG REACTIONS

	The variants listed below have been associated with a higher likelihood of specific adverse drug reactions, compared to non-carriers.
	Increased risk of adverse drug reactions
Variant(s) detected / tested	4/13

Increased risk of adverse drug reactions

Gene	Reference SNP cluster ID	Variant detected	Associated medication(s)
ANKK1	rs1800497	yes	weight gain: valproic acid
INSIG2	rs17047764	yes	antipsychotic-induced weight gain: clozapine, olanzapine, risperidone
MC4R	rs489693	yes	antipsychotic-induced weight gain: clozapine, olanzapine, quetiapine, risperidone
MC4R	rs17782313	yes	antipsychotic-induced weight gain: quetiapine
ADRA2A	rs1800544	no	antipsychotic-induced weight gain: clozapine, olanzapine, risperidone
DRD2	rs6275	no	antipsychotic-induced weight gain: clozapine, olanzapine, risperidone
GNB3	rs5443	no	antipsychotic-induced weight gain: clozapine, olanzapine, risperidone
HLA-A	*31:01	no	cutaneous adverse reactions: carbamazepine
HLA-B	*15:02	no	cutaneous adverse reactions: carbamazepine, oxcarbazepine, phenytoin
HTR2A	rs6311	no	gastrointestinal side effects (nausea, vomiting): citalopram, escitalopram, sertraline
HTR2C	rs3813929	no	antipsychotic-induced weight gain: clozapine, olanzapine, risperidone
SLC6A2	rs28386840	no	hypertension: esketamine
SLC6A5	rs2298826	no	extrapyramidal side effects: haloperidol

ANALYTICAL RESULTS

The following analytical results were used to generate the pharmacogenomic interpretations found in this report. Technical limitations inherent with the methods used to produce these results may hinder the attribution of a definitive phenotype (see "TEST METHODOLOGY AND LIMITATIONS").

Genes	Variant Details (GRCH38.p12)		Result
ABCB1	rs1045642	chr7:87509329	A|G
	rs2032582	chr7:87531302	C|C
	rs2032583	chr7:87531245	C|T
ABCG2	rs2231142	chr4:88131171	G|G
ADRA2A	rs1800544	chr10:111076745	C|C
ANKK1	rs1800497	chr11:113400106	G|G
BDNF	rs6265	chr11:27658369	C|C
CACNG2	rs2283967	chr22:36567486	C|T
CES1	rs71647871	chr16:55823658	C|C
CNR1	rs806380	chr6:88154934	A|G
COMT	rs4680	chr22:19963748	A|G
CYP1A2	rs762551	chr15:74749576	A|A
	rs2069514	chr15:74745879	G|G
CYP2A6	rs1801272	chr19:40848628	A|A
	rs5031017	chr19:40843845	G|G
	rs28399433	chr19:40850474	A|A
CYP2B6	rs2279343	chr19:41009358	A|A
	rs3745274	chr19:41006936	G|G
	rs28399499	chr19:41012316	T|T
CYP2C9	rs1057910	chr10:94981296	C|A
	rs1799853	chr10:94942290	C|C
	rs7900194	chr10:94942309	G|G
	rs9332131	chr10:94949282-94949283	A|A
	rs9332239	chr10:94989020	C|C
	rs28371685	chr10:94981224	C|C
	rs28371686	chr10:94981301	C|C
	rs72558187	chr10:94941958	T|T
	rs72558190	chr10:94947782	C|C
CYP2C19	rs4244285	chr10:94781859	G|G
	rs4986893	chr10:94780653	G|G
	rs6413438	chr10:94781858	C|C
	rs12248560	chr10:94761900	C|C
	rs12769205	chr10:94775367	A|A
	rs17884712	chr10:94775489	G|G
	rs28399504	chr10:94762706	A|A
	rs41291556	chr10:94775416	T|T
	rs56337013	chr10:94852738	C|C
	rs72552267	chr10:94775453	G|G
	rs72558186	chr10:94781999	T|T
CYP2D6	rs16947	chr22:42127941	G|A
	rs1065852	chr22:42130692	G|G
	rs1135840	chr22:42126611	C|G
	rs3892097	chr22:42128945	C|C
	rs5030655	chr22:42129084	A|A
	rs5030656	chr22:42128174-42128178	A|A
	rs5030862	chr22:42130668	C|C
	rs5030865	chr22:42129033	C|C
	rs5030867	chr22:42127856	T|T
	rs28371725	chr22:42127803	C|C
	rs28371706	chr22:42129770	G|G
	rs35742686	chr22:42128242	T|T
	rs59421388	chr22:42127608	C|C
	rs72549354	chr22:42128815-42128817	D|D
	rs201377835	chr22:42129910	C|C
	Gene Deletion	n/a	Not Detected
	Gene Duplication	n/a	Detected

Genes	Variant Details (GRCH38.p12)		Result
CYP3A4	rs4986907	chr7:99769804	C|C
	rs35599367	chr7:99768693	G|G
	rs55785340	chr7:99768360	A|A
	rs67666821	chr7:99758184-99758188	D|D
	rs72552799	chr7:99770165	C|C
CYP3A5	rs776746	chr7:99672916	C|C
	rs10264272	chr7:99665212	C|C
	rs28365083	chr7:99652613	G|G
	rs28383479	chr7:99660516	C|C
	rs41303343	chr7:99652771	D|D
	rs55817950	chr7:99676198	G|G
	rs56411402	chr7:99665237	T|T
DRD2	rs6275	chr11:113412755	G|G
DRD3	rs963468	chr3:114144040	A|G
FAAH	rs324420	chr1:46405089	C|C
FKBP5	rs4713916	chr6:35702206	G|G
GNB3	rs5443	chr12:6845711	C|C
GRIK1	rs2832407	chr21:29595188	A|C
GRIK4	rs1954787	chr11:120792654	C|C
*HLA-A*31:01*	rs1061235	chr6:29945521	A|A
*HLA-B*15:02*	rs144012689	chr6:31355003	T|T
HTR2A	rs6311	chr13:46897343	C|T
	rs6313	chr13:46895805	A|G
	rs2770296	chr13:46866425	T|T
HTR2C	rs3813929	chrX:114584047	C|T
HTR7	rs7905446	chr10:90859404	G|G
INSIG2	rs17047764	chr2:118111006	C|C
long non-coding (lnc) RNA	rs74795342	chr21:18954018	G|G
	rs75222709	chr21:18955109	T|T
MC4R	rs489693	chr18:60215554	A|A
	rs17782313	chr18:60183864	C|C
MTHFR	rs1801131	chr1:11794419	T|T
	rs1801133	chr1:11796321	G|G
OPRM1	rs1799971	chr6:154039662	A|A
POR	rs2868177	chr7:75960585	A|G
SLC6A2	rs5569	chr16:55697923	G|G
	rs2242446	chr16:55656513	C|T
	rs28386840	chr16:55652906	A|A
SLC6A4	5-HTTLPR	chr17:30190154-30240133	S|L
SLC6A5	rs2298826	chr11:20638211	G|G
TH	rs2070762	chr11:2165105	A|A
TPH2	rs1487278	chr12:72007071	T|T
UGT1A1	rs4148323	chr2:233760498	G|G
	rs34815109	chr2:233760234-233760248	6|7
UGT1A4	rs2011425	chr2:233718962	T|T
UGT2B7	rs7439366	chr4:69098620	C|C
UGT2B15	rs1902023	chr4:68670366	C|A

TEST METHODOLOGY AND LIMITATIONS

The Biron pharmacogenomic test for psychiatry and pain management is a MALDI-TOF-based single nucleotide primer extension genotyping test; laboratory developed and validated test (LDT), not approved by Health Canada. Nucleic acid amplification techniques may be subject to general interference by factors such as reaction inhibitors and low quality or quantity of extracted DNA. Factors influencing the amount and quality of extracted DNA include but are not limited to patient oral hygiene, collection technique and presence of dietary or microbial source of nucleic acids and nuclease. When present, these interferents typically yield no result rather than an inaccurate one. Risk of suboptimal DNA quantity or quality is significantly reduced by automated DNA extraction which uses chemistry without PCR inhibitors (magnetic beads) and systematic dilution, quantitation and normalization of DNA before nucleic acid amplification. Very infrequent variants or polymorphisms occurring in primer-binding regions may also affect testing and could produce an erroneous result or assay failure. The test does not detect all known and unknown variations in the genes tested, nor does absence of a detectable variant (typically reported as *1 for metabolic enzymes) rule out the presence of other, non-detected variants. The test detects CYP2D6 deletion and duplication but cannot differentiate duplication in the presence of deletion. CYP2D6 deletion and duplication assays can translate into equivocal phenotype results where a range of enzyme activity level must be reported. Test results and clinical interpretation may be inaccurate for individuals who have undergone or are receiving non-autologous blood transfusions, tissue, and/or organ transplant therapies.

DISCLAIMER

Biron Health Group developed this pharmacogenomic report. This test does not diagnose any disorder, condition or disease. The interpretations and recommendations provided in this report are intended as a clinical support tool (DST) to be used solely by a healthcare professional. Treatment decisions for the patient remain the sole responsibility of the treating healthcare provider. The interpretations of the results provided by this report were determined by Biron's data curation protocol, which were established as per the current available scientific evidence available at the time this report version was created. As more evidence becomes available in the future, these interpretations may change. Some variants tested may not be used to provide report interpretations due to a lack of clear gene-drug association as determined by Biron's data curation protocol. The presence of a notification within the "Exposure", "Efficacy" or "Adverse Drug Reactions" categories for a given drug indicates that an associated genetic variant was detected. The lack of a notification within these categories for a given drug does not eliminate the requirement for dose adjustments for optimal dosage, does not guarantee effective drug therapy and does not eliminate the risks of adverse drug reactions. Commercial names are indicated as examples and do not consist an exhaustive list.

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For the full list of references, contact pgxinfo@biron.com

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