

Interpretation Guide

Pharmacogenomic (PGx) Report

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

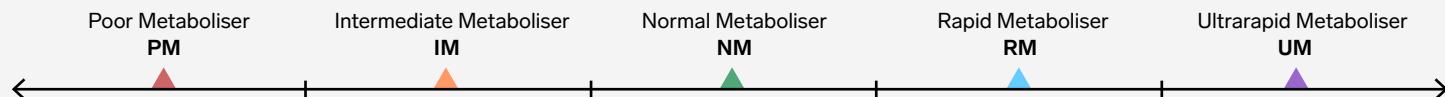
1. Only medications relevant for your patient need to be consulted.
2. Use the **Exposure** column to adjust doses for adequate plasma concentrations.
3. Use the **Efficacy** and **Risk of atypical effect** columns to choose the most compatible medication.

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

Exposure	Efficacy	Risk of atypical effect
 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.	 Signifies the presence of a high-impact gene variant, which increases the probability of a poorer response.	 Signifies the presence of variants associated with an increased risk of particular side effects, compared to non-carriers.
 Drug not recommended by peer-reviewed guidelines due to a risk of toxicity or lack of efficacy.	 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.	 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**.

For any questions regarding this report, contact Michel Cameron, PhD:

Phone: 1-866-923-9222 ext 8702

Email: mcameron@biron.com

biron.com/pgx-healthcare



PHARMACOGENOMIC REPORT



Psychiatry and ADHD, Pain Management, Cardiology

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DO NOT DISTRIBUTE. As per the Genetic Non-Discrimination Act, the information herein is intended for the patient and his/her healthcare providers. Without explicit patient consent, this report cannot be shared and/or used with other persons or organisations, including insurers and employers.

Many factors may affect the choice of optimal medication (e.g. diagnosis, environmental factors, epigenetics), hence this report is intended as a clinical decision support tool, does not constitute medical advice and does not supersede the professional judgement of the clinician. When supported by published guidelines, firm recommendations are provided and referenced, otherwise the evidence is directional in nature. For additional online resources, visit biron.com/pgxtest.

ADMINISTRATIVE DATA

Patient Name Michel The Great	Ordering Clinician N/A	Sample ID: bio022043 Sample Type: saliva
Sex assigned at birth: Male Date of birth: 1982-01-29 Phone Number: N/A Email: N/A	Patient Address 123 Rue des Tuileries Québec, QC G2G1K5	Date ordered: 2025-11-28 Date of sample reception: 2025-11-28 Date of report: 2025-11-28
Clinical Support Email: genetique@biron.com	Phone: 1-855-943-6379	Fax: (514) 317-2241

ATYPICAL PHENOTYPES

CYP1A2 IND, CYP2B6 IM, CYP4F2 PM, DPYD IM, POR PA, NUDT15 PM, SLCO1B1 Poor function, TPMT PM, UGT2B15 IM.

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

Medication	Identified risk	Recommendation
Capecitabine, 5-fluorouracil	Decreased DPD activity (DPD activity at 30% to 70% that of the normal population) and increased risk for severe or even fatal drug toxicity when treated with fluoropyrimidines.	Reduce starting dose by 50% followed by titration of dose based on toxicity or therapeutic drug monitoring, if available. Increase the dose in patients experiencing no or clinically tolerable toxicity in the first two cycles to maintain efficacy; decrease the dose in patients who do not tolerate the starting dose to minimize toxicities (DPYD IM, c.2846A>T/c.2846A>T). ¹
Azathioprine	Extremely high concentrations of TGN metabolites; fatal toxicity possible without dose decrease; no MeTIMP metabolites. Greatly increased risk of thiopurine-related leukopenia, neutropenia, myelosuppression.	For nonmalignant conditions, consider alternative nonthiopurine immunosuppressant therapy. For malignancy, start with drastically reduced doses (reduce daily dose by 10-fold and dose thrice weekly instead of daily) and adjust doses of azathioprine based on degree of myelosuppression and disease-specific guidelines. Allow 4–6 weeks to reach steady-state after each dose adjustment (TPMT PM, NUDT15 PM). ²
Mercaptopurine	Extremely high concentrations of TGN metabolites; fatal toxicity possible without dose decrease; no MeTIMP metabolites. Greatly increased risk of thiopurine-related leukopenia, neutropenia, myelosuppression.	For malignancy, start with drastically reduced doses (reduce daily dose by 10-fold and reduce frequency to thrice weekly instead of daily (e.g., 10 mg/m ² /day given just 3 days/week) and adjust doses of mercaptopurine based on degree of myelosuppression and disease-specific guidelines. Allow 4–6 weeks to reach steady-state after each dose adjustment. If myelosuppression occurs, emphasis should be on reducing mercaptopurine over other agents. For nonmalignant conditions, consider alternative nonthiopurine immunosuppressant therapy (TPMT PM, NUDT15 PM). ²

CAUTIONARY INFORMATION

Medication	Identified risk	Recommendation
Thioguanine	Extremely high concentrations of TGN metabolites; fatal toxicity possible without dose decrease. Greatly increased risk of thiopurine-related leukopenia, neutropenia, myelosuppression.	Start with drastically reduced doses (reduce daily dose by 10-fold and dose thrice weekly instead of daily) and adjust doses of thioguanine based on degree of myelosuppression and disease-specific guidelines. Allow 4–6 weeks to reach steady-state after each dose adjustment. If myelosuppression occurs, emphasis should be on reducing thioguanine over other agents. For nonmalignant conditions, consider alternative nonthiopurine immunosuppressant therapy (TPMT PM, NUDT15 PM). ²
Cisplatin	Increased risk of cisplatin-induced hearing loss (ototoxicity).	To reduce the risk of ototoxicity, monitor hearing loss more closely and consider the use of otoprotectants. Alternative treatments may be considered based on disease-specific guidelines (TPMT PM). ³

PGx RECOMMENDATIONS - PSYCHIATRY AND ADHD

- ↑ Dose increase may be required due to lower exposure to active metabolite(s) with standard dosing. ✓ Increased probability of a better response.
- ↓ Dose reduction may be required due to higher exposure to active metabolite(s) with standard dosing. ! Greater potential for a poorer response or atypical effect.
- ⌚ Exposure is difficult to predict, insufficient data to calculate dose adjustments. ✗ 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®)	Normal exposure (CYP2D6 NM, CYP2C9 NM).	4/6 variants: increased likelihood of a poorer response (FKBP5, BDNF, GRIK4, HTR7).	Normal risk*
Fluvoxamine (Luvox®)	Initiate with recommended dose; a low dose may be adequate (CYP2D6 NM, ABCB1).	4/6 variants: increased likelihood of a poorer response (FKBP5, BDNF, GRIK4, HTR7).	Normal risk*
Paroxetine (Paxil®)	Initiate therapy with recommended starting dose; a low dose may be adequate (CYP2D6 NM, ABCB1).	4/6 variants: increased likelihood of a poorer response (FKBP5, BDNF, GRIK4, HTR7).	Normal risk*
Citalopram (Celexa®)	Initiate with recommended dose; a low dose may be adequate (CYP2C19 NM, CYP3A4 NM, ABCB1).	4/6 variants: increased likelihood of a poorer response (FKBP5, BDNF, GRIK4, HTR7).	! 1/1 variant: increased risk of gastrointestinal side effects (HTR2A).
Escitalopram (Cipralex®)	Initiate with recommended dose; a low dose may be adequate (CYP2C19 NM, CYP3A4 NM, ABCB1).	4/6 variants: increased likelihood of a poorer response (FKBP5, BDNF, GRIK4, HTR7).	! 1/1 variant: increased risk of gastrointestinal side effects (HTR2A).
Sertraline (Zoloft®)	↓ Initiate therapy with recommended starting dose but with a slower titration schedule and a lower maintenance dose (CYP2B6 IM, CYP2C19 NM). ⁴	4/5 variants: increased likelihood of a poorer response (BDNF, FKBP5, GRIK4, HTR7)	! 1/1 variant: increased risk of gastrointestinal side effects (HTR2A).
Serotonin–norepinephrine reuptake inhibitors (SNRIs)			
Desvenlafaxine (Pristiq®)	Initiate with recommended dose (UGT1A1 NM, UGT2B15 IM, CYP3A4 NM).	2/2 variants: increased likelihood of a poorer response (FKBP5, GRIK4).	Normal risk*
Levomilnacipran (Fetzima®)	Initiate with recommended dose; a low dose may be adequate (CYP3A4 NM, ABCB1).	2/2 variants: increased likelihood of a poorer response (FKBP5, GRIK4).	Normal risk*
Venlafaxine-XR (Effexor XR®)	Initiate with recommended dose; a low dose may be adequate (CYP2D6 NM, ABCB1).	4/4 variants: increased likelihood of a poorer response (COMT, FKBP5, GRIK4, SLC6A2).	Normal risk*
Duloxetine (Cymbalta®)	↑ Initiate therapy with recommended starting dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke (CYP1A2 Ind, CYP2D6 NM).	2/3 variants: increased likelihood of a poorer response (FKBP5, GRIK4).	Normal risk*
Other antidepressants			
Trazodone (Desyrel®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Vilazodone (Viibryd®)	Initiate with recommended dose; a low dose may be adequate (CYP3A4 NM, ABCB1).	Normal efficacy*	Normal risk*

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Vortioxetine (Trintellix®)	Normal exposure (CYP2D6 NM, CYP3A4 NM).	Normal efficacy*	Normal risk*
Mirtazapine (Remeron®)	↑ Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke (CYP1A2 Ind, CYP2D6 NM, CYP3A4 NM).	2/2 variants: increased likelihood of a poorer response (FKBP5, TPH2).	Normal risk*
Bupropion (Wellbutrin®)	↓ Consider using a lower dose (CYP2B6 IM, POR).	0/1 variant: no increased likelihood of a poorer response for treatment of depressive symptoms (HTR2A).	Normal risk*
Esketamine (Spravato®)	↓ Consider using a lower dose (CYP2B6 IM, POR).	0/1 variant: no increased likelihood of a poorer response.	0/1 variant: no increased risk of emergent hypertension.
Ketamine (Ketalar®)	↓ Consider using a lower dose (CYP2B6 IM, POR).	0/1 variant: no increased likelihood of a poorer response.	0/1 variant: no increased risk of emergent hypertension.
Tricyclic antidepressants (TCAs)			
Amitriptyline (Elavil®)	CYP2C19 NM, CYP2D6 NM, ABCB1 - Initiate with recommended dose; a low dose may be adequate.	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Clomipramine (Anafranil®)	CYP2C19 NM, CYP2D6 NM - Normal exposure ⁵	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Desipramine (Norpramin®)	CYP2D6 NM, ABCB1 - Initiate with recommended dose; a low dose may be adequate.	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Doxepin (Sinequan®)	CYP2C19 NM, CYP2D6 NM, ABCB1 - Initiate with recommended dose; a low dose may be adequate.	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Imipramine (Tofranil®)	CYP2C19 NM, CYP2D6 NM - Normal exposure ⁵	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Nortriptyline (Aventyl®)	CYP2D6 NM, ABCB1 - Initiate with recommended dose; a low dose may be adequate.	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Trimipramine (Surmontil®)	CYP2C19 NM, CYP2D6 NM, ABCB1 - Initiate with recommended dose; a low dose may be adequate.	1/1 variant: increased likelihood of a poorer response (TPH2)	Genetic influence not available
Monoamine oxidase inhibitors (MAOs)			
Moclobemide (Manerix®)	Normal exposure (CYP2D6 NM, CYP2C19 NM).	Normal efficacy*	Normal risk*
Phenelzine (Nardil®)	Normal exposure*	Normal efficacy*	Normal risk*
Tranylcypromine (Parnate®)	Normal exposure*	Normal efficacy*	Normal risk*
Antipsychotics			
1st generation antipsychotics			
Chlorpromazine (Largactil®)	Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke (CYP2D6 NM, CYP1A2 Ind).	Normal efficacy*	Normal risk*
Fluphenazine (Moditen®)	Normal exposure (CYP2D6 NM).	Normal efficacy*	Normal risk*
Haloperidol (Haldol®)	Normal exposure (CYP2D6 NM).	Normal efficacy*	0/1 variant: no increased risk of extrapyramidal side effects.
Perphenazine (Trilafon®)	Normal exposure (CYP2D6 NM).	Normal efficacy*	Normal risk*

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Pimozide (Orap®)	Normal exposure (CYP2D6 NM).	Normal efficacy*	Normal risk*
Zuclopentixol (Clopixol®)	Normal exposure (CYP2D6 NM).	Normal efficacy*	Normal risk*
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*
2nd generation antipsychotics			
Aripiprazole (Abilify®)	Normal exposure (CYP2D6 NM).	1/1 variant: increased likelihood of a poorer response (ANKK1).	Normal risk*
Brexpiprazole (Rexulti®)	Normal exposure (CYP2D6 NM, CYP3A4 NM).	Normal efficacy*	Normal risk*
Cariprazine (Vraylar®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Lurasidone (Latuda®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Paliperidone (Invega®)	Initiate with recommended dose; a low dose may be adequate (CYP3A4 NM, ABCB1).	Normal efficacy*	Normal risk*
Quetiapine (Seroquel®)	Initiate with recommended dose; a low dose may be adequate (CYP3A4 NM, ABCB1).	Normal efficacy*	1/2 variants: increased risk of antipsychotic-induced weight gain (MC4Ra).
Risperidone (Risperdal®)	Normal exposure (CYP2D6 NM).	1/1 variant: increased likelihood of a poorer response (ANKK1).	1/6 variants: increased risk of antipsychotic-induced weight gain (MC4R).
Ziprasidone (Zeldox®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
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*
Clozapine (Clozaril®)	↑ Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke (CYP1A2 Ind, CYP2D6 NM).	Normal efficacy*	1/6 variants: increased risk of antipsychotic-induced weight gain (MC4R).
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 (MC4R).
Anxiolytics			
Alprazolam (Xanax®)	Normal exposure (CYP3A4 NM, CYP3A5 PM).	Normal efficacy*	Normal risk*
Buspirone (Buspar®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Chlordiazepoxide (Librium®)	Initiate with recommended dose; a low dose may be adequate (CYP3A4 NM, UGT2B15 IM).	Normal efficacy*	Normal risk*
Clobazam (Frismium®)	Normal exposure (CYP2C19 NM).	Normal efficacy*	Normal risk*
Clonazepam (Rivotril®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Clorazepate (Tranxene®)	Initiate with recommended dose; a low dose may be adequate (CYP3A4 NM, UGT2B15 IM).	Normal efficacy*	Normal risk*

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Diazepam (Valium®)	Normal exposure (CYP2C19 NM, CYP3A4 NM, UGT2B15 IM).	Normal efficacy*	Normal risk*
Flurazepam (Dalmane®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Hydroxyzine (Atarax®)	Normal exposure (CYP3A4 NM, CYP3A5 PM).	Normal efficacy*	Normal risk*
Lorazepam (Ativan®)	Initiate with recommended dose; a low dose may be adequate (UGT2B15 IM).	Normal efficacy*	Normal risk*
Midazolam (Versed®)	Normal exposure (CYP2C19 NM, CYP3A5 PM, CYP3A4 NM).	Normal efficacy*	Normal risk*
Nitrazepam (Mogadon®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Oxazepam (Serax®)	Initiate with recommended dose; a low dose may be adequate (UGT2B15 IM).	Normal efficacy*	Normal risk*
Temazepam (Restoril®)	Initiate with recommended dose; a low dose may be adequate (UGT2B15 IM).	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*

Central alpha-adrenergic agonists

Clonidine (Catapres®)	Normal exposure (CYP2D6 NM).	1/1 variant: increased likelihood of a poorer response (GNB3).	Normal risk*
Guanfacine (Intuniv XR®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*

Mood Stabilizers

Carbamazepine (Tegretol®)	Normal exposure (CYP3A4 NM, CYP3A5 PM, UGT2B7 NM, ABCB1).	Normal efficacy*	HLA-A*31:01 negative, HLA-B*15:02 negative - Normal risks of cutaneous adverse reactions.
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 cutaneous adverse reactions.
Pregabalin (Lyrica®)	Normal exposure*	Normal efficacy*	Normal risk*
Topiramate (Topamax®)	Genetic influence not available	1/1 variant: increased likelihood of a poorer response for treatment of alcohol-related disorders (GRIK1).	Normal risk*
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

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Atomoxetine (Strattera®)	Normal exposure (CYP2D6 NM). ^{6, 7}	Genetic influence not available	Genetic influence not available
Psychostimulants			
Amphetamine / Dextroamphetamine (Adderall XR®)	Normal exposure (CYP2D6 NM).	Normal efficacy*	Normal risk*
Dextroamphetamine (Dexedrine®)	Normal exposure (CYP2D6 NM).	Normal efficacy*	Normal risk*
Lisdexamfetamine (Vyvanse®)	Normal exposure (CYP2D6 NM).	Normal efficacy*	Normal risk*
Methylphenidate - Biphentin®	Normal exposure (CES1 NM).	3/5 variants: increased likelihood of a poorer response (ADRA2A, SLC6A2a, SLC6A2b).	Normal risk*
Methylphenidate - Concerta®	Normal exposure (CES1 NM).	3/5 variants: increased likelihood of a poorer response (ADRA2A, SLC6A2a, SLC6A2b).	Normal risk*
Methylphenidate - Foquest®	Normal exposure (CES1 NM).	3/5 variants: increased likelihood of a poorer response (ADRA2A, SLC6A2a, SLC6A2b).	Normal risk*
Methylphenidate - Quillivant®	Normal exposure (CES1 NM).	3/5 variants: increased likelihood of a poorer response (ADRA2A, SLC6A2a, SLC6A2b).	Normal risk*
Methylphenidate - Ritalin®	Normal exposure (CES1 NM).	3/5 variants: increased likelihood of a poorer response (ADRA2A, SLC6A2a, SLC6A2b).	Normal risk*
Sedative-Hypnotics			
Daridorexant (Quviquiq®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Diphenhydramine (Benadryl®)	Normal exposure*	Normal efficacy*	Normal risk*
Eszopiclone (Lunesta®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Lemborexant (Dayvigo®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Melatonin	Normal exposure*	Normal efficacy*	Normal risk*
Phenobarbital (Phenobarb®)	Normal exposure (CYP2C9 NM).	Normal efficacy*	Normal risk*
Triazolam (Halcion®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Zolpidem (Sublinox®)	Normal exposure (CYP3A4 NM, CYP2C9 NM).	Normal efficacy*	Normal risk*
Zopiclone (Imovane®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Wakefulness-promoting agents			
Modafinil (Alertec®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Pitolisant (Wakix®)	Normal exposure (CYP2D6 NM, CYP3A4 NM).	Normal efficacy*	Normal risk*
Sodium oxybate (Xyrem®)	Normal exposure*	Normal efficacy*	Normal risk*
Solriamfetol (Sunosi®)	Normal exposure*	Normal efficacy*	Normal risk*

PGx RECOMMENDATIONS - PAIN MANAGEMENT

- ▲ Dose increase may be required due to lower exposure to active metabolite(s) with standard dosing. ✓ Increased probability of a better response.
- ▼ Dose reduction may be required due to higher exposure to active metabolite(s) with standard dosing. ! Greater potential for a poorer response or atypical effect.
- ~ Exposure is difficult to predict, insufficient data to calculate dose adjustments. ✖ 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
Analgesic			
Acetaminophen (Tylenol®)	Normal exposure*	Normal efficacy*	Normal risk*
Antimetabolite			
Methotrexate	▼ Consider using a lower dose (ABCB1, MTHFR).	Normal efficacy*	Normal risk*
Cannabinoids			
Cannabidiol (CBD)	Normal exposure (CYP3A4 NM, CYP2C9 NM).	Normal efficacy*	Normal risk*
Nabilone (Cesamet®)	Normal exposure*	Normal efficacy*	Normal risk*
Tetrahydrocannabinol (THC)	Normal exposure (CYP3A4 NM, CYP2C9 NM).	Normal efficacy*	! 1/2 variants: increased risk of cannabis use disorder (CNR1).
Muscle Relaxant			
Carisoprodol (Soma®)	Normal exposure (CYP2C19 NM).	Normal efficacy*	Normal risk*
Methocarbamol (Robaxin®)	Normal exposure*	Normal efficacy*	Normal risk*
Cyclobenzaprine (Flexeril®)	▲ Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke (CYP3A4 NM, CYP1A2 Ind).	Normal efficacy*	Normal risk*
Tizanidine (Zanaflex®)	▲ Initiate with recommended dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke (CYP1A2 Ind).	Normal efficacy*	Normal risk*
Nonsteroidal Anti-Inflammatory Drugs (NSAID)			
Acetylsalicylic acid (Aspirin®)	Normal exposure*	Normal efficacy*	Normal risk*
Celecoxib (Celebrex®)	Normal exposure (CYP2C9 NM).	Normal efficacy*	Normal risk*
Diclofenac (Voltaren®)	Normal exposure (UGT2B7 NM).	Normal efficacy*	Normal risk*
Etodolac (Ultradol®)	Normal exposure (CYP2C9 NM).	Normal efficacy*	Normal risk*
Flurbiprofen (Ansaid®)	Normal exposure (CYP2C9 NM).	Normal efficacy*	Normal risk*

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Ibuprofen (Advil®)	Normal exposure (CYP2C9 NM).	Normal efficacy*	Normal risk*
Indomethacin (Indocid®)	Normal exposure (CYP2C9 NM).	Normal efficacy*	Normal risk*
Ketorolac (Toradol®)	Normal exposure (CYP2C9 NM).	Normal efficacy*	Normal risk*
Meloxicam (Mobicox®)	Normal exposure (CYP2C9 NM).	Normal efficacy*	Normal risk*
Naproxen (Naprosyn®)	Normal exposure*	Normal efficacy*	Normal risk*
Piroxicam (Feldene®)	Initiate with recommended dose; normal exposure (CYP2C9 MM).	Normal efficacy*	Normal risk*
Tenoxicam (Mobicflex®)	Initiate with recommended dose; normal exposure (CYP2C9 MM).	Normal efficacy*	Normal risk*
Nabumetone (Relafen®)	↓ Initiate with recommended dose but monitor tolerance more closely; may require a lower dose, especially with CYP1A2 inducers, such as smoke (CYP1A2 Ind, CYP2C9 NM).	Normal efficacy*	Normal risk*
Opioids			
Buprenorphine (Butrans®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Butorphanol (Stadol®)	Normal exposure*	Normal efficacy*	Normal risk*
Fentanyl (Duragesic®)	Normal exposure (CYP3A4 NM, CYP3A5 PM).	Normal efficacy*	Normal risk*
Nalbuphine (Nubain®)	Normal exposure*	Normal efficacy*	Normal risk*
Remifentanil (Ultiva®)	Normal exposure*	Normal efficacy*	Normal risk*
Sufentanil (Sufenta®)	Normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Tapentadol (Nucynta®)	Normal exposure*	Normal efficacy*	Normal risk*
Meperidine (Demerol®)	↓ Consider using a lower dose (CYP2B6 IM, POR, CYP3A4 NM).	Normal efficacy*	Normal risk*
Methadone	↓ Consider using a lower dose (CYP2B6 IM, POR, CYP3A4 NM).	Normal efficacy*	Normal risk*
Codeine	Normal exposure (CYP2D6 NM, UGT2B7 NM).	! 1/1 variant: increased likelihood of a poorer response (OPRM1).	Normal risk*
Hydrocodone (Hycodan®)	Normal exposure (CYP2D6 NM).	! 1/1 variant: increased likelihood of a poorer response (OPRM1).	Normal risk*
Hydromorphone (Dilaudid®)	Normal exposure*	! 1/1 variant associated with an increased likelihood of a poorer response (OPRM1).	Normal risk*
Morphine (Statex®)	Normal exposure (UGT2B7 NM).	! 1/1 variant: increased likelihood of a poorer response (OPRM1).	0/1 variant: no increased risk of gastrointestinal side effects (FAAH).
Oxycodone (Suepdol®)	Normal exposure (CYP3A4 NM, CYP2D6 NM).	! 1/1 variant: increased likelihood of a poorer response (OPRM1).	Normal risk*
Tramadol (Ultram®)	Normal exposure (CYP2D6 NM).	! 1/1 variant: increased likelihood of a poorer response (OPRM1).	Normal risk*
Opioid antagonists			
Naloxone (Narcan®)	Normal exposure*	0/1 variant: no increased likelihood of a poorer response.	Normal risk*

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Naltrexone (Revia®)	Normal exposure*	1/1 variant: increased likelihood of a poorer response when used in combination with bupropion for weight loss (ANKK1).	Normal risk*

PGx RECOMMENDATIONS - CARDIOLOGY

- ▲ Dose increase may be required due to lower exposure to active metabolite(s) with standard dosing. ✓ Increased probability of a better response.
- ▼ Dose reduction may be required due to higher exposure to active metabolite(s) with standard dosing. ! Greater potential for a poorer response or atypical effect.
- ~ Exposure is difficult to predict, insufficient data to calculate dose adjustments. ✖ 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
Angiotensin-Converting Enzyme Inhibitors (ACEI)			
Benazepril (Lotensin®)	Initiate with recommended starting dose, normal exposure (CES1 NM).	Normal efficacy*	Normal risk*
Captopril (Capoten®)	Normal exposure*	Normal efficacy*	Normal risk*
Cilazapril (Inhibace®)	Initiate with recommended starting dose, normal exposure (CES1 NM).	Normal efficacy*	Normal risk*
Fosinopril (Monopril®)	Initiate with recommended starting dose, normal exposure (CES1 NM).	Normal efficacy*	Normal risk*
Lisinopril (Prinivil/Zestril®)	Normal exposure*	Normal efficacy*	Normal risk*
Perindopril (Coversyl®)	Initiate with recommended starting dose, normal exposure (CES1 NM).	Normal efficacy*	Normal risk*
Quinapril (Accupril®)	Initiate with recommended starting dose, normal exposure (CES1 NM).	Normal efficacy*	Normal risk*
Ramipril (Altace®)	Initiate with recommended starting dose, normal exposure (CES1 NM).	Normal efficacy*	Normal risk*
Trandolapril (Mavik®)	Initiate with recommended starting dose, normal exposure (CES1 NM).	Normal efficacy*	Normal risk*
Enalapril (Vasotec®)	! Initiate with recommended starting dose but monitor side effects and the risk of hypotension more closely (CES1 NM, SLCO1B1 poor function).	Normal efficacy*	Normal risk*
Antiarrhythmics			
Amiodarone (Pacerone®/Cordarone®)	Initiate therapy with recommended starting dose (CYP3A4 NM).	Normal efficacy*	Normal risk*
Digoxin (Lanoxin®)	Initiate with recommended dose; a low dose may be adequate (ABCB1).	Normal efficacy*	Normal risk*
Disopyramide (Rythmodan®)	Initiate therapy with recommended starting dose (CYP3A4 NM).	Normal efficacy*	Normal risk*
Flecainide (Tambocor®)	Initiate therapy with recommended starting dose, normal exposure (CYP2D6 NM). ⁸	Normal efficacy*	Normal risk*
Propafenone (Rythmol®)	Initiate therapy with recommended starting dose, normal exposure (CYP2D6 NM). ⁸	Normal efficacy*	Normal risk*
Anticoagulants			

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Acenocoumarol-Nicoumalone (Sintrom®)	Initiate with recommended dose, normal exposure (VKORC1 -1639 GG). ⁸	Normal efficacy*	Normal risk*
Apixaban (Eliquis®)	Initiate with recommended starting dose, normal exposure (CYP3A4 NM, ABCB1).	Normal efficacy*	Normal risk*
Dabigatran (Pradaxa®)	Initiate with recommended starting dose (CES1 NM, UGT2B15 IM).	Normal efficacy*	Normal risk*
Edoxaban (Lixiana®/Savaysa®)	! Initiate with recommended starting dose but monitor more closely for potential bleeding risks (SLCO1B1 PA).	Normal efficacy*	Normal risk*
Rivaroxaban (Xarelto®)	! Initiate with recommended starting dose but monitor more closely for potential bleeding risks (ABCB1).	Normal efficacy*	Normal risk*
Warfarin (Coumadin®)	! A dose adjustment may be required; go to warfarindosing.org to calculate the average recommended dose using a validated pharmacogenetic algorithm (CYP2C9 NM, VKORC1 -1639 GG, CYP4F2 TT, rs12777823 GG). ⁹	Normal efficacy*	Normal risk*
Antiplatelets			
Clopidogrel (Plavix®)	Initiate with recommended starting dose, normal exposure (CYP2C19 NM). ¹⁰	Normal efficacy*	Normal risk*
Prasugrel (Effient®)	Normal exposure*	Normal efficacy*	Normal risk*
Ticagrelor (Brilinta®)	Normal exposure*	Normal efficacy*	Normal risk*
Angiotensin II Receptor Blockers (ARBs)			
Azilsartan (Edarbi®)	Initiate with recommended starting dose, normal exposure (CYP2C9 NM).	Normal efficacy*	Normal risk*
Irbesartan (Avapro®)	Initiate with recommended starting dose, normal exposure (CYP2C9 NM).	Normal efficacy*	Normal risk*
Losartan (Cozaar®)	Initiate with recommended starting dose, normal exposure (CYP2C9 NM).	Normal efficacy*	Normal risk*
Olmesartan (Olmotec®/Benicar®)	Normal exposure*	Normal efficacy*	Normal risk*
Telmisartan (Micardis®)	Normal exposure*	Normal efficacy*	Normal risk*
Valsartan (Diovan®)	Initiate with recommended starting dose, normal exposure (ABCB1).	Normal efficacy*	Normal risk*
Beta-blockers			
Acebutolol (Sectral®/Monitan®)	Initiate with recommended dose; normal exposure (CYP2C19 NM).	Normal efficacy*	Normal risk*
Atenolol (Tenormin®)	Normal exposure; eliminated largely unchanged by the kidneys.	Normal efficacy*	Normal risk*
Bisoprolol (Monocor®/Zebeta®)	Initiate with recommended starting dose, normal exposure (CYP2D6 NM, CYP3A4 NM, CYP3A5 PM).	Normal efficacy*	Normal risk*
Carvedilol (Coreg®)	Initiate with recommended starting dose, normal exposure (CYP2D6 NM, CYP2C9 NM, UGT1A1 NM).	Normal efficacy*	Normal risk*
Labetalol (Trandate®)	CYP2C19 NM - Initiate with recommended dose; normal exposure.	Normal efficacy*	Normal risk*

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Metoprolol (Lopressor/Betaloc®/ Toprol XL®)	Initiate with recommended starting dose, normal exposure (CYP2D6 NM).	Normal efficacy*	Normal risk*
Nadolol (Corgard®)	Initiate with recommended starting dose but monitor bradycardia more closely; a low dose may be adequate (ABCB1).	Normal efficacy*	Normal risk*
Sotalol (Sotacor®/Betapace®)	Normal exposure; eliminated largely unchanged by the kidneys.	Normal efficacy*	Normal risk*
Propranolol (Inderal®)	↑ Initiate therapy with recommended starting dose but may require a higher dose, especially with CYP1A2 inducers, such as smoke (CYP2D6 NM, CYP1A2 Ind).	Normal efficacy*	Normal risk*
Calcium channel blockers (CCBs)			
Amlodipine (Norvasc®)	Initiate with recommended starting dose, normal exposure (CYP3A4 NM, CYP3A5 PM).	Normal efficacy*	Normal risk*
Diltiazem (Cardizem®/Tiazac®)	Initiate with recommended starting dose, normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Felodipine (Plendil®)	Initiate with recommended starting dose, normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Nifedipine (Adalat/Procardia®)	Initiate with recommended starting dose, normal exposure (CYP3A4 NM, CYP3A5 PM).	Normal efficacy*	Normal risk*
Verapamil (Isoptin®/Verelan®/ Calan®)	Initiate with recommended starting dose, normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Diuretics			
Acetazolamide (Diamox®)	Normal exposure; eliminated largely unchanged by the kidneys.	Normal efficacy*	Normal risk*
Amiloride (Midamor®)	Normal exposure; eliminated largely unchanged by the kidneys.	Normal efficacy*	Normal risk*
Chlorthalidone (Hygroton®)	Normal exposure; eliminated largely unchanged by the kidneys.	Normal efficacy*	Normal risk*
Eplerenone (Inspira®)	Initiate with recommended starting dose, normal exposure (CYP3A4 NM, CYP3A5 PM).	Normal efficacy*	Normal risk*
Furosemide (Lasix®)	Normal exposure*	Normal efficacy*	Normal risk*
Hydrochlorothiazide (HCTZ) (Hydrodiuril®/ Microzide®)	Normal exposure; eliminated largely unchanged by the kidneys.	Normal efficacy*	Normal risk*
Indapamide (Izide®/Lozol®)	Initiate with recommended starting dose, normal exposure (CYP3A4 NM).	Normal efficacy*	Normal risk*
Spirostanolactone (Aldactone®)	Normal exposure; eliminated largely unchanged by the kidneys.	Normal efficacy*	Normal risk*
Triamterene (Dyrenium®)	↑ Initiate with recommended starting dose but monitor efficacy more closely, especially with CYP1A2 inducers, such as smoke (CYP1A2 Ind).	Normal efficacy*	Normal risk*
Lipid-lowering agent			
Fenofibrate (Lipidil®/Tricor®)	Normal exposure*	Normal efficacy*	Normal risk*

Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Selective cholesterol-absorption inhibitor			
Ezetimibe (Ezetrol®/Zetia®)	Normal exposure*	Normal efficacy*	Normal risk*
Statins			
Atorvastatin (Lipitor®/Caduet®)	<p>⬇️ Prescribe ≤20 mg as a starting dose and adjust doses based on disease-specific guidelines. If dose >20 mg is needed for desired efficacy, consider rosuvastatin or combination therapy (i.e., atorvastatin plus nonstatin guideline-directed medical therapy) (SLCO1B1 poor function).¹¹</p>	Normal efficacy*	Normal risk*
Fluvastatin (Lescol®)	<p>⬇️ Prescribe ≤40 mg per day as a starting dose and adjust doses based on disease-specific guidelines. If patient is tolerating 40 mg per day but higher potency is needed, a higher dose (>40 mg) or an alternative statin or combination therapy (i.e., fluvastatin plus nonstatin guideline-directed medical therapy) could be considered. Be aware of possible increased risk for myopathy with fluvastatin especially with doses >40 mg per day (SLCO1B1 poor function, CYP2C9 NM).¹¹</p>	Normal efficacy*	Normal risk*
Pitavastatin (Livalo®)	<p>⬇️ Prescribe ≤1 mg as a starting dose and adjust doses based on disease-specific guidelines. If dose >1 mg needed for desired efficacy, consider an alternative statin or combination therapy (i.e., pitavastatin plus nonstatin guideline-directed medical therapy) (SLCO1B1 poor function).¹¹</p>	Normal efficacy*	Normal risk*
Pravastatin (Pravachol®)	<p>⬇️ Prescribe ≤40 mg as a starting dose and adjust doses based on disease-specific guidelines. If patient is tolerating 40-mg dose but higher potency is needed, a higher dose (>40 mg) or an alternative statin or combination therapy (i.e., pravastatin plus nonstatin guideline-directed medical therapy) could be considered. Be aware of possible increased risk for myopathy especially with pravastatin doses >40 mg (SLCO1B1 poor function).¹¹</p>	Normal efficacy*	Normal risk*
Rosuvastatin (Crestor®)	<p>⬇️ Prescribe ≤20 mg as a starting dose and adjust doses based on disease-specific and population-specific guidelines. If dose >20 mg needed for desired efficacy, consider combination therapy (i.e., rosuvastatin plus nonstatin guideline-directed medical therapy) (SLCO1B1 poor function, ABCG2 normal function).⁵</p>	Normal efficacy*	Normal risk*
Lovastatin (Mevacor®)	<p>✗ Prescribe an alternative statin depending on the desired potency (SLCO1B1 poor function).¹¹</p>	Normal efficacy*	Normal risk*
Simvastatin (Zocor®)	<p>✗ Prescribe an alternative statin depending on the desired potency (SLCO1B1 poor function).¹¹</p>	Normal efficacy*	Normal risk*

PGx RECOMMENDATIONS - COMPLEMENTARY TREATMENTS

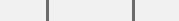
- ▲ Dose increase may be required due to lower exposure to active metabolite(s) with standard dosing. ✓ Increased probability of a better response.
- ▼ Dose reduction may be required due to higher exposure to active metabolite(s) with standard dosing. ! Greater potential for a poorer response or atypical effect.
- ~ Exposure is difficult to predict, insufficient data to calculate dose adjustments. ✖ 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.

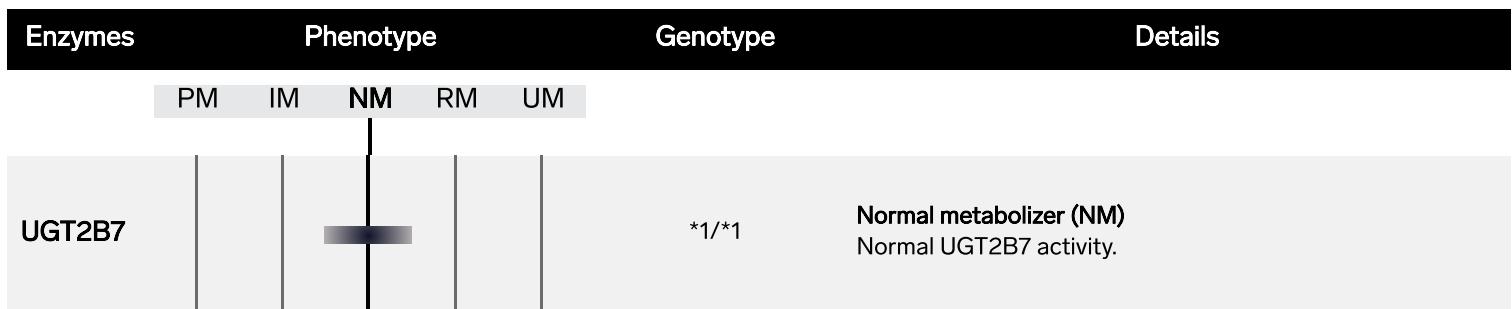
Genetic Associations Identified

Medications	Exposure	Efficacy	Risk of atypical effect
Antiemetics			
Dimenhydrinate (Gravol®)	Normal exposure*	Normal efficacy*	Normal risk*
Granisetron (Kytril®)	Normal exposure (CYP3A4 NM, CYP3A5 PM).	Normal efficacy*	Normal risk*
Ondansetron (Zofran®)	Normal exposure (CYP2D6 NM).	Normal efficacy*	Normal risk*
Palonosetron (Aloxi®)	Normal exposure (CYP2D6 NM).	Normal efficacy*	Normal risk*
Proton pump inhibitors (PPI)			
Dexlansoprazole (Dexilant®)	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 (CYP2C19 NM). ¹²	Normal efficacy*	Normal risk*
Esomeprazole (Nexium®)	Normal exposure*	Normal efficacy*	Normal risk*
Lansoprazole (Prevacid®)	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 (CYP2C19 NM). ¹²	Normal efficacy*	Normal risk*
Omeprazole (Losec®)	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 (CYP2C19 NM). ¹²	Normal efficacy*	Normal risk*
Pantoprazole (Pantoloc®)	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 (CYP2C19 NM). ¹²	Normal efficacy*	Normal risk*

PGx ASSOCIATIONS - EXPOSURE

Enzymes	Phenotype					Genotype	Details
	PM	IM	NM	RM	UM		
CYTOCHROME P450 (CYP450)							
CYP4F2						*3/*3	Poor metabolizer (PM) Total loss of CYP4F2 function.
CYP3A5						*3/*3	Poor metabolizer (PM) Low CYP3A5 activity is the most common phenotype and has been used to establish standard doses.
CYP2B6						*1/*6 or *4/*9	Intermediate metabolizer (IM) Reduced CYP2B6 activity compared to normal metabolizers.
CYP2A6						*1/*1	Normal metabolizer (NM) Normal CYP2A6 activity.
CYP2C9						*1/*1	Normal metabolizer (NM) Normal CYP2C9 activity.
CYP2C19						*1/*1	Normal metabolizer (NM) Normal CYP2C19 activity.
CYP2D6						*2/*41	Normal metabolizer (NM) Normal CYP2D6 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		
OTHER METABOLIC ENZYMES AND FACTORS							
POR						A/A	Poor activity (PA) Greatly reduced cytochrome P450 oxicoreductase (POR) activity compared to normal phenotypes (POR participates in CYP2B6 activation).
SLCO1B1						*5/*5	Poor function Greatly reduced solute carrier organic anion transporter family member 1B1 (SLCO1B1) activity compared to a normal function.
TPMT						*3C/*3C	Poor metabolizer (PM) Greatly reduced thiopurine S-methyltransferase (TPMT) activity compared to normal metabolizers.
NUDT15						*3/*3	Poor metabolizer (PM) Greatly reduced or absent nudix hydrolase 15 (NUDT15) activity compared to normal metabolizers.
DPYD						c.868A>G/c.868A>G	Intermediate metabolizer (IM) Reduced dihydropyrimidine dehydrogenase (DPYD) activity compared to normal metabolizers.
CES1						C/C	Normal metabolizer (NM) Normal carboxylesterase-1 (CES1) activity.
UDP-GLUCURONOSYLTRANSFERASES (UGT)							
UGT2B15						*1/*2	Intermediate metabolizer (IM) Reduced UGT2B15 activity compared to normal metabolizers.
UGT1A1						*1/*1	Normal metabolizer (NM) Normal UGT1A1 activity.
UGT1A4						*1/*1	Normal metabolizer (NM) Normal UGT1A4 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	Genes	Variant Details (GRCH38.p12)	Result		
<i>ABCB1</i>	rs1045642 rs2032582 rs2032583	chr7:87509329 chr7:87531302 chr7:87531245	A G A C C T	<i>CYP3A5</i>	rs776746 rs10264272 rs41303343	chr7:99672916 chr7:99665212 chr7:99652771	C C C C D D
<i>ABCG2</i>	rs2231142	chr4:88131171	G G	<i>CYP4F2</i>	rs2108622	chr19:15879621	1 2
<i>ADRA2A</i>	rs1800544	chr10:111076745	C C	<i>DPYD</i>	rs75017182 rs55886062 rs3918290 rs112766203 rs67376798 rs115232898 rs146356975	chr1:97579893 chr1:97515787 chr1:97450058 chr1:97305279 chr1:97082391 chr1:97699474 chr1:97595149	2 2 1 1 0 0 5 5 6 6 3 3 4 4
<i>ANKK1</i>	rs1800497	chr11:113400106	G G	<i>DRD2</i>	rs6275	chr11:113412755	G G
<i>BDNF</i>	rs6265	chr11:27658369	C C	<i>DRD3</i>	rs963468	chr3:114144040	A G
<i>CACNG2</i>	rs2283967	chr22:36567486	C C	<i>FAAH</i>	rs324420	chr1:46405089	C C
<i>CES1</i>	rs71647871	chr16:55823658	C C	<i>FKBP5</i>	rs4713916	chr6:35702206	G G
<i>CNR1</i>	rs806380	chr6:88154934	A A	<i>GNB3</i>	rs5443	chr12:6845711	C C
<i>COMT</i>	rs4680	chr22:19963748	G G	<i>GRIK1</i>	rs2832407	chr21:29595188	A C
<i>CYP1A2</i>	rs762551 rs2069514	chr15:74749576 chr15:74745879	A A G G	<i>GRIK4</i>	rs1954787	chr11:120792654	C T
<i>CYP2A6</i>	rs1801272 rs28399433	chr19:40848628 chr19:40850474	A A A A	<i>HLA-A*31:01</i>	rs1061235	chr6:29945521	A A
<i>CYP2B6</i>	rs2279343 rs3745274 rs28399499	chr19:41009358 chr19:41006936 chr19:41012316	G A G T T T	<i>HLA-B*15:02</i>	rs144012689	chr6:31355003	T T
<i>CYP2C2 cluster</i>	rs12777823	chr10:94645745	1 4	<i>HTR2A</i>	rs6311 rs6313 rs2770296	chr13:46897343 chr13:46895805 chr13:46866425	C C G G C C
<i>CYP2C9</i>	rs1057910 rs1799853 rs7900194 rs9332131 rs9332239 rs28371685 rs28371686 rs72558187 rs72558190	chr10:94981296 chr10:94942290 chr10:94942309 chr10:94949282-94949283 chr10:94989020 chr10:94981224 chr10:94981301 chr10:94941958 chr10:94947782	A A C C G G A A C C C C C C T T C C	<i>HTR2C</i>	rs3813929	chrX:114584047	C T
<i>CYP2C19</i>	rs4244285 rs4986893 rs6413438 rs12248560 rs12769205 rs17884712 rs28399504 rs41291556 rs56337013 rs72552267 rs72558186	chr10:94781859 chr10:94780653 chr10:94781858 chr10:94761900 chr10:94775367 chr10:94775489 chr10:94762706 chr10:94775416 chr10:94852738 chr10:94775453 chr10:94781999	G G G G C C C C A A G G A A T T C C G G T T	<i>HTR7</i>	rs7905446	chr10:90859404	G T
<i>CYP2D6</i>	rs16947 rs1065852 rs1135840 rs3892097 rs5030655 rs5030656 rs5030862 rs5030865 rs5030867 rs28371725 rs28371706 rs35742686 rs59421388 rs774671100 rs201377835 Gene Deletion Gene Duplication	chr22:42127941 chr22:42130692 chr22:42126611 chr22:42128945 chr22:42129084 chr22:42128174-42128178 chr22:42130668 chr22:42129033 chr22:42127856 chr22:42127803 chr22:42129770 chr22:42128242 chr22:42127608 chr22:42129910 n/a n/a	A A G G G G C C C C A A A A C C T T C T G G T T C C G G C C Not Detected Not Detected	<i>INSIG2</i> <i>long non-coding (lnc) RNA</i> <i>MC4R</i> <i>MTHFR</i> <i>NUDT15</i> <i>OPRM1</i> <i>POR</i> <i>SLC6A2</i> <i>SLC6A4</i> <i>SLC6A5</i> <i>SLCO1B1</i> <i>TH</i> <i>TPH2</i> <i>TPMT</i> <i>UGT1A1</i> <i>UGT1A4</i> <i>UGT2B7</i> <i>UGT2B15</i> <i>VKORC1</i>	rs17047764 rs74795342 rs489693 rs17782313 rs1801131 rs1801133 rs116855232 rs1799971 rs2868177 rs5569 rs2242446 rs28386840 chr17:30190154-30240133 chr11:20638211 chr12:21178615 rs2070762 rs1487278 rs1800462 rs1800460 rs1142345 chr2:233760498 chr2:233760234-233760248 chr2:233718962 chr4:69098620 chr4:68670366 chr16:31096368	chr2:118111006 chr21:18954018 C G G G A C T T G T A G 1 0 A G A A A G A G G G T T A G C T C T 7 7 8 8 9 9 G G 6 6 T T T T C A 1 3	
<i>CYP3A4</i>	rs4986907 rs35599367 rs55785340 rs67666821 rs72552799	chr7:99769804 chr7:99768693 chr7:99768360 chr7:99758184-99758188 chr7:99770165	C C G G A A D D 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.

REFERENCES

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

Reference(s) cited in this report:

1. Amstutz U, et al. *Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for Dihydropyrimidine Dehydrogenase Genotype and Fluoropyrimidine Dosing: 2017 Update*. *Clin Pharmacol Ther* (2018).
2. Relling MV, et al. *Clinical Pharmacogenetics Implementation Consortium Guideline for Thiopurine Dosing Based on TPMT and NUDT15 Genotypes: 2018 Update*. *Clin Pharmacol Ther* (2019).
3. Lee JW, et al. *Clinical Practice Recommendations for the Management and Prevention of Cisplatin-Induced Hearing Loss Using Pharmacogenetic Markers*. *Ther Drug Monit* (2016).
4. 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).
5. Hicks JK, et al. *Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update*. *Clin Pharmacol Ther* (2017).
6. Brown JT, et al. *Clinical Pharmacogenetics Implementation Consortium Guideline for Cytochrome P450 (CYP)2D6 Genotype and Atomoxetine Therapy*. *Clin Pharmacol Ther* (2019).
7. Dutch Pharmacogenetics Working Group (DPWG) 2021 update
(https://api.pharmgkb.org/v1/download/file/attachment/DPWG_May_2021.pdf)
8. Dutch Pharmacogenetics Working Group (DPWG) 2018 update
(https://api.pharmgkb.org/v1/download/file/attachment/DPWG_November_2018.pdf)
9. Johnson JA, et al. *Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for Pharmacogenetics-Guided Warfarin Dosing: 2017 Update*. *Clin Pharmacol Ther* (2017).

10. Lee CR, et al. *Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2C19 Genotype and Clopidogrel Therapy: 2022 Update*. *Clin Pharmacol Ther* (2022).
11. Cooper-DeHoff RM, et al. *The Clinical Pharmacogenetics Implementation Consortium Guideline for SLCO1B1, ABCG2, and CYP2C9 genotypes and Statin-Associated Musculoskeletal Symptoms*. *Clin Pharmacol Ther* (2022).
12. Lima JJ, et al. *Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C19 and Proton Pump Inhibitor Dosing*. *Clin Pharmacol Ther* (2021).