CLIA # 18D1100471
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PATIENT INFORMATION		PHYSICIAN		SPECIMEN DETAILS	
Name:		Provider:	**Oliveira, Rennan**	Specimen ID:	**22090900003**
Test Low Risk Result Frost Test		Location:	**Gravity+**	Specimen Type:	**Buccal**
Patient ID:	**P2225200003**	Client #:	**G+**	Collection Date:	**09/14/2022**
DOB:	**01/12/1999**	Phone:		Received Date:	**09/09/2022**
Sex:	**Female**			Report Date:	**09/09/2022**

Order Choice: *GetMyDNA PWN*

Substantial Drug-Gene Interaction
Genetic information should be strongly considered to change the prescribing of the indicated medication due to an increased risk of adverse reactions or a reduction in efficacy.

Moderate Drug-Gene Interaction
Genetic information should be considered as the identified medication may have an increased risk of adverse reactions or a reduction in efficacy.

Limited Drug-Gene Interaction
The standard precautions for prescribing the indication medication should be followed.

LEVEL OF EVIDENCE

FDA: The FDA labeling for the identified drug may contain specific actions to be taken based on genetic information. There may be alleles not accounted for based on the inferred phenotypes.

CPIC Level A: Preponderance of evidence is high or moderate in favor of changing prescribing of identified drug based on genetic information.

CPIC Level B: Preponderance of evidence is weak with little conflicting data in favor of changing prescribing of identified drug based on genetic information and alternative therapies/dosing are extremely likely to be as effective and as safe as non-genetically based dosing.

CPIC Level C: There are published studies at varying levels of evidence, some with mechanistic rationale, but no prescribing actions are recommended.

The reported drug-gene interactions are based on consensus scientific evidence referenced from the dosing guidelines on the FDA label or the Clinical Pharmacogenetics Implementation Consortium (CPIC) recommendations.

! Please note: Do not make any changes to your medication without consulting a physician. This report is intended to aid healthcare providers in determining the proper treatment options for a patient and should be used in the context of other clinical factors to change or select medications and dosage.

Current Patient Medications

Clopidogrel

Clopidogrel | Cardiovascular
CYP2C19 Normal (Extensive) Metabolizer
CPIC Level A, FDA

POTENTIALLY IMPACTED MEDICATIONS

Disclaimer: The medications listed in this report are not fully inclusive of all medications available in each category.

Cardiovascular

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Antiarrhythmics			Propafenone
Anticoagulants		Acenocoumarol Warfarin	
Antiplatelets			Clopidogrel
Beta Blockers			Carvedilol Metoprolol Nebivolol Propranolol
Statins			Simvastatin
Thrombopoietin Receptor Agonists		Avatrombopag	

Gastroenterology

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Antiemetics		Dronabinol	Metoclopramide Ondansetron
Proton Pump Inhibitors			Dexlansoprazole Esomeprazole Lansoprazole Omeprazole Pantoprazole Rabeprazole

Gynecology

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Gynecology Pain Medication			Elagolix
HSDD Agents-Mixed Serotonin Agonist/Antagonists			Flibanserin

Neurology

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Anticonvulsants		Fosphenytoin Phenytoin	Brivaracetam
Benzodiazepines			Clobazam Diazepam
Cholinesterase Inhibitors			Donepezil Galantamine
Movement Disorder Therapy			Deutetrabenazine Tetrabenazine Valbenazine
Multiple Sclerosis Treatment		Siponimod	
Vertigo Treatment			Meclizine

Oncology

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Antineoplastic		Erdafitinib	Gefitinib Tamoxifen

Other

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Dental			Cevimeline
Immunosuppressive			Tacrolimus
Metabolic Modifier			Eliglustat

Pain Management

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Analgesic Opioid		Methadone	Codeine Hydrocodone Oliceridine Tramadol
NSAID		Ibuprofen Lornoxicam Meloxicam Tenoxicam	

Psychiatry

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
ADHD Therapy		Atomoxetine	Amphetamine
Antiaddictives			Lofexidine
Antidepressant			Amitriptyline Amoxapine Citalopram Clomipramine Desipramine Doxepin Escitalopram Fluvoxamine Imipramine Nortriptyline Paroxetine Protriptyline Sertraline Trimipramine Venlafaxine Vortioxetine
Antipsychotics			Aripiprazole Aripiprazole Lauroxil Brexpiprazole Clozapine Iloperidone Perphenazine Pimozide Risperidone Thioridazine
Narcolepsy Therapy Agents			Pitolisant

Rheumatology

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Hyperuricemia Therapy		Lesinurad	
Muscle Relaxant			Carisoprodol
NSAID Analgesic		Celecoxib Flurbiprofen Piroxicam	

Urology

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Alpha Blocker			Tamsulosin
Urinary Antispasmodic			Darifenacin Fesoterodine Mirabegron Tolterodine

DOSING GUIDANCE

Acenocoumarol | Anticoagulants — CPIC Level B

CYP2C9 Intermediate Metabolizer

Implications: In patients with one or more reduced function variants of the CYP2C9 allele the clearance of Acenocoumarol is reduced.

Therapeutic Recommendations: No recommendation based on CYP2C9 genotype.

Atomoxetine | ADHD Therapy — CPIC Level A, FDA

CYP2D6 Normal (Extensive) Metabolizer

Implications: Normal (Extensive) Metabolizers of atomoxetine have a lower likelihood of response as compared to poor metabolizers. This is associated with increased discontinuation due to lack of efficacy as compared with poor metabolizers.

Therapeutic Recommendations: If no clinical response and in the absence of adverse events after 2 weeks, consider obtaining a peak plasma concentration (1-2 hours after dose administered).

Avatrombopag | Thrombopoietin Receptor Agonists — CPIC Level B/C, FDA

CYP2C9 Intermediate Metabolizer

Implications: The CYP2C9*2 and CYP2C9*3 loss-of-function polymorphisms result in reduced CYP2C9 enzymatic activity. In a pooled pharmacogenomic analysis of avatrombopag studies, subjects heterozygous for CYP2C9 loss-of-function polymorphisms (intermediate metabolizers) had approximately 1.4-fold higher exposure and subjects homozygous for CYP2C9 loss-of-function polymorphisms (poor metabolizers) had approximately 2-fold higher exposure compared to subjects wild-type for CYP2C9 (Normal (Extensive) Metabolizers).

Therapeutic Recommendations: No recommendation based on CYP2C9 genotype.

Celecoxib | NSAID Analgesic — CPIC Level A, FDA

CYP2C9 Intermediate Metabolizer

Implications: Reduced celecoxib metabolism; higher plasma concentrations may increase probability of toxicities.

Therapeutic Recommendations: Initiate therapy with recommended starting dose.

Dronabinol | Antiemetics — CPIC Level B/C, FDA

CYP2C9 Intermediate Metabolizer

Implications: Published data indicates a 2 to 3 fold higher dronabinol exposure in individuals carrying genetic variants associated with diminished CYP2C9 function.

Therapeutic Recommendations: Published data suggest that systemic clearance of dronabinol may be reduced and concentrations may be increased in presence of CYP2C9 genetic polymorphism. Monitoring for increased adverse reactions is recommended in patients known to carry genetic variants associated with diminished CYP2C9 function.

Efavirenz | Anti-HIV Drugs — CPIC Level A, FDA

CYP2B6 Intermediate Metabolizer

Implications: Higher dose-adjusted trough concentrations of efavirenz compared with Normal (Extensive) Metabolizers; increased risk of CNS adverse events.

Therapeutic Recommendations: Consider initiating efavirenz with a decreased dose.

Erdafitinib | Antineoplastic — CPIC Level B/C, FDA

CYP2C9 Intermediate Metabolizer

Implications: CYP2C9 activity is reduced in individuals with genetic variants, such as the CYP2C9*2 and CYP2C9*3 polymorphisms. Erdafitinib exposure was similar in subjects with CYP2C9*1/*2 and *1/*3 genotypes relative to subjects with CYP2C9*1/*1 genotype (wild type). No data are available in subjects characterized by other genotypes (e.g., *2/*2, *2/*3, *3/*3). Simulation suggested no clinically meaningful differences in erdafitinib exposure in subjects with CYP2C9*2/*2 and *2/*3 genotypes.

Therapeutic Recommendations: No recommendation based on CYP2C9 genotype.

Flurbiprofen | NSAID Analgesic — CPIC Level A, FDA

CYP2C9 Intermediate Metabolizer

Implications: Reduced flurbiprofen metabolism; higher plasma concentrations may increase probability of toxicities.

Therapeutic Recommendations: Initiate therapy with recommended starting dose.

Fosphenytoin | Anticonvulsants — CPIC Level A, FDA

CYP2C9 Intermediate Metabolizer

Implications: Reduced fosphenytoin metabolism; higher plasma concentrations may increase probability of toxicities.

Therapeutic Recommendations: For first dose, use typical initial or loading dose. For subsequent doses, use approximately 25% less than typical maintenance dose. Subsequent doses should be adjusted according to therapeutic drug monitoring, response and side effects.

Ibuprofen | NSAID — CPIC Level A

CYP2C9 Intermediate Metabolizer

Implications: Reduced ibuprofen metabolism; higher plasma concentrations may increase probability of toxicities.

Therapeutic Recommendations: Initiate therapy with recommended starting dose.

Lesinurad | Hyperuricemia Therapy — CPIC Level B/C, FDA

CYP2C9 Intermediate Metabolizer

Implications: The patient's genotype may be associated with increased lesinurad exposure when following standard dosing guidelines.

Therapeutic Recommendations: Follow standard dosing guidelines

Lornoxicam | NSAID — CPIC Level A

CYP2C9 Intermediate Metabolizer

Implications: Reduced lornoxicam metabolism; higher plasma concentrations may increase probability of toxicities.

Therapeutic Recommendations: Initiate therapy with recommended starting dose.

Meloxicam | NSAID — CPIC Level A, FDA

CYP2C9 Intermediate Metabolizer

Implications: Reduced meloxicam metabolism; higher plasma concentrations may increase probability of toxicities.

Therapeutic Recommendations: Initiate therapy with recommended starting dose.

Methadone | Analgesic Opioid — CPIC Level B

CYP2B6 Intermediate Metabolizer

Implications: Patients with one copy of the *6 allele (e.g. *1/*6) may have decreased methadone clearance compared to patients without the *6 allele.

Therapeutic Recommendations: No recommendation based on CYP2B6 genotype.

Phenytoin | Anticonvulsants — CPIC Level A, FDA

CYP2C9 Intermediate Metabolizer

Implications: Reduced phenytoin metabolism; higher plasma concentrations may increase probability of toxicities.

Therapeutic Recommendations: For first dose, use typical initial or loading dose. For subsequent doses, use approximately 25% less than typical maintenance dose. Subsequent doses should be adjusted according to therapeutic drug monitoring, response and side effects.

Piroxicam | NSAID Analgesic — CPIC Level A, FDA

CYP2C9 Intermediate Metabolizer

Implications: Reduced piroxicam metabolism; higher plasma concentrations may increase probability of toxicities.

Therapeutic Recommendations: Initiate therapy with recommended starting dose, or Choose an alternative therapy not metabolized by CYP2C9 or not significantly impacted by CYP2C9 genetic variants in vivo or choose an NSAID metabolized by CYP2C9 but with a shorter half-life.

Siponimod | Multiple Sclerosis Treatment — CPIC Level A, FDA

CYP2C9 Intermediate Metabolizer

Implications: The patient's genotype may be associated with increased siponimod exposure when following standard dosing guidelines.

Therapeutic Recommendations: Adjust dosage based on genotype. Refer to FDA labeling for specific dosing recommendations.

··· Tenoxicam | NSAID — CPIC Level A

CYP2C9 Intermediate Metabolizer

Implications: Reduced tenoxicam metabolism; higher plasma concentrations may increase probability of toxicities.

Therapeutic Recommendations: Initiate therapy with recommended starting dose, or Choose an alternative therapy not metabolized by CYP2C9 or not significantly impacted by CYP2C9 genetic variants in vivo or choose an NSAID metabolized by CYP2C9 but with a shorter half-life.

··· Warfarin | Anticoagulants — CPIC Level A, FDA

VKORC1 Increased Warfarin Sensitivity

Implications: A common variant upstream of VKORC1 rs9923231 is significantly associated with warfarin sensitivity and patients with one or two T alleles require progressively lower warfarin doses than those homozygous for the C allele.

Therapeutic Recommendations: Patients with one or two T alleles require progressively lower warfarin doses.

··· Warfarin | Anticoagulants — CPIC Level A, FDA

CYP2C9 Intermediate Metabolizer

Implications: Decreased warfarin metabolism resulting in increased warfarin exposure.

Therapeutic Recommendations: Consider a lower starting dose, recommend using a pharmacogenetic algorithm-based warfarin dosing.

The following medications have no recommended actions for the identified pharmacogenetic interaction.

Medication	Category	Interaction	Level of Evidence
Elagolix	Gynecology	SLCO1B1 Normal	CPIC Level B/C, FDA

Test Details

Gene	Diplotype	Phenotype
CYP1A2	*1A/*1F	Rapid Metabolizer
CYP2B6	*1/*6	Intermediate Metabolizer
CYP2C19	*1/*1	Normal (Extensive) Metabolizer
CYP2C9	*1/*11	Intermediate Metabolizer
CYP2D6	*1/*1	Normal (Extensive) Metabolizer
CYP3A4	*1/*1	Normal (Extensive) Metabolizer
CYP3A5	*3/*3	Poor Metabolizer
SLC6A4	La/La	Normal Serotonin Transporter Expression

Gene	Result	Phenotype
ADRA2A		
rs1800544	C/C	Homozygous for C allele
COMT		
rs4680	A/G	Heterozygous for the A/G alleles
F2		
rs1799963	G/G	Homozygous for the G allele
F5		
rs6025	C/C	Homozygous for the C allele
HTR2A		
rs6311	C/C	Homozygous for C allele
rs7997012	G/G	Homozygous for the G allele
OPRM1		
rs1799971	G/A	Heterozygous for the A/G alleles
SLCO1B1		
rs4149056	T/T	Normal
VKORC1		
rs9923231	C/T	Increased Warfarin Sensitivity

Limitation: The information presented in this report is for medical professionals and does not constitute medical advice for the diagnosis or treatment of a patient. The medical professional is solely responsible for the treatment of the patient. This test does not detect all alleles known to result in altered or inactive function. This test does not account for all variations that may be present in the individual tested. Absence of a detectable variant does not rule out the possibility that a patient carries undetected polymorphisms that may confer a phenotype other than that reported. Phenotypes are also affected by factors such as drug-drug interactions, comorbidities, and lifestyle habits.

Methodology: Genomic DNA was extracted from buccal swabs or EDTA blood as indicated by the sample type listed on the first page of the report. Testing was performed using MassARRAY® technology (Agena Biosciences) for all tests except SLC6A4, which was performed by PCR-RFLP analysis using MspI restriction endonuclease. The alleles tested are: **ADRA2A** rs1800544; **COMT** rs4680; **CYP1A2** *1A *1C *1E *1F *1K *1L *7 *11 *1J; **CYP2B6** *1 *4 *5 *6 *7 *18 *9; **CYP2C19** *1 *2 *3 *4A *4B *5 *6 *7 *8 *9 *10 *17; **CYP2C9** *1 *2 *3 *4 *5 *6 *8 *11 *12 *13 *15 *25 *27; **CYP2D6** *1 *2 *3 *4 *6 *7 *8 *9 *10 *11 *12 *14 *15 *17 *18 *19 *20 *29 *41 *69 *114 *5 *13; **CYP3A4** *1 *1B *2 *17 *22; **CYP3A5** *1A *2 *3 *6 *7; **F2** rs1799963; **F5** rs6025; **HTR2A** rs7997012 rs6311; **OPRM1** rs1799971; **SLC6A4** S La Lg XL; **SLCO1B1** rs4149056 rs2306283 rs11045819; **VKORC1** rs9923231; In the rare instances that multiple alleles could be inferred based on the observed data, the allele with the highest population frequency will be reported.

Lab Disclaimer: Gravity Diagnostics developed and determined the performance characteristics of this laboratory-developed genotype test. It has not been reviewed or approved by the U.S. Food and Drug Administration. The information is this report is provided for clinical use, and not as an investigational or research use only. However, the educational information provided needs the appropriate clinical context of the patient and is not a substitute for clinical monitoring by a medical professional.

Signed By: **Matthew Harper B.S.**