Interpretation Guide

Pharmacogenomic (PGx) Report - for your healthcare provider

Biron

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.

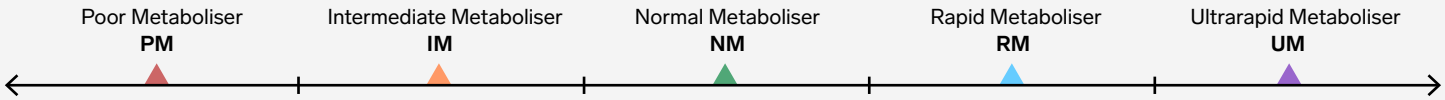
Risk of atypical effect

- ! 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 Normal efficacy* or Normal risk* 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**.

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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

Sex assigned at birth: Female
Date of birth: 1999-01-01
Phone Number: (418) 999-9999
Email: test-sample.BIO2409071579@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: BIO2409071579
Sample Type: test

Date ordered: 2022-08-21
Date of sample reception: 2025-10-02
Date of report: 2025-10-02

Fax: (514) 317-2241

VARIANT(S) OF VERY IMPORTANT PHARMACOGENES (VIPS)

CYP1A2 IND, CYP2C19 IM, CYP2D6 PM, CYP3A4 IM, UGT1A1 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
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: consider alternative P2Y12 inhibitor at standard dose if clinically indicated and no contraindication.[1]
Tamoxifen	Lower endoxifen concentrations compared to normal metabolizers; higher risk of breast cancer recurrence, reduced probability of event-free and recurrence-free survival (CYP2D6 PM).	Recommend alternative hormonal therapy such as an aromatase inhibitor for post-menopausal women or aromatase inhibitor along with ovarian function suppression in premenopausal women. Note, higher dose tamoxifen (40mg/day) increases but does not normalize endoxifen concentrations and can be considered if aromatase inhibitors are contraindicated.[2]

PGx RECOMMENDATIONS - PSYCHIATRY AND ADHD

↑ 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.

Normal exposure*, Normal efficacy* or Normal risk*: Based on currently available genetic data, the efficacy or risk of an atypical effect is likely similar to that of most other individuals; further research is needed to better understand genetic influence.

Genetic Associations Identified			
Medications	Exposure	Efficacy	Risk of atypical effect
Antidepressants			
Selective serotonin reuptake inhibitors (SSRIs)			
Fluoxetine (Prozac®)	Initiate with recommended dose but monitor more closely for side effects; a low dose may be adequate (CYP2D6 PM, CYP2C9 NM).	5/6 variants: increased likelihood of a poorer response (BDNF, FKBP5, GRIK4, HTR2A, HTR7).	Normal risk*
Citalopram (Celexa®)	↓ 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 (CYP2C19 IM).[3, 4]	5/6 variants: increased likelihood of a poorer response (BDNF, FKBP5, GRIK4, HTR2A, HTR7).	0/3 variants: no increased risk of gastrointestinal or SSRI-induced sexual side effects.
Escitalopram (Cipralex®)	↓ 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 (CYP2C19 IM).[3, 4]	5/6 variants: increased likelihood of a poorer response (BDNF, FKBP5, GRIK4, HTR2A, HTR7).	0/3 variants: no increased risk of gastrointestinal or SSRI-induced sexual side effects.
Fluvoxamine (Luvox®)	↓ Consider reducing the starting dose by 25-50% and a slower titration schedule, or consider clinically appropriate alternative antidepressant not predominantly metabolized by CYP2D6 (CYP2D6 PM).[3]	5/6 variants: increased likelihood of a poorer response (BDNF, FKBP5, GRIK4, HTR2A, HTR7).	Normal risk*
Paroxetine (Paxil®)	↓ Consider reducing the starting dose by 50%, slower titration schedule, and a 50% lower maintenance dose than normal (CYP2D6 PM).[3]	5/6 variants: increased likelihood of a poorer response (BDNF, FKBP5, GRIK4, HTR2A, HTR7).	Normal risk*
Sertraline (Zoloft®)	↓ Initiate therapy with recommended starting dose but with a slower titration schedule and a lower maintenance dose (CYP2B6 NM, CYP2C19 IM).[3]	4/5 variants: increased likelihood of a poorer response (BDNF, FKBP5, GRIK4, HTR7)	0/3 variants: no increased risk of gastrointestinal or SSRI-induced sexual side effects.
Serotonin–norepinephrine reuptake inhibitors (SNRIs)			
Desvenlafaxine (Pristiq®)	Initiate with recommended dose; a low dose may be adequate (UGT1A1 IM, UGT2B15 NM, CYP3A4 IM).	2/2 variants: increased likelihood of a poorer response (FKBP5, GRIK4).	Normal risk*
Levomilnacipran (Fetzima®)	↓ Consider using a lower dose (CYP3A4 IM).	2/2 variants: increased likelihood of a poorer response (FKBP5, GRIK4).	Normal risk*
Duloxetine (Cymbalta®)	~ Initiate therapy with recommended starting dose but monitor response and tolerance more closely; insufficient data to calculate dose adjustments, especially with CYP1A2 inducers, such as smoke (CYP1A2 Ind, CYP2D6 PM).	2/3 variants: increased likelihood of a poorer response (FKBP5, GRIK4).	Normal risk*

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Venlafaxine-XR (Effexor XR®)	✖ Consider an alternative drug not predominantly metabolized by CYP2D6 due to increased risk of adverse effects (CYP2D6 PM).[3]	4/4 variants: increased likelihood of a poorer response (COMT, FKBP5, GRIK4, SLC6A2).	Normal risk*
Other antidepressants			
Bupropion (Wellbutrin®)	Normal exposure (CYP2B6 NM).	1/1 variant: increased likelihood of a poorer response for treatment of depressive symptoms (HTR2A).	Normal risk*
Esketamine (Spravato®)	Normal exposure (CYP2B6 NM).	0/1 variant: no increased likelihood of a poorer response.	0/1 variant: no increased risk of emergent hypertension.
Ketamine (Ketalar®)	Normal exposure (CYP2B6 NM).	0/1 variant: no increased likelihood of a poorer response.	0/1 variant: no increased risk of emergent hypertension.
Trazodone (Desyrel®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Vilazodone (Viibryd®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Vortioxetine (Trintellix®)	↓ Reduce the starting dose by 50% (e.g., 5mg) and titrate to a maximum dose of 10mg/day or consider an alternative drug not predominantly metabolized by CYP2D6. Reduce the dose an additional 50% with concomitant CYP2D6 inhibitor (CYP2D6 PM).[3, 5]	Normal efficacy*	Normal risk*
Mirtazapine (Remeron®)	∿ Initiate with recommended dose but monitor response and tolerance more closely, especially with CYP1A2 inducers, such as smoke; insufficient data to calculate dose adjustments (CYP2D6 PM, CYP3A4 IM, CYP1A2 Ind).	2/2 variants: increased likelihood of a poorer response (FKBP5, TPH2).	Normal risk*
Tricyclic antidepressants (TCAs)			
Amitriptyline (Elavil®)	✖ CYP2C19 IM, CYP2D6 PM - Avoid tricyclic use, or consider a 50% reduction of the recommended starting dose.[6]	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Clomipramine (Anafranil®)	✖ CYP2C19 IM, CYP2D6 PM - Avoid tricyclic use, or consider a 50% reduction of the recommended starting dose.[6]	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Desipramine (Norpramin®)	✖ CYP2D6 PM - Avoid tricyclic use, or consider a 50% reduction of the recommended starting dose.[6]	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Doxepin (Sinequan®)	✖ CYP2C19 IM, CYP2D6 PM - Avoid tricyclic use, or consider a 50% reduction of the recommended starting dose.[6]	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Imipramine (Tofranil®)	✖ CYP2C19 IM, CYP2D6 PM - Avoid tricyclic use, or consider a 50% reduction of the recommended starting dose.[6]	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Nortriptyline (Aventyl®)	✖ CYP2D6 PM - Avoid tricyclic use, or consider a 50% reduction of the recommended starting dose.[6]	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Trimipramine (Surmontil®)	✖ CYP2C19 IM, CYP2D6 PM - Avoid tricyclic use, or consider a 50% reduction of the recommended starting dose.[6]	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Monoamine oxidase inhibitors (MAOs)			
Phenelzine (Nardil®)	Normal exposure*	Normal efficacy*	Normal risk*

Genetic Associations Identified			
Medications	Exposure	Efficacy	Risk of atypical effect
Tranylcypromine (Parnate®)	Normal exposure*	Normal efficacy*	Normal risk*
Moclobemide (Manerix®)	↓ Consider using a lower dose (CYP2D6 PM, CYP2C19 IM).[7]	Normal efficacy*	Normal risk*
Antipsychotics			
1st generation antipsychotics			
Loxapine (Loxapac®)	↑ Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke (CYP1A2 Ind).	Normal efficacy*	Normal risk*
Trifluoperazine (Stelazine®)	↑ Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke (CYP1A2 Ind).	Normal efficacy*	Normal risk*
Chlorpromazine (Largactil®)	↓ Consider using a lower dose and monitor response and tolerance more closely, especially with CYP1A2 inducers, such as smoke (CYP2D6 PM, CYP1A2 Ind).	Normal efficacy*	Normal risk*
Fluphenazine (Moditen®)	↓ Consider using a lower dose (CYP2D6 PM).	Normal efficacy*	Normal risk*
Haloperidol (Haldol®)	↓ Reduce the starting dose by 50% and titrate based on response and tolerance, or consider an alternative drug not predominantly metabolized by CYP2D6, such as flupentixol, fluphenazine, quetiapine, olanzapine or clozapine (CYP2D6 PM).[8]	Normal efficacy*	0/1 variant: no increased risk of extrapyramidal side effects.
Perphenazine (Trilafon®)	↓ Consider reducing the starting dose (CYP2D6 PM).	Normal efficacy*	Normal risk*
Pimozide (Orap®)	↓ Consider reducing the starting dose and do not exceed 50% of the maximum standard dose (i.e., adults: 4mg/day, children: 0.05mg/kg/day to a maximum of 2mg/day). Doses should not be increased earlier then 14 days (CYP2D6 PM).[8, 9]	Normal efficacy*	Normal risk*
Zuclopenthixol (Clopixol®)	↓ Consider reducing the starting dose by 50%, or consider using an alternative drug not predominantly metabolized by CYP2D6, such as flupentixol, fluphenazine, quetiapine, olanzapine or clozapine (CYP2D6 PM).[8]	Normal efficacy*	Normal risk*
2nd generation antipsychotics			
Asenapine (Saphris®)	↑ Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke (CYP1A2 Ind, UGT1A4 NM).	Normal efficacy*	Normal risk*
Olanzapine (Zyprexa®)	↑ Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke (CYP1A2 Ind).	Normal efficacy*	1/6 variants: increased risk of antipsychotic-induced weight gain (HTR2C).
Aripiprazole (Abilify®)	↓ Consider reducing the standard dose by 50% and do not exceed 10 mg/day or 300 mg/month (68-75% of the standard maximum dose); maximum should be 200 mg/month with concomitant CYP3A4 inhibitor (CYP2D6 PM).[10, 8]	1/1 variant: increased likelihood of a poorer response (ANKK1).	Normal risk*

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Brexpiprazole (Rexulti®)	↓ Consider reducing the standard dose by 75% (CYP2D6 PM, CYP3A4 IM)[11, 8]	Normal efficacy*	Normal risk*
Cariprazine (Vraylar®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Lurasidone (Latuda®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Paliperidone (Invega®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Quetiapine (Seroquel®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	0/2 variants: no increased risk of antipsychotic-induced weight gain.
Risperidone (Risperdal®)	↓ Consider reducing the starting dose by 33%. If problematic side effects originating in the central nervous system occur, consider reducing the dose to 50% of the standard dose (CYP2D6 PM).[8]	1/1 variant: increased likelihood of a poorer response (ANKK1).	1/6 variants: increased risk of antipsychotic-induced weight gain (HTR2C).
Ziprasidone (Zeldox®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Clozapine (Clozaril®)	∿ Initiate with recommended dose but monitor response and tolerance more closely, especially with CYP1A2 inducers, such as smoke; insufficient data to calculate dose adjustments (CYP1A2 Ind, CYP2D6 PM).	Normal efficacy*	1/6 variants: increased risk of antipsychotic-induced weight gain (HTR2C).
Anxiolytics			
Alprazolam (Xanax®)	Initiate with recommended dose; a low dose may be adequate (CYP3A4 IM, CYP3A5 PM).	Normal efficacy*	Normal risk*
Chlordiazepoxide (Librium®)	Initiate with recommended dose; a low dose may be adequate (CYP3A4 IM, UGT2B15 NM).	Normal efficacy*	Normal risk*
Clobazam (Frisium®)	Initiate with recommended dose; a low dose may be adequate (CYP2C19 IM).	Normal efficacy*	Normal risk*
Diazepam (Valium®)	Initiate with recommended dose; a low dose may be adequate (CYP2C19 IM, CYP3A4 IM, UGT2B15 NM).	Normal efficacy*	Normal risk*
Lorazepam (Ativan®)	Normal exposure (UGT2B15 NM).	Normal efficacy*	Normal risk*
Oxazepam (Serax®)	Normal exposure (UGT2B15 NM).	Normal efficacy*	Normal risk*
Temazepam (Restoril®)	Normal exposure (UGT2B15 NM).	Normal efficacy*	Normal risk*
Bromazepam (Lectopam®)	↑ Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke (CYP1A2 Ind).	Normal efficacy*	Normal risk*
Buspirone (Buspar®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Clonazepam (Rivotril®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Clorazepate (Tranxene®)	↓ Consider using a lower dose (CYP3A4 IM, UGT2B15 NM).	Normal efficacy*	Normal risk*
Flurazepam (Dalmane®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Hydroxyzine (Atarax®)	↓ Consider using a lower dose (CYP3A4 IM, CYP3A5 PM).	Normal efficacy*	Normal risk*

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Midazolam (Versed®)	↓ Consider reducing the dose (CYP2C19 IM, CYP3A5 PM, CYP3A4 IM).	Normal efficacy*	Normal risk*
Nitrazepam (Mogadon®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Central alpha-adrenergic agonists			
Clonidine (Catapres®)	↓ Consider using a lower dose (CYP2D6 PM).	1/1 variant: increased likelihood of a poorer response (GNB3).	Normal risk*
Guanfacine (Intuniv XR®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Mood Stabilizers			
Gabapentin (Neurontin®)	Normal exposure (ABCB1).	Normal efficacy*	Normal risk*
Lamotrigine (Lamictal®)	Normal exposure (ABCG2, UGT2B7 NM).	Normal efficacy*	HLA-B*15:02 negative - Normal risks of cutaneous adverse reactions.
Levetiracetam (Keppra®)	Normal exposure (ABCB1).	Normal efficacy*	Normal risk*
Lithium (Carbolith®)	Normal exposure*	0/1 variant: no increased likelihood of a poorer response (CACNG2); 1/1 variant: increased likelihood of relapse after successful lithium therapy (lncRNA) - for bipolar disorder.	Normal risk*
Oxcarbazepine (Trileptal®)	Normal exposure (UGT2B7 NM).	Normal efficacy*	HLA-B*15:02 negative - Normal risks of cutaneous adverse reactions.
Phenytoin (Dilantin®)	Normal exposure (CYP2C9 NM).	Normal efficacy*	HLA-B*15:02 negative - normal risks of cutaneaous adverse reactions.
Pregabalin (Lyrica®)	Normal exposure*	Normal efficacy*	Normal risk*
Topiramate (Topamax®)	Genetic influence not available	0/1 variant: no increased likelihood of a poorer response for treatment of alcohol-related disorders.	Normal risk*
Carbamazepine (Tegretol®)	↓ Consider using a lower dose (CYP3A4 IM, CYP3A5 PM, UGT2B7 NM).	Normal efficacy*	HLA-A*31:01 negative, HLA-B*15:02 negative - Normal risks of cutaneous adverse reactions.
Valproic acid, Divalproex (Depakene®, Epival®)	Normal exposure (CYP2A6 NM, CYP2C9 NM).	Normal efficacy*	! 1/1 variant: increased likelihood of weight gain (ANKK1).
Norepinephrine Reuptake Inhibitor			
Atomoxetine (Strattera®)	↓ Children: Initiate with a dose of 0.5mg/kg/day and if no clinical response and in the absence of adverse events after 2 weeks, consider a gradual dose increase. If unacceptable side effects are present at any time, consider a reduction in dose (CYP2D6 PM). Adults: Initiate with a dose of 40mg/day and if no clinical response and in the absence of adverse events after 2 weeks increase dose gradually to 80mg/day. If response is inadequate after 2 weeks, consider a dose increase. If unacceptable side effects are present at any time, consider a reduction in dose (CYP2D6 PM).[12, 8]	Genetic influence not available	Genetic influence not available
Psychostimulants			
Methylphenidate - Biphentin®	Normal exposure (CES1 NM).	2/5 variants: increased likelihood of a poorer response (COMT, SLC6A2).	Normal risk*

Genetic Associations Identified			
Medications	Exposure	Efficacy	Risk of atypical effect
Methylphenidate - Concerta®	Normal exposure (CES1 NM).	2/5 variants: increased likelihood of a poorer response (COMT, SLC6A2).	Normal risk*
Methylphenidate - Foquest®	Normal exposure (CES1 NM).	2/5 variants: increased likelihood of a poorer response (COMT, SLC6A2).	Normal risk*
Methylphenidate - Quillivant®	Normal exposure (CES1 NM).	2/5 variants: increased likelihood of a poorer response (COMT, SLC6A2).	Normal risk*
Methylphenidate - Ritalin®	Normal exposure (CES1 NM).	2/5 variants: increased likelihood of a poorer response (COMT, SLC6A2).	Normal risk*
Amphetamine / Dextroamphetamine (Adderall XR®)	↓ Consider using a lower dose (CYP2D6 PM).	Normal efficacy*	Normal risk*
Dextroamphetamine (Dexedrine®)	↓ Consider using a lower dose (CYP2D6 PM).	Normal efficacy*	Normal risk*
Lisdexamfetamine (Vyvanse®)	↓ Consider using a lower dose (CYP2D6 PM).	Normal efficacy*	Normal risk*
Sedative-Hypnotics			
Diphenydramine (Benadryl®)	Normal exposure*	Normal efficacy*	Normal risk*
Melatonin	Normal exposure*	Normal efficacy*	Normal risk*
Phenobarbital (Phenobarb®)	Normal exposure (CYP2C9 NM).	Normal efficacy*	Normal risk*
Zolpidem (Sublinox®)	Normal exposure (CYP3A4 IM, CYP2C9 NM).	Normal efficacy*	Normal risk*
Daridorexant (Quviviq®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Eszopiclone (Lunesta®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Lemborexant (Dayvigo®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Triazolam (Halcion®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Zopiclone (Imovane®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Wakefulness-promoting agents			
Sodium oxybate (Xyrem®)	Normal exposure*	Normal efficacy*	Normal risk*
Solriamfetol (Sunosi®)	Normal exposure*	Normal efficacy*	Normal risk*
Modafinil (Alertec®)	↓ Consider using a lower dose (CYP3A4 IM).	Normal efficacy*	Normal risk*
Pitolisant (Wakix®)	↓ Initiate at 8.9mg/day and titrate to 17.8mg/day after 7 days; total daily dose should not exceed 20mg. Closer monitoring is recommended. For children <40 kg: consider lowering the dose further (CYP2D6 PM).[13]	Normal efficacy*	Normal risk*

PGx RECOMMENDATIONS - CARDIOLOGY

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.

Normal exposure*, Normal efficacy* or Normal risk*: Based on currently available genetic data, the efficacy or risk of an atypical effect is likely similar to that of most other individuals; further research is needed to better understand genetic influence.

Genetic Associations Identified			
Medications	Exposure	Efficacy	Risk of atypical effect
Beta-blockers			
Propranolol (Inderal®)	Initiate therapy with recommended starting dose but monitor response and tolerance more closely; insufficient data to calculate dose adjustments, especially with CYP1A2 inducers, such as smoke (CYP1A2 Ind, CYP2D6 PM).	Normal efficacy*	Normal risk*

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.

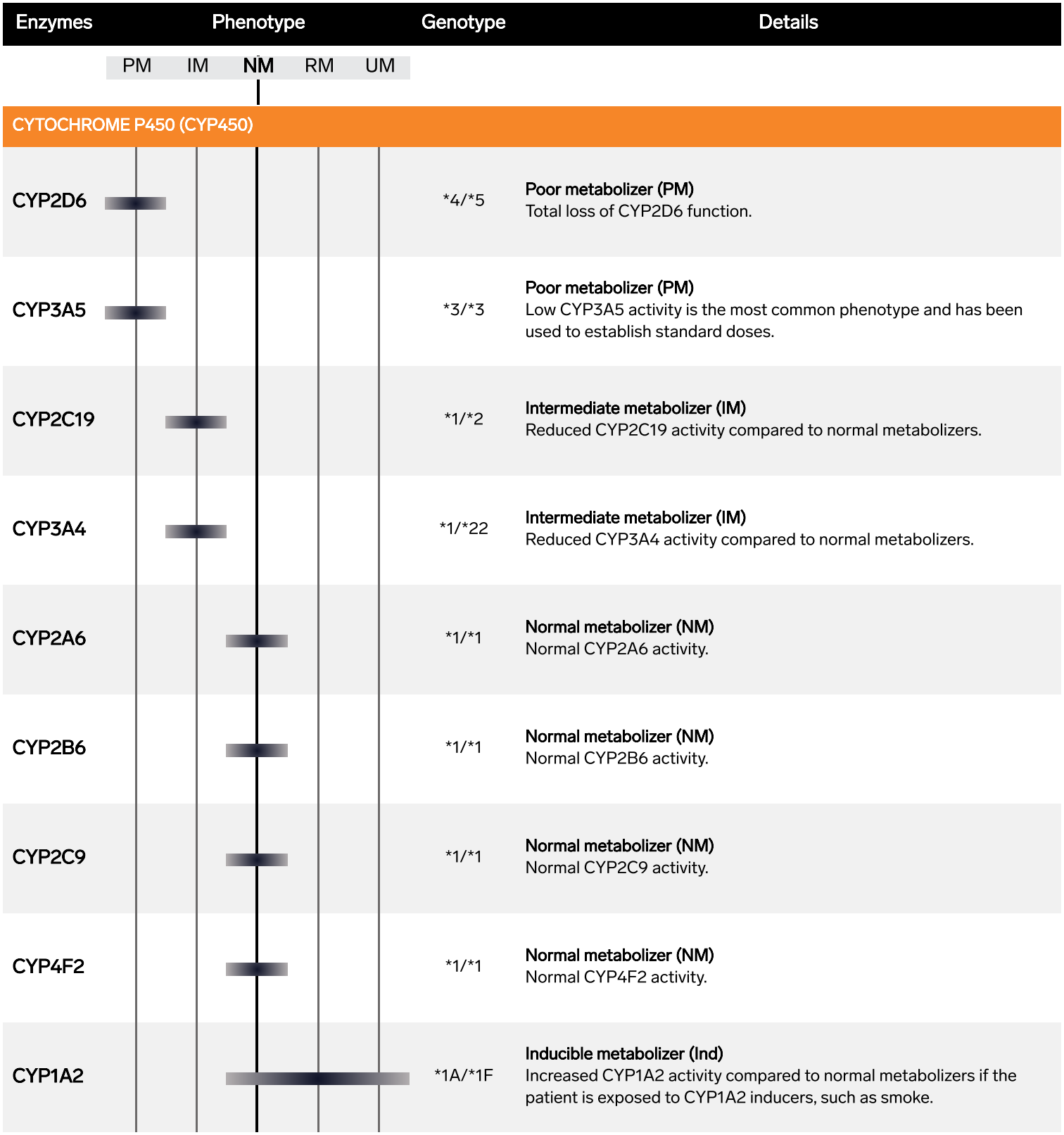
Greater potential for a poorer response or atypical effect.

Medication not recommended by peer-reviewed guidelines.

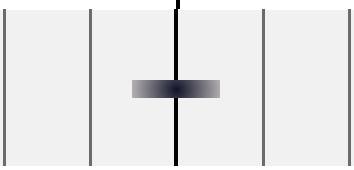
Normal exposure*, Normal efficacy* or Normal risk*: Based on currently available genetic data, the efficacy or risk of an atypical effect is likely similar to that of most other individuals; further research is needed to better understand genetic influence.

Genetic Associations Identified			
Medications	Exposure	Efficacy	Risk of atypical effect
Antiemetics			
Dimenhydrinate (Gravol®)	Normal exposure*	Normal efficacy*	Normal risk*
Granisetron (Kytril®)	Initiate therapy with recommended starting dose; a low dose may be adequate (CYP3A4 IM, CYP3A5 PM).	Normal efficacy*	Normal risk*
Ondansetron (Zofran®)	Initiate therapy with recommended starting dose; a low dose may be adequate (CYP2D6 PM).	Normal efficacy*	Normal risk*
Palonosetron (Aloxi®)	Consider using a lower dose (CYP2D6 PM).	Normal efficacy*	Normal risk*
Proton pump inhibitors (PPI)			
Esomeprazole (Nexium®)	Normal exposure*	Normal efficacy*	Normal risk*
Dexlansoprazole (Dexilant®)	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 (CYP2C19 IM).[14]	Normal efficacy*	Normal risk*
Lansoprazole (Prevacid®)	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 (CYP2C19 IM).[14]	Normal efficacy*	Normal risk*
Omeprazole (Losec®)	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 (CYP2C19 IM).[14]	Normal efficacy*	Normal risk*
Pantoprazole (Pantoloc®)	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 (CYP2C19 IM).[14]	Normal efficacy*	Normal risk*

PGx ASSOCIATIONS - EXPOSURE



Enzymes	Phenotype (PM / IM / **NM** / RM / UM)	Genotype	Details
OTHER METABOLIC ENZYMES AND FACTORS			
POR	NM	A/A	**Normal activity (NA)** Normal cytochrome P450 oxicoreductase (POR) activity (POR participates in CYP2B6 activation).
CES1	NM	C/C	**Normal metabolizer (NM)** Normal carboxylesterase-1 (CES1) activity.
SLCO1B1	NM	*1/*1	**Normal function** Normal solute carrier organic anion transporter family member 1B1 (SLCO1B1) activity.
DPYD	NM	REF/REF	**Normal metabolizer (NM)** Normal dihydropyrimidine dehydrogenase activity (DPYD).
TPMT	NM	*1/*1	**Normal metabolizer (NM)** Normal thiopurine S-methyltransferase (TPMT) activity.
NUDT15	NM	*1/*1	**Normal metabolizer (NM)** Normal nudix hydrolase 15 (NUDT15) activity.
UDP-GLUCURONOSYLTRANSFERASES (UGT)			
UGT1A1	IM	*1/*28	**Intermediate metabolizer (IM)** Reduced UGT1A1 activity compared to normal metabolizers.
UGT1A4	NM	*1/*1	**Normal metabolizer (NM)** Normal UGT1A4 activity.
UGT2B7	NM	*1/*1	**Normal metabolizer (NM)** Normal UGT2B7 activity.

Enzymes	Phenotype	Genotype	Details
	PM IM **NM** RM UM		
UGT2B15		*1/*1	**Normal metabolizer (NM)** Normal UGT2B15 activity.

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	G|G
	rs2032582	chr7:87531302	C|C
	rs2032583	chr7:87531245	T|T
ABCG2	rs2231142	chr4:88131171	G|G
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|C
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
	rs28399433	chr19:40850474	A|A
CYP2B6	rs2279343	chr19:41009358	A|A
	rs3745274	chr19:41006936	G|G
	rs28399499	chr19:41012316	T|T
CYP2C cluster	rs12777823	chr10:94645745	A|G
CYP2C9	rs1057910	chr10:94981296	A|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	A|A
	rs1135840	chr22:42126611	G|G
	rs3892097	chr22:42128945	T|T
	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
	rs774671100	chr22:42130555-42130755	G|G
	rs201377835	chr22:42129910	C|C
	Gene Deletion	n/a	Detected
	Gene Duplication	n/a	Not Detected
CYP3A4	rs4986907	chr7:99769804	C|C
	rs35599367	chr7:99768693	A|G
	rs55785340	chr7:99768360	A|A
	rs67666821	chr7:99758184-99758188	D|D
	rs72552799	chr7:99770165	C|C

Genes	Variant Details (GRCH38.p12)		Result
CYP3A5	rs776746	chr7:99672916	C|C
	rs10264272	chr7:99665212	C|C
	rs41303343	chr7:99652771	D|D
CYP4F2	rs2108622	chr19:15879621	C|C
DPYD	rs75017182	chr1:97579893	G|G
	rs55886062	chr1:97515787	A|A
	rs3918290	chr1:97450058	C|C
	rs112766203	chr1:97305279	G|G
	rs67376798	chr1:97082391	T|T
	rs115232898	chr1:97699474	T|T
	rs146356975	chr1:97595149	T|T
DRD2	rs6275	chr11:113412755	A|G
DRD3	rs963468	chr3:114144040	A|G
FAAH	rs324420	chr1:46405089	A|C
FKBP5	rs4713916	chr6:35702206	A|G
GNB3	rs5443	chr12:6845711	C|T
GRIK1	rs2832407	chr21:29595188	C|C
GRIK4	rs1954787	chr11:120792654	C|T
*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|C
HTR7	rs7905446	chr10:90859404	G|T
INSIG2	rs17047764	chr2:118111006	C|G
long non-coding (lnc) RNA	rs74795342	chr21:18954018	G|G
MC4R	rs489693	chr18:60215554	C|C
	rs17782313	chr18:60183864	T|T
MTHFR	rs1801131	chr1:11794419	T|T
	rs1801133	chr1:11796321	A|G
NUDT15	rs116855232	chr13:48045719	C|C
OPRM1	rs1799971	chr6:154039662	A|A
POR	rs2868177	chr7:75960585	A|A
SLC6A2	rs5569	chr16:55697923	G|G
	rs2242446	chr16:55656513	T|T
	rs28386840	chr16:55652906	A|A
SLC6A4	5-HTTLPR	chr17:30190154-30240133	L|L
SLC6A5	rs2298826	chr11:20638211	A|G
SLCO1B1	rs4149056	chr12:21178615	T|T
TH	rs2070762	chr11:2165105	A|G
TPH2	rs1487278	chr12:72007071	C|T
TPMT	rs1800462	chr6:18143724	C|C
	rs1800460	chr6:18138997	C|C
	rs1142345	chr6:18130687	T|T
UGT1A1	rs4148323	chr2:233760498	G|G
	rs34815109	chr2:233760234-233760248	6|7
UGT1A4	rs2011425	chr2:233718962	T|T
UGT2B7	rs7439366	chr4:69098620	T|T
UGT2B15	rs1902023	chr4:68670366	C|C
VKORC1	rs9923231	chr16:31096368	C|C

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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