Interpretation Guide

Pharmacogenomic (PGx) Report - for your healthcare provider

Biron Genetics

The following PGx report is a clinical decision support tool based on individual genetic results. It contributes to a better understanding and prediction of medication response and tolerability. This test does not predict the risk of any health problem. **Since response to medications is multifactorial, clinical judgment supersedes any recommendations provided.**

The report notifies you if the patient carries any genetic variant that can alter the following pharmacological parameters:

- pharmacokinetics: overall **exposure** to a medication depending on metabolic and efflux pump function;
- pharmacodynamics: the potential **efficacy** of a drug and whether the patient is predisposed to certain **atypical effects**.

These results do not change with age, but their interpretation can evolve as new data becomes available. Therefore, the Biron PGx reports are updated periodically. These results can also be useful for other medications, not covered by the report.

How to use pharmacogenomic recommendations

1. Only medications relevant for your patient need to be consulted.
2. Use the **Exposure** column to adjust doses for adequate plasma concentrations.
3. Use the **Efficacy** and **Risk of atypical effect** columns to choose the most compatible medication.

The **Exposure**, **Efficacy** and **Risk of atypical effect** columns are interpreted i ndependently from each other. Medications are ordered by class with the most compatible options listed first within each class.

Exposure

- ↑ A higher dose may be required to achieve adequate plasma concentrations.
- ↓ A lower dose may be required to achieve adequate plasma concentrations.
- ∿ Several metabolic pathways are involved, but their capacities are opposed (e.g., PM and UM). Thus, a calculation of dose adjustments is not possible based on current data and closer monitoring is recommended.
- ✗ Drug not recommended by peer-reviewed guidelines due to a risk of toxicity or lack of efficacy.

Efficacy

When choosing between multiple clinically appropriate medications, you may give preference to a medication in which a lower number of variants have been identified (e.g., 2/2 is better than 4/6), in terms of their association with an increased likelihood of a poorer response or an atypical effect.

- ! Signifies the presence of a high-impact gene variant, which increases the probability of a poorer response.
- ✓ Signifies that all of the tested variants predict an increased likelihood of a better response, compared to non-carriers. This medication may be a good option.

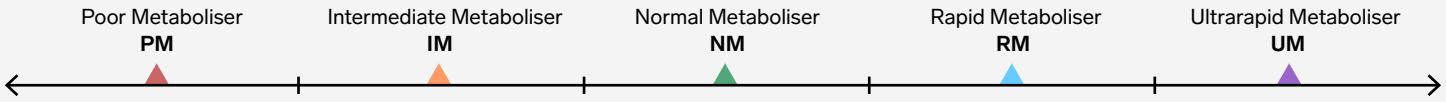
Risk of atypical effect

- ! Signifies the presence of variants associated with an increased risk of particular side effects, compared to non-carriers.
- ✗ Medication not recommended by peer-reviewed guidelines due to a risk of severe side effects,

The notification "**Genetic influence not available**" signifies that there is currently no available data allowing for a genetically-based prediction of medication effect.

Nomenclature for enzyme phenotypes

(e.g., cytochrome P450s or CYP)



NM is generally used to establish standard doses. This dose may be too high for **PM/IM** or too low for **RM/UM**, warranting a dose adjustments or the consideration of an alternative agent. For a pro-drug (e.g., clopidogrel, tramadol), phenotype variability will have the opposite effect.

Inducible Metaboliser **(Ind)** - Specific for CYP1A2, which can have increased function in the presence of an inducer, such as tobacco smoke, comparable to **RM/UM**.

Phone: 1-855-943-6379 **Email: genetics@biron.com**
biron.com/en/genetics/pharmacogenomics

PHARMACOGENOMIC REPORT

Biron

Psychiatry and ADHD

To download the latest version, go here: secur.biron.com/login.

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. For more information, visit biron.com/pgxtest.

ADMINISTRATIVE DATA

Patient Name
Test-Firstname Test-Lastname

Gender: Female
Date of birth: 1999-01-01
Phone Number: (418) 999-9999
Email: test-sample.BIO2107270327@biron.local

Clinical Support
Email: genetique@biron.com

Ordering Clinician
Meredith Grey

Patient Address
1212 some street
Ste-foy, Québec
G2J 4M5

Phone: 1-855-943-6379

Sample ID: BIO2107270327
Sample Type: test

Date ordered: 2022-08-21
Date of sample reception: 2025-01-14
Date of report: 2025-01-14

Fax: (514) 317-2241

VARIANT(S) OF VERY IMPORTANT PHARMACOGENES (VIPS)

CYP1A2 IND, CYP2C9 IM, CYP2C19 IM, POR IA, CES1 IM, UGT1A1 IM, UGT1A4 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
Carbamazepine Tegretol®	Risk of hypersensitivity reaction due to the presence of the HLA-B*15:02 allele.	If patient is carbamazepine-naïve, avoid carbamazepine. If the patient has previously used carbamazepine consistently for longer than three months without incidence of cutaneous adverse reactions, cautiously consider using carbamazepine.[1]
Oxcarbazepine Trileptal®	Risk of hypersensitivity reaction due to the presence of the HLA-B*15:02 allele.	If patient is oxcarbazepine-naïve, avoid oxcarbazepine. If the patient has previously used oxcarbazepine consistently for longer than three months without incidence of cutaneous adverse reactions, cautiously consider use of oxcarbazepine.[1]
Phenytoin Dilantin®	Risk of hypersensitivity reaction due to the presence of the HLA-B*15:02 allele.	If patient is phenytoin-naïve, avoid phenytoin. If the patient has previously used phenytoin consistently for longer than three months without incidence of cutaneous adverse reactions, cautiously consider use of phenytoïn.[1]
Clopidogrel Plavix®	Reduced clopidogrel active metabolite formation; increased on-treatment platelet reactivity; increased risk for adverse cardiac and cerebrovascular events (CYP2C19 IM).	Cardiovascular indications: avoid standard dose (75mg/day) if possible; use prasugrel or ticagrelor at standard dose if no contraindication. Neurovascular:

CAUTIONARY INFORMATION - MEDICATIONS TO AVOID OR USE WITH CAUTION

Medication	Identified risk	Recommendation
		consider alternative P2Y12 inhibitor at standard dose if clinically indicated and no contraindication.[2]

PGx RECOMMENDATIONS - PSYCHIATRY

- Dose increase may be required.
- Dose reduction may be required.
- Exposure is difficult to predict, insufficient data to calculate dose adjustments.
- Increased probability of a better response.
- Greater potential for a poorer response or atypical effect.
- Medication not recommended by peer-reviewed guidelines.

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Antidepressants			
Selective serotonin reuptake inhibitors (SSRIs)			
Fluoxetine (Prozac®)	CYP2D6 NM, CYP2C9 IM - Initiate with recommended dose; a low dose may be adequate.	! 4/6 variants: increased likelihood of a poorer response (SLC6A4 - association demonstrated mainly in Caucasians, not observed in Asians, BDNF, FKBP5, HTR7); consider adding L-methylfolate 15mg/day (MTHFR).	Genetic influence not available
Fluvoxamine (Luvox®)	CYP2D6 NM, ABCB1 - Initiate with recommended dose but may require a higher dose.	! 4/6 variants: increased likelihood of a poorer response (SLC6A4 - association demonstrated mainly in Caucasians, not observed in Asians, BDNF, FKBP5, HTR7); consider adding L-methylfolate 15mg/day (MTHFR).	Genetic influence not available
Paroxetine (Paxil®)	CYP2D6 NM, ABCB1 - Initiate therapy with recommended starting dose but may require a higher dose.	! 4/6 variants: increased likelihood of a poorer response (SLC6A4 - association demonstrated mainly in Caucasians, not observed in Asians, BDNF, FKBP5, HTR7); consider adding L-methylfolate 15mg/day (MTHFR).	Genetic influence not available
Citalopram (Celexa®)	↓ CYP2C19 IM - Initiate with recommended dose but consider a slower titration schedule and do not exceed the following daily doses: 30mg for adults up to 65 yrs; 15mg for adults 65 yrs or older.[3,4]	! 4/6 variants: increased likelihood of a poorer response (SLC6A4 - association demonstrated mainly in Caucasians, not observed in Asians, BDNF, FKBP5, HTR7); consider adding L-methylfolate 15mg/day (MTHFR).	! 1/1 variant: increased risk of gastrointestinal side effects (HTR2A).
Escitalopram (Cipralex®)	↓ CYP2C19 IM - Initiate with recommended dose but consider a slower titration schedule and do not exceed the following daily doses: 15mg for adults up to 65 yrs; 7.5mg for adults 65 yrs or older.[3,4]	! 4/6 variants: increased likelihood of a poorer response (SLC6A4 - association demonstrated mainly in Caucasians, not observed in Asians, BDNF, FKBP5, HTR7); consider adding L-methylfolate 15mg/day (MTHFR).	! 1/1 variant: increased risk of gastrointestinal side effects (HTR2A).
Sertraline (Zoloft®)	↓ CYP2B6 NM, CYP2C19 IM - Initiate therapy with recommended starting dose but with a slower titration schedule and a lower maintenance dose.[3]	! 4/5 variants: increased likelihood of a poorer response (SLC6A4 - association demonstrated mainly in Caucasians, not observed in Asians, BDNF, FKBP5, HTR7); consider adding L-methylfolate 15mg/day (MTHFR).	! 1/1 variant: increased risk of gastrointestinal side effects (HTR2A).
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); consider adding L-methylfolate 15mg/day (MTHFR).	Genetic influence not available
Levomilnacipran (Fetzima®)	CYP3A4 NM, ABCB1 - Initiate therapy with recommended starting dose but may require a higher dose.	1/2 variants: increased likelihood of a poorer response (FKBP5); consider adding L-methylfolate 15mg/day (MTHFR).	Genetic influence not available

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Venlafaxine-XR (Effexor XR®)	CYP2D6 NM, ABCB1 - Initiate with recommended dose but may require a higher dose.	3/4 variants: increased likelihood of a poorer response (COMT, FKBP5, SLC6A2); consider adding L-methylfolate 15mg/day (MTHFR).	Genetic influence not available
Duloxetine (Cymbalta®)	CYP1A2 Ind, CYP2D6 NM - 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); consider adding L-methylfolate 15mg/day (MTHFR).	Genetic influence not available
Other antidepressants			
Bupropion (Wellbutrin®)	CYP2B6 NM, POR - Initiate with recommended dose; a low dose may be adequate.	0/1 variant: no increased likelihood of a poorer response for treatment of depressive symptoms (HTR2A).	Genetic influence not available
Esketamine (Spravato®)	CYP2B6 NM, 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®)	CYP2B6 NM, 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	Genetic influence not available	Genetic influence not available
Vilazodone (Viibryd®)	CYP3A4 NM, ABCB1 - Initiate with recommended dose but may require a higher dose.	Genetic influence not available	Genetic influence not available
Vortioxetine (Trintellix®)	CYP2D6 NM, CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Mirtazapine (Remeron®)	CYP1A2 Ind, CYP2D6 NM - 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).	Genetic influence not available
Tricyclic antidepressants (TCAs)			
Clomipramine (Anafranil®)	Normal exposure	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Desipramine (Norpramin®)	CYP2D6 NM, ABCB1 - Initiate with recommended dose but may require a higher dose.	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Imipramine (Tofranil®)	Normal exposure	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Nortriptyline (Aventyl®)	CYP2D6 NM, ABCB1 - Initiate with recommended dose but may require a higher dose.	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Amitriptyline (Elavil®)	ABCB1, CYP2C19 IM, CYP2D6 NM - Initiate therapy with recommended starting dose but monitor response and tolerance more closely; insufficient data to calculate dose adjustments.	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Doxepin (Sinequan®)	ABCB1, CYP2C19 IM, CYP2D6 NM - Initiate therapy with recommended starting dose but monitor response and tolerance more closely; insufficient data to calculate dose adjustments.	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Trimipramine (Surmontil®)	ABCB1, CYP2C19 IM, CYP2D6 NM - Initiate therapy with recommended starting dose but monitor response and tolerance more closely; insufficient data to calculate dose adjustments.	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Monoamine oxidase inhibitors (MAOs)			

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Moclobemide (Manerix®)	CYP2D6 IM - Initiate with recommended dose; a low dose may be adequate.	Genetic influence not available	Genetic influence not available
Phenelzine (Nardil®)	Genetic influence not available	Genetic influence not available	Genetic influence not available
Tranylcypromine (Parnate®)	Genetic influence not available	Genetic influence not available	Genetic influence not available
Antipsychotics			
1st generation antipsychotics			
Chlorpromazine (Largactil®)	CYP1A2 Ind - Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	Genetic influence not available	Genetic influence not available
Fluphenazine (Moditen®)	CYP2D6 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Haloperidol (Haldol®)	CYP2D6 NM - Normal exposure	Genetic influence not available	0/1 variant: no increased risk of extrapyramidal side effects.
Perphenazine (Trilafon®)	CYP2D6 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Pimozide (Orap®)	CYP2D6 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Zuclopenthixol (Clopixol®)	CYP2D6 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Loxapine (Loxapac®)	↑ CYP1A2 Ind - Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	Genetic influence not available	Genetic influence not available
Trifluoperazine (Stelazine®)	↑ CYP1A2 Ind - Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	Genetic influence not available	Genetic influence not available
2nd generation antipsychotics			
Aripiprazole (Abilify®)	CYP2D6 NM - Normal exposure	1/1 variant: increased likelihood of a poorer response (ANKK1).	Genetic influence not available
Brexpiprazole (Rexulti®)	CYP2D6 NM, CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Cariprazine (Vraylar®)	CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Lurasidone (Latuda®)	CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Paliperidone (Invega®)	CYP3A4 NM, ABCB1 - Initiate with recommended dose but may require a higher dose.	Genetic influence not available	Genetic influence not available
Quetiapine (Seroquel®)	CYP3A4 NM, ABCB1 - Initiate with recommended dose but may require a higher dose.	Genetic influence not available	1/2 variants: increased risk of antipsychotic-induced weight gain (MC4Ra).
Risperidone (Risperdal®)	CYP2D6 NM - Normal exposure	1/1 variant: increased likelihood of a poorer response (ANKK1).	2/6 variants: increased risk of antipsychotic-induced weight gain (MC4R, HTR2C).
Ziprasidone (Zeldox®)	CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Asenapine (Saphris®)	↑ CYP1A2 Ind, UGT1A4 IM - Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	Genetic influence not available	Genetic influence not available

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Clozapine (Clozaril®)	↑ CYP1A2 Ind - Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	Genetic influence not available	2/6 variants: increased risk of antipsychotic-induced weight gain (MC4R, HTR2C).
Olanzapine (Zyprexa®)	↑ CYP1A2 Ind - Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	Genetic influence not available	2/6 variants: increased risk of antipsychotic-induced weight gain (MC4R, HTR2C).
Anxiolytics			
Alprazolam (Xanax®)	CYP3A4 NM, CYP3A5 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Buspirone (Buspar®)	CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Chlordiazepoxide (Librium®)	CYP3A4 NM, UGT2B15 IM - Initiate with recommended dose; a low dose may be adequate.	Genetic influence not available	Genetic influence not available
Clobazam (Frisium®)	CYP2C19 IM - Initiate with recommended dose; a low dose may be adequate.	Genetic influence not available	Genetic influence not available
Clonazepam (Rivotril®)	CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Clorazepate (Tranxene®)	CYP3A4 NM, UGT2B15 IM - Initiate with recommended dose; a low dose may be adequate.	Genetic influence not available	Genetic influence not available
Diazepam (Valium®)	CYP3A4 NM, UGT2B15 IM, CYP2C19 IM - Normal exposure	Genetic influence not available	Genetic influence not available
Flurazepam (Dalmane®)	CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Hydroxyzine (Atarax®)	CYP3A4 NM, CYP3A5 PM - Normal exposure	Genetic influence not available	Genetic influence not available
Lorazepam (Ativan®)	UGT2B15 IM - Initiate with recommended dose; a low dose may be adequate.	Genetic influence not available	Genetic influence not available
Midazolam (Versed®)	CYP2C19 IM, CYP3A5 PM, CYP3A4 NM - Initiate with recommended dose; a low dose may be adequate.	Genetic influence not available	Genetic influence not available
Nitrazepam (Mogadon®)	CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Oxazepam (Serax®)	UGT2B15 IM - Initiate with recommended dose; a low dose may be adequate.	Genetic influence not available	Genetic influence not available
Temazepam (Restoril®)	UGT2B15 IM - Initiate with recommended dose; a low dose may be adequate.	Genetic influence not available	Genetic influence not available
Bromazepam (Lectopam®)	↑ CYP1A2 Ind - Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	Genetic influence not available	Genetic influence not available
Beta blocker			
Propranolol	↑ CYP2D6 NM, CYP1A2 Ind - Initiate therapy with recommended starting dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke.	Genetic influence not available	Genetic influence not available
Central alpha-adrenergic agonists			
Clonidine (Catapres®)	CYP2D6 NM - Normal exposure	1/1 variant: increased likelihood of a poorer response (GNB3).	Genetic influence not available

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Guanfacine (Intuniv XR®)	CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Mood Stabilizers			
Gabapentin (Neurontin®)	ABCB1 - Normal exposure	Genetic influence not available	Genetic influence not available
Levetiracetam (Keppra®)	ABCB1 - Initiate with recommended dose; a low dose may be adequate.	Genetic influence not available	Genetic influence not available
Lithium (Carbolith®)	Genetic influence not available	0/1 variant: no increased likelihood of a poorer response; 0/2 variants: normal likelihood of relapse after successful lithium therapy (lncRNA) - for bipolar disorder.	Genetic influence not available
Pregabalin (Lyrica®)	Genetic influence not available	Genetic influence not available	Genetic influence not available
Topiramate (Topamax®)	Genetic influence not available	0/1 variant: no increased likelihood of a poorer response for treatment of alcohol-related disorders.	Genetic influence not available
Valproic acid, Divalproex (Depakene®, Epival®)	CYP2A6 NM, CYP2C9 IM - Normal exposure	Genetic influence not available	! 1/1 variant: increased likelihood of weight gain (ANKK1).
Lamotrigine (Lamictal®)	ABCG2, UGT2B7 IM - Initiate with recommended dose; a low dose may be adequate.	Genetic influence not available	✖ HLA-B*15:02 positive, the risk of hypersensitivity reaction is increased by a factor of 3.6 and estimated to be 0.4%. Avoid lamotrigine if an alternative is available. If not, advise the patient to report any rash immediately.[5]
Carbamazepine (Tegretol®)	↑ UGT2B7 RM - Initiate with recommended dose but may require a higher dose.	Genetic influence not available	✖ HLA-B*15:02 positive,HLA-A*31:01 negative, increased risk of hypersensitivity reaction - If patient is carbamazepine-naïve, avoid carbamazepine. If the patient has previously used carbamazepine consistently for longer than three months without incidence of cutaneous adverse reactions, cautiously consider using carbamazepine.[1]
Oxcarbazepine (Trileptal®)	↑ UGT2B7 RM - Initiate with recommended dose but may require a higher dose.	Genetic influence not available	✖ HLA-B*15:02 positive, increased risk of hypersensitivity reaction - If patient is oxcarbazepine-naïve, avoid oxcarbazepine. If the patient has previously used oxcarbazepine consistently for longer than three months without incidence of cutaneous adverse reactions, cautiously consider use of oxcarbazepine.[1]
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]	Genetic influence not available	✖ HLA-B*15:02 positive - If patient is phenytoin-naïve, avoid phenytoin. If the patient has previously used phenytoin consistently for longer than three months without incidence of cutaneous adverse reactions, cautiously consider use of phenytoin.[6]
Norepinephrine Reuptake Inhibitor			
Atomoxetine (Strattera®)	CYP2D6 NM - Normal exposure[5,7]	Genetic influence not available	Genetic influence not available

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Psychostimulants			
Amphetamine / Dextroamphetamine (Adderall XR®)	CYP2D6 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Dextroamphetamine (Dexedrine®)	CYP2D6 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Lisdexamfetamine (Vyvanse®)	CYP2D6 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Methylphenidate - Biphentin®	↓ CES1 IM - Consider using a lower dose.	2/5 variants: increased likelihood of a poorer response (COMT, SLC6A2).	Genetic influence not available
Methylphenidate - Concerta®	↓ CES1 IM - Consider using a lower dose.	2/5 variants: increased likelihood of a poorer response (COMT, SLC6A2).	Genetic influence not available
Methylphenidate - Foquest®	↓ CES1 IM - Consider using a lower dose.	2/5 variants: increased likelihood of a poorer response (COMT, SLC6A2).	Genetic influence not available
Methylphenidate - Ritalin®	↓ CES1 IM - Consider using a lower dose.	2/5 variants: increased likelihood of a poorer response (COMT, SLC6A2).	Genetic influence not available
Sedative-Hypnotics			
Daridorexant (Quviviq®)	CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Diphenydramine (Benadryl®)	Genetic influence not available	Genetic influence not available	Genetic influence not available
Eszopiclone (Lunesta®)	CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Lemborexant (Dayvigo®)	CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Melatonin	Genetic influence not available	Genetic influence not available	Genetic influence not available
Phenobarbital (Phenobarb®)	CYP2C9 IM - Initiate therapy with recommended starting dose; a low dose may be adequate.	Genetic influence not available	Genetic influence not available
Triazolam (Halcion®)	CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Zolpidem (Sublinox®)	CYP3A4 NM, CYP2C9 IM - Normal exposure	Genetic influence not available	Genetic influence not available
Zopiclone (Imovane®)	CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Wakefulness-promoting agents			
Modafinil (Alertec®)	CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Pitolisant (Wakix®)	CYP2D6 NM, CYP3A4 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Sodium oxybate (Xyrem®)	Genetic influence not available	Genetic influence not available	Genetic influence not available
Solriamfetol (Sunosi®)	Genetic influence not available	Genetic influence not available	Genetic influence not 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.

Increased probability of a better response.

Greater potential for a poorer response or atypical effect.

Medication not recommended by peer-reviewed guidelines.

Genetic Associations Identified			
Medications	Exposure	Efficacy	Risk of atypical effect
Antiemetics			
Dimenhydrinate (Gravol®)	Genetic influence not available	Genetic influence not available	Genetic influence not available
Granisetron (Kytril®)	CYP3A4 NM, CYP3A5 PM - Normal exposure	Genetic influence not available	Genetic influence not available
Ondansetron (Zofran®)	CYP2D6 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Palonosetron (Aloxi®)	CYP2D6 NM - Normal exposure	Genetic influence not available	Genetic influence not available
Proton pump inhibitors (PPI)			
Esomeprazole (Nexium®)	Genetic influence not available	Genetic influence not available	Genetic influence not available
Dexlansoprazole (Dexilant®)	CYP2C19 IM - Initiate therapy with standard dose but for chronic therapy (> 12 weeks) and efficacy achieved, consider reducing the daily dose by 50% and monitor for continued efficacy.[8]	Genetic influence not available	Genetic influence not available
Lansoprazole (Prevacid®)	CYP2C19 IM - Initiate therapy with standard dose but for chronic therapy (> 12 weeks) and efficacy achieved, consider reducing the daily dose by 50% and monitor for continued efficacy.[8]	Genetic influence not available	Genetic influence not available
Omeprazole (Losec®)	CYP2C19 IM - Initiate therapy with standard dose but for chronic therapy (> 12 weeks) and efficacy achieved, consider reducing the daily dose by 50% and monitor for continued efficacy.[8]	Genetic influence not available	Genetic influence not available
Pantoprazole (Pantoloc®)	CYP2C19 IM - Initiate therapy with standard dose but for chronic therapy (> 12 weeks) and efficacy achieved, consider reducing the daily dose by 50% and monitor for continued efficacy.[8]	Genetic influence not available	Genetic influence not available

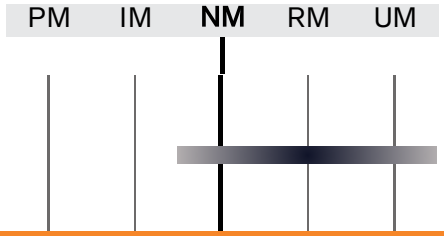
PGx ASSOCIATIONS - EXPOSURE

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	1/1	4/4

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.
CYP2C19		*1/*2	**Intermediate metabolizer (IM)** Reduced CYP2C19 activity compared to normal metabolizers.
CYP2A6		*1/*1	**Normal metabolizer (NM)** Normal CYP2A6 activity.
CYP2B6		*1/*1	**Normal metabolizer (NM)** Normal CYP2B6 activity.
CYP2D6		*1/*1	**Normal metabolizer (NM)** Normal CYP2D6 activity.
CYP3A4		*1/*1	**Normal metabolizer (NM)** Normal CYP3A4 activity.

Enzymes	Phenotype	Genotype	Details
			
CYP1A2		*1A/*1F	**Inducible metabolizer (Ind)** Increased CYP1A2 activity compared to normal metabolizers if the patient is exposed to CYP1A2 inducers, such as smoke.
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/T	**Intermediate metabolizer (IM)** Reduced CES1 activity compared to normal metabolizers.
UDP-GLUCURONOSYLTRANSFERASES (UGT)			
UGT1A1		*1/*28	**Intermediate metabolizer (IM)** Reduced UGT1A1 activity compared to normal metabolizers.
UGT1A4		*1/*3	**Intermediate metabolizer (IM)** Reduced UGT1A4 activity compared to normal metabolizers.
UGT2B15		*1/*2	**Intermediate metabolizer (IM)** Reduced UGT2B15 activity compared to normal metabolizers.
UGT2B7		*1/*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	1/1

Efflux Pump	Phenotype	Genotype	Details
	Poor activity / Intermediate activity / **Normal activity**		
EFFLUX PUMPS (P-GLYCOPROTEIN, MULTIDRUG RESISTANCE PROTEIN)			
ABCB1		AAT/ACT	**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/T	**Intermediate activity (IA)** Reduced efflux pump activity may result in higher substrate concentrations, increasing the likelihood of response but also increasing the risk of adverse drug reactions.

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	10/23

Poorer response more likely

Gene	Reference SNP cluster ID	Variant detected	Associated medication(s)
ANKK1	rs1800497	yes	aripiprazole, risperidone
BDNF	rs6265	yes	citalopram, escitalopram, sertraline, fluoxetine, fluvoxamine, paroxetine
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
HTR7	rs7905446	yes	citalopram, escitalopram, sertraline, fluoxetine, fluvoxamine, paroxetine
SLC6A2	rs2242446	yes	venlafaxine
SLC6A2	rs28386840	yes	methylphenidate
SLC6A4	5-HTTLPR	yes	citalopram, escitalopram, sertraline, fluoxetine, fluvoxamine, paroxetine
TPH2	rs1487278	yes	amitriptyline, clomipramine, desipramine, doxepin, imipramine, mirtazapine, nortriptyline, trimipramine
ADRA2A	rs1800544	no	methylphenidate
ANKK1	rs1800497	no	bupropion
BDNF	rs6265	no	esketamine, ketamine
CACNG2	rs2283967	no	lithium
DRD3	rs963468	no	duloxetine
GRIK1	rs2832407	no	topiramate
GRIK4	rs1954787	no	citalopram, desvenlafaxine, duloxetine, escitalopram, fluoxetine, fluvoxamine, levomilnacipran, paroxetine, sertraline, venlafaxine
HTR2A	rs2770296	no	bupropion

Gene	Reference SNP cluster ID	Variant detected	Associated medication(s)
HTR2A	rs6311	no	citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine
lncRNA	rs74795342	no	lithium
lncRNA	rs75222709	no	lithium
SLC6A2	rs5569	no	methylphenidate
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	5/13

Increased risk of adverse drug reactions

Gene	Reference SNP cluster ID	Variant detected	Associated medication(s)
ANKK1	rs1800497	yes	weight gain: valproic acid
HLA-B	*15:02	yes	cutaneous adverse reactions: carbamazepine, oxcarbazepine, phenytoin
HTR2A	rs6311	yes	gastrointestinal side effects (nausea, vomiting): citalopram, escitalopram, sertraline
HTR2C	rs3813929	yes	antipsychotic-induced weight gain: clozapine, olanzapine, risperidone
MC4R	rs489693	yes	antipsychotic-induced weight gain: clozapine, olanzapine, quetiapine, risperidone
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
INSIG2	rs17047764	no	antipsychotic-induced weight gain: clozapine, olanzapine, risperidone
MC4R	rs17782313	no	antipsychotic-induced weight gain: quetiapine
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|A
	rs2032582	chr7:87531302	A|C
	rs2032583	chr7:87531245	T|T
ABCG2	rs2231142	chr4:88131171	G|T
ADRA2A	rs1800544	chr10:111076745	C|G
ANKK1	rs1800497	chr11:113400106	G|G
BDNF	rs6265	chr11:27658369	C|C
CACNG2	rs2283967	chr22:36567486	C|C
CES1	rs71647871	chr16:55823658	C|T
CNR1	rs806380	chr6:88154934	A|A
COMT	rs4680	chr22:19963748	A|G
CYP1A2	rs762551	chr15:74749576	C|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	G|G
	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|A
	rs4986893	chr10:94780653	G|G
	rs6413438	chr10:94781858	C|C
	rs12248560	chr10:94761900	C|C
	rs12769205	chr10:94775367	G|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|G
	rs1065852	chr22:42130692	G|G
	rs1135840	chr22:42126611	C|C
	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
	rs774671100	chr22:42130555-42130755	G|G
	rs201377835	chr22:42129910	C|C
	Gene Deletion	n/a	Not Detected
	Gene Duplication	n/a	Not 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	A|G
GNB3	rs5443	chr12:6845711	C|T
GRIK1	rs2832407	chr21:29595188	C|C
GRIK4	rs1954787	chr11:120792654	C|C
*HLA-A*31:01*	rs1061235	chr6:29945521	A|A
*HLA-B*15:02*	rs144012689	chr6:31355003	A|A
HTR2A	rs6311	chr13:46897343	C|C
	rs6313	chr13:46895805	G|G
	rs2770296	chr13:46866425	C|C
HTR2C	rs3813929	chrX:114584047	C|C
HTR7	rs7905446	chr10:90859404	G|T
INSIG2	rs17047764	chr2:118111006	G|G
long non-coding (lnc) RNA	rs74795342	chr21:18954018	A|G
	rs75222709	chr21:18955109	G|T
MC4R	rs489693	chr18:60215554	A|C
	rs17782313	chr18:60183864	T|T
MTHFR	rs1801131	chr1:11794419	G|G
	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	T|T
	rs28386840	chr16:55652906	A|A
SLC6A4	5-HTTLPR	chr17:30190154-30240133	S|S
SLC6A5	rs2298826	chr11:20638211	G|G
TH	rs2070762	chr11:2165105	A|G
TPH2	rs1487278	chr12:72007071	C|T
UGT1A1	rs4148323	chr2:233760498	G|G
	rs34815109	chr2:233760234-233760248	6|7
UGT1A4	rs2011425	chr2:233718962	G|T
UGT2B7	rs7439366	chr4:69098620	T|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.

REFERENCES

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

Reference(s) cited in this report:

1. *Phillips EJ, et al. Clinical Pharmacogenetics Implementation Consortium Guideline for HLA Genotype and Use of Carbamazepine and Oxcarbazepine: 2017 Update. Clin Pharmacol Ther (2017).*
2. *Lee CR, et al. Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2C19 Genotype and Clopidogrel Therapy: 2022 Update. Clin Pharmacol Ther (2022).*
3. *Bousman CA, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A Genotypes and Serotonin Reuptake Inhibitor Antidepressants. Clin Pharmacol Ther (2023).*
4. *Brouwer J, et al. Dutch Pharmacogenetics Working Group (DPWG) guideline for the gene-drug interaction between CYP2C19 and CYP2D6 and SSRIs. Eur J Hum Genet (2021).*
5. *Dutch Pharmacogenetics Working Group (DPWG) 2021 update (https://api.pharmgkb.org/v1/download/file/attachment/DPWG_May_2021.pdf)*
6. *Karnes JH, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C9 and HLA-B Genotypes and Phenytoin Dosing: 2020 Update. Clin Pharmacol Ther (2021).*
7. *Brown JT, et al. Clinical Pharmacogenetics Implementation Consortium Guideline for Cytochrome P450 (CYP)2D6 Genotype and Atomoxetine Therapy. Clin Pharmacol Ther (2019).*
8. *Lima JJ, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C19 and Proton Pump Inhibitor Dosing. Clin Pharmacol Ther (2021).*