PATIENT INFORMATION		SPECIMEN DETAILS		PROVIDER INFORMATION
NAME:	**Sample**	**SPECIMEN TYPE:**	Buccal Swab	Genovive Box File
ACC #:	00000000000	**COLLECTION DATE:**		
DOB:	DD/MM/YYYY	**RECEIVED DATE:**	11/13/2018	
SEX:		**REPORT DATE:**	11/29/2018	

Comprehensive Pharmacogenetic Report

Risk Management

✓ Atrial Fibrillation

No increased risk of atrial fibrillation

The patient does not have a mutation in 4q25 variant rs2200733.

Unless other risk factors are present, noncarriers of 4q25 variant rs2200733 do not have an increased risk of atrial fibrillation.

No action is needed for this patient unless other cardiovascular risk factors are present.

✓ Hyperuricemia and Gout

Normal Risk of Gout

The patient carries two copies of ABCG2 rs2231142 C allele.

The ABCG2 rs2231142 C allele is associated with normal ABCG2 activity and subsequent normal renal elimination of uric acid. The patient's genotype is associated with a normal risk of hyperuricemia and gout.

No action is needed for this patient unless other genetic or non-genetic risk factors are present.

⚠ Antipsychotic-Induced Tardive Dyskinesia

Moderate Risk of Antipsychotic-Induced Tardive Dyskinesia

The patient carries one copy of the Taq1A variant (heterozygous for the A1 allele).

The genotype results predict that the patient may have reduced dopamine receptor DRD2 density and hypodopaminergic functioning. The patient has moderate risk for tardive dyskinesia when treated with antipsychotics.

Monitor the patient for any signs of tardive dyskinesia.

⚠ Antipsychotic-Induced Hyperprolactinemia

Moderate Risk of Antipsychotic-induced Hyperprolactinemia

The patient carries one copy of the Taq1A variant (heterozygous for the A1 allele).

The genotype results predict that the patient may have reduced dopamine receptor DRD2 density and hypodopaminergic functioning. The patient has moderate risk of hyperprolactinemia when treated with antipsychotics.

Monitor patient closely for signs of hyperprolactinemia. An evaluation of the risk-benefit profile of the antipsychotic medication may be required.

⚠ Antipsychotic-Induced Weight Gain

Moderate Risk of Antipsychotic-Induced Weight Gain

The patient carries one copy of the Taq1A variant (heterozygous for the A1 allele).

The genotype results predict that the patient may have reduced dopamine receptor DRD2 density and hypodopaminergic functioning. The patient has moderate risk for weight gain when treated with antipsychotics.

Monitor patient closely for signs of weight gain.

✓ Type III Hyperlipoproteinemia

Not Associated with Type III Hyperlipoproteinemia

The patient is negative for both the APOE c.388 T>C (Cys130Arg) and c.526 C>T (Arg176Cys) mutations. The patient's genotype is wild-type, which is the most common genotype in the general population (frequency: >60%).

A patient with wild-type genotype does not have a defect in the apolipoprotein E (APOE), which is an integral structure of lipoprotein particles that have critical roles in blood lipid metabolism and transport. The APOE ε3/ε3 genotype is not associated with increased risk of cardiovascular disease.

No action is needed when a patient is normolipidemic.

⚠ Platelet Hyperactivity

Possible Altered Response to Aspirin

The patient carries one ITGB3 176T>C (Leu59Pro) mutation.

Preliminary studies have found an association between the 176T>C mutation of the integrin β3 gene and the possible resistance to the antithrombotic effects of aspirin. However, because the variability in response to antiplatelet drugs is multifactorial and not caused by single gene mutations, testing for the ITGB3 mutation alone should not be used as a diagnostic tool.

✓ Hyperhomocysteinemia - Depression

No Increased Risk of Hyperhomocysteinemia

The patient carries one MTHFR C677T mutation (heterozygous). MTHFR enzyme activity is reduced (60% of normal activity).

Patients diagnosed with depression often have low folate levels and homocysteine is a highly sensitive marker of folate status. Functional folate deficiency is indicated by elevated homocysteine. The patient's small reduction in MTHFR activity is not a risk factor for hyperhomocysteinemia.

Patients diagnosed with depression: as lower folate levels are associated with poorer antidepressant response, and baseline levels of folate within the normal range predict antidepressant response, testing for homocysteine levels and serum folate levels may be informative for this patient before prescribing methylfolate as an antidepressant-augmenting agent.

✓ Nitric Oxide Production and Coronary Artery Disease

Normal Risk of Coronary Artery Disease

The patient does not carry the NOS3 G894T risk allele.

The endothelial nitric oxide synthase (NOS3) protein is involved in the synthesis of nitric oxide from L-arginine. The G allele of NOS3 G894T is associated with a normal basal nitric oxide production. The G/G genotype is not associated with an increased risk of developing coronary artery disease, hypertension and ischemic stroke.

No action is needed for this patient unless other cardiovascular risk factors are present.

✓ Alcohol Related Co-morbidities

Normal Alcohol and Acetaldehyde Metabolism After Alcohol Ingestion

ALDH2 rs671 A risk allele or the ADH1B rs1229984 T risk allele are absent.

Test results indicate normal alcohol dehydrogenase (ADH1B) activity and normal aldehyde dehydrogenase activity (ALDH2). ADH1B and ALDH2 play a role in alcohol metabolism. ADH1B is responsible for converting ethanol to acetaldehyde and ALDH2 subsequently converts this acetaldehyde into acetate.

Elevated and sustained aldehyde exposure after frequent alcohol consumption plays a key role in the pathogenesis of tissue and organ damage. In East Asians, abnormal ADH1B and/or ALDH2 activities appears to be associated with various health issues such as cancer, liver and cardiovascular diseases.

Consider optimal drinking habits by reducing the amount and the frequency of alcohol consumption.

✓ Hyperlipidemia/Atherosclerotic Cardiovascular Disease

No increased risk of cardiovascular disease

The patient is a non carrier of the risk alleles in LPA gene for both the variants (rs3798220 and rs10455872).

The patient's genotype is associated with normal lipoprotein levels. The patient has no increased risk of atherosclerosis and cardiovascular disease as compared to the general population unless other risk factors are present.

No action is needed for this patient unless other genetic and non genetic risk factors (e.g. high blood pressure, smoking, diabetes, obesity, high blood cholesterol and excessive alcohol use) are present.

⚠ Calcium Channels Function and Bipolar Disorder

Risk of Bipolar Disorder: Caucasians - Increased; Asians - Normal

The patient carries one copy of the rs1006737 A allele and one copy of the rs1051375 G allele. Caucasians: Risk allele for CACNA1C rs1006737 is present. Asians: Risk allele for CACNA1C rs1051375 is present.

The patient carries a variant in the gene coding for the voltage-dependent calcium channel L-type, alpha 1C subunit (CACNA1C). This genotype is associated with an altered calcium gating, excessive neuronal depolarization and an altered mood regulation function. This genotype has been associated with higher rates of mood disorder recurrence and an increased risk of bipolar disorder in Caucasians. The patient carries one copy of the risk allele for bipolar disorder in Asians. A single copy of this variant is associated with normal risk of bipolar disorder in patients of Asian origin and the exact functional significance of this variant remains unknown.
Bipolar disorder is a polygenic disorder and, as such, several genes are implicated in the etiology of the disease. Identification of one or more risk alleles in genes such as CACNA1C cannot replace standard clinical diagnostic tests, and this test should not be used as a diagnostic test for bipolar disorder.

⚠ Coronary Artery Disease

Slightly increased risk for coronary artery disease

The patient carries one mutation in each of the two variants of 9p21. There is a heterozygous mutation in 9p21 variant rs1333049 and a heterozygous mutation in 9p21 variant rs10757278.

The patient's genotype is associated with a 25 - 50% increased risk of coronary artery disease as compared to the general population.

Patient needs to be monitored for cardiovascular health and for other genetic and non-genetic cardiovascular risk factors such as diabetes, hypertension, high cholesterol and alcohol use.

✓ Hyperhomocysteinemia - Thrombosis

No Increased Risk of Hyperhomocysteinemia

The patient carries one MTHFR C677T mutation (heterozygous). MTHFR enzyme activity is reduced (60% of normal activity).

The patient's small reduction in MTHFR activity is not a risk factor for hyperhomocysteinemia. Unless other risk factors are present, the patient is not expected to have an increased risk for venous thromboembolism (VTE).

The patient's MTHFR activity is slightly reduced.

⊗ A medication has potentially reduced efficacy, increased toxicity or the patient has an increased risk for the indicated condition.	**ACTIONABLE**	Recommendations based upon publications by international pharmacogenetic expert groups, consortia or regulatory bodies (CPIC, DPWG, FDA, EMA). Recommendations are suitable for implementation in a clinical setting. Guidelines may change as knowledge arises.
⚠ Guidelines exist for adjusting dosage, increased vigilance or the patient has a moderate risk for the indicated condition.		
✓ The medication can be prescribed according to standard regimens or the patient's risk for the indicated condition is not increased.	**INFORMATIVE**	There are insufficient or contradictory findings documenting the impact of a given genetic polymorphism or drug interaction. Recommendations are informative and implementation in a clinical setting is optional.

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Potentially Impacted Medications

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Anesthesia	Injectable Anesthetics		Propofol (Diprivan®)	
Anticancer Agents	Antifolates		Methotrexate (Trexall®)	
Cardiovascular	**Angiotensin II Receptor Antagonists**	Azilsartan (Edarbi®, Edarbyclor®) Candesartan (Atacand®) Eprosartan (Teveten®) Irbesartan (Avapro®) Losartan (Cozaar®, Hyzaar®) Olmesartan (Benicar®) Telmisartan (Micardis®) Valsartan (Diovan®, Entresto®)		
	Antianginal Agents	Nitroglycerin (Gonitro®, Minitran®, Nitro-Dur®, Nitromist®, Nitrostat®) Ranolazine (Ranexa®)		
	Antiarrhythmics	Flecainide (Tambocor®) Mexiletine (Mexitil®) Propafenone (Rythmol®)		
	Anticoagulants	Apixaban (Eliquis®) Betrixaban (Bevyxxa®) Dabigatran Etexilate (Pradaxa®) Edoxaban (Savaysa®) Fondaparinux (Arixtra®) Rivaroxaban (Xarelto®) Warfarin (Coumadin®)		
	Antiplatelets	Prasugrel (Effient®) Ticagrelor (Brilinta®) Vorapaxar (Zontivity®)		Clopidogrel (Plavix®)
	Beta Blockers	Atenolol (Tenormin®) Bisoprolol (Zebeta®) Carvedilol (Coreg®) Labetalol (Normodyne®, Trandate®) Metoprolol (Lopressor®) Nebivolol (Bystolic®) Propranolol (Inderal®) Timolol (Timoptic®)		
	Calcium Channel Blockers	Verapamil (Covera-HS®, Verelan®, Isoptin®)		
	Diuretics	Hydrochlorothiazide (Esidrix®, Microzide®) Torsemide (Demadex®)		

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
	Statins	Atorvastatin (Lipitor®) Fluvastatin (Lescol®) Lovastatin (Mevacor®, Altoprev®, Advicor®) Pitavastatin (Livalo®) Pravastatin (Pravachol®) Rosuvastatin (Crestor®) Simvastatin (Zocor®)		
Diabetes	Biguanides		Metformin (Glucophage®)	
	Meglitinides	Nateglinide (Starlix®) Repaglinide (Prandin®, Prandimet®)		
	Sulfonylureas	Chlorpropamide (Diabinese®) Glimepiride (Amaryl®) Glipizide (Glucotrol®) Glyburide (Micronase®) Tolbutamide (Orinase®)		
Gastrointestinal	Antiemetics	Aprepitant (Emend-oral®) Dolasetron (Anzemet®) Dronabinol (Marinol®) Fosaprepitant (Emend-i.v®) Granisetron (Sancuso®, Sustol®) Metoclopramide (Reglan®) Netupitant-Palonosetron (Akynzeo®) Ondansetron (Zofran®, Zuplenz®) Palonosetron (Aloxi®) Rolapitant (Varubi®)		
	Proton Pump Inhibitors	Dexlansoprazole (Dexilant®, Kapidex®) Esomeprazole (Nexium®) Lansoprazole (Prevacid®) Omeprazole (Prilosec®) Pantoprazole (Protonix®) Rabeprazole (Aciphex®)		
Gaucher Disease	Endocrine-Metabolic Agents	Eliglustat (Cerdelga®) Imiglucerase (Cerezyme®) Miglustat (Zavesca®) Taliglucerase alfa (Elelyso®) Velaglucerase alfa (Vpriv®)		
Infections	Antifungals	Amphotericin B (AmBisome®, Abelcet®) Anidulafungin (Eraxis®) Caspofungin (Cancidas®) Fluconazole (Diflucan®) Isavuconazonium (Cresemba®) Itraconazole (Sporanox®) Micafungin (Mycamine®) Posaconazole (Noxafil®)		Voriconazole (Vfend®)

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
	Anti-HIV Agents	Dolutegravir (Tivicay®, Triumeq®) Raltegravir (Isentress®, Dutrebis®)		
	Antimalarials	Proguanil (Malarone®)		
	Interferons			Peginterferon alfa-2a (Pegasys®) Peginterferon alfa-2b (Pegintron®, Sylatron®)
Pain	Fibromyalgia Agents	Milnacipran (Savella®)		
	Muscle Relaxants	Cyclobenzaprine (Flexeril®, Amrix®) Metaxalone (Skelaxin®) Methocarbamol (Robaxin®)	Carisoprodol (Soma®)	
	NSAIDs	Celecoxib (Celebrex®) Diclofenac (Voltaren®) Flurbiprofen (Ansaid®) Ibuprofen (Advil®, Motrin®) Indomethacin (Indocin®) Ketoprofen (Orudis®) Ketorolac (Toradol®) Meloxicam (Mobic®) Nabumetone (Relafen®) Naproxen (Aleve®) Piroxicam (Feldene®) Sulindac (Clinoril®)		
	Opioids	Alfentanil (Alfenta®) Benzhydrocodone (Apadaz®) Buprenorphine (Butrans®, Buprenex®) Codeine (Codeine; Fioricet® with Codeine) Dihydrocodeine (Synalgos-DC®) Fentanyl (Actiq®) Hydrocodone (Vicodin®) Hydromorphone (Dilaudid®, Exalgo®) Levorphanol (Levo Dromoran®) Meperidine (Demerol®) Oxycodone (Percocet®, Oxycontin®) Oxymorphone (Opana®, Numorphan®) Sufentanil (Sufenta®) Tapentadol (Nucynta®) Tramadol (Ultram®)	Methadone (Dolophine®) Morphine (MS Contin®)	
	Antiaddictives	Levodopa / Carbidopa (Sinemet®)	Acamprosate (Campral®) Bupropion (Wellbutrin®, Zyban®, Aplenzin®, Contrave®) Disulfiram (Antabuse®) Naltrexone (Vivitrol®, Contrave®)	

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Psychotropic	Anti-ADHD Agents	Amphetamine (Adderall®, Evekeo®) Atomoxetine (Strattera®) Clonidine (Kapvay®) Dexmethylphenidate (Focalin®) Dextroamphetamine (Dexedrine®) Guanfacine (Intuniv®) Lisdexamfetamine (Vyvanse®) Methylphenidate (Ritalin®, Aptensio XR®, Concerta®, Metadate ER®, Quillivant ER®)		
	Anticonvulsants	Carbamazepine (Tegretol®, Carbatrol®, Epitol®) Eslicarbazepine (Aptiom®) Ethosuximide (Zarontin®) Ezogabine (Potiga®) Felbamate (Felbatol®) Fosphenytoin (Cerebyx®) Gabapentin (Neurontin®) Lacosamide (Vimpat®) Lamotrigine (Lamictal®) Levetiracetam (Keppra®) Oxcarbazepine (Trileptal®, Oxtellar XR®) Perampanel (Fycompa®) Phenytoin (Dilantin®) Pregabalin (Lyrica®) Rufinamide (Banzel®) Tiagabine (Gabitril®) Topiramate (Topamax®) Valproic Acid (Depakote®, Depakene®) Vigabatrin (Sabril®)	Brivaracetam (Briviact®) Phenobarbital (Luminal®) Primidone (Mysoline®) Zonisamide (Zonegran®)	
	Antidementia Agents	Donepezil (Aricept®) Galantamine (Razadyne®) Memantine (Namenda®)		
	Antidepressants	Amoxapine (Amoxapine®) Desipramine (Norpramin®) Desvenlafaxine (Pristiq®) Duloxetine (Cymbalta®) Fluoxetine (Prozac®, Sarafem®) Fluvoxamine (Luvox®) Levomilnacipran (Fetzima®) Maprotiline (Ludiomil®) Mirtazapine (Remeron®) Nefazodone (Serzone®) Nortriptyline (Pamelor®) Paroxetine (Paxil®, Brisdelle®) Protriptyline (Vivactil®) Trazodone (Oleptro®) Venlafaxine (Effexor®) Vilazodone (Viibryd®) Vortioxetine (Trintellix®)	Amitriptyline (Elavil®) Citalopram (Celexa®) Clomipramine (Anafranil®) Doxepin (Silenor®) Escitalopram (Lexapro®) Imipramine (Tofranil®) Sertraline (Zoloft®) Trimipramine (Surmontil®)	

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
	Antipsychotics	Aripiprazole (Abilify®, Aristada®) Asenapine (Saphris®) Brexpiprazole (Rexulti®) Cariprazine (Vraylar®) Chlorpromazine (Thorazine®) Fluphenazine (Prolixin®) Haloperidol (Haldol®) Iloperidone (Fanapt®) Loxapine (Loxitane®, Adasuve®) Lurasidone (Latuda®) Paliperidone (Invega®) Perphenazine (Trilafon®) Pimavanserin (Nuplazid®) Pimozide (Orap®) Quetiapine (Seroquel®) Thioridazine (Mellaril®) Thiothixene (Navane®) Trifluoperazine (Stelazine®) Ziprasidone (Geodon®)	Clozapine (Clozaril®) Olanzapine (Zyprexa®) Risperidone (Risperdal®)	
	Benzodiazepines	Alprazolam (Xanax®) Clonazepam (Klonopin®)	Clobazam (Onfi®) Diazepam (Valium®)	
	Mood Stabilizers		Lithium (Eskalith®, Lithobid®)	
	Other Neurological Agents	Deutetrabenazine (Austedo®) Dextromethorphan / Quinidine (Nuedexta®) Valbenazine (Ingrezza®)	Flibanserin (Addyi®) Tetrabenazine (Xenazine®)	
Rheumatology	**Anti-Hyperuricemics and Anti-Gout Agents**	Allopurinol (Zyloprim®, Liopurin®, Aloprim®) Colchicine (Mitigare®) Febuxostat (Uloric®) Lesinurad (Zurampic®)		
	Immunomodulators	Apremilast (Otezla®)	Leflunomide (Arava®) Tofacitinib (Xeljanz®)	
	Other Antirheumatic Agents		Sulfasalazine (Azulfidine®, Sulfazine®)	
Sjogren's Syndrome	**Cholinergic Agonists**	Cevimeline (Evoxac®)		
Transplantation	**Immunosuppressants**	Tacrolimus (Prograf®)		
	5-Alpha Reductase Inhibitors for Benign Prostatic Hyperplasia	Dutasteride (Avodart®) Finasteride (Proscar®)		
	Alpha-Blockers for Benign Prostatic Hyperplasia	Alfuzosin (UroXatral®) Doxazosin (Cardura®) Silodosin (Rapaflo®) Tamsulosin (Flomax®) Terazosin (Hytrin®)		

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Urologicals	**Antispasmodics for Overactive Bladder**	Darifenacin (Enablex®) Fesoterodine (Toviaz®) Mirabegron (Myrbetriq®) Oxybutynin (Ditropan®) Solifenacin (Vesicare®) Tolterodine (Detrol®) Trospium (Sanctura®)		
	Phosphodiesterase Inhibitors for Erectile Dysfunction	Avanafil (Stendra®) Sildenafil (Viagra®) Tadalafil (Cialis®) Vardenafil (Levitra®)		

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Dosing Guidance

Clopidogrel
Plavix®

Significantly Reduced Response to Clopidogrel (CYP2C19: Poor Metabolizer) — **ACTIONABLE**

Consider alternative therapy. Examples of alternative drugs: prasugrel (contraindicated in TIA/Stroke patients), ticagrelor, aspirin, aspirin plus dipyridamole.

Scott S A SA, Sangkuhl K K, Stein C M CM, Hulot J-S JS, Mega J L JL, Roden D M DM, Klein T E TE, Sabatine M S MS, Johnson J A JA, Shuldiner A R AR, . Clinical Pharmacogenetics Implementation Consortium guidelines for CYP2C19 genotype and clopidogrel therapy: 2013 update., Clin. Pharmacol. Ther. 2013 08;94 (3):317-23.

Peginterferon alfa-2a
Pegasys®

Unfavorable Response to Peginterferon alfa-2a and Ribavirin Based Regimen for Hepatitic C Genotype 1 (IFNL3: Heterozygous for rs12979860 T allele) — **ACTIONABLE**

Pegylated interferon alfa-2a and ribavirin regimen: Hepatitis C genotype 1 patients with this genotype have only a 30% chance of sustained virologic response after 48 weeks of treatment.

Pegylated interferon alfa-2a and ribavirin in combination with protease inhibitor regimen: Hepatitis C genotype 1 patients with this genotype have a 60% chance of sustained virologic response after 24 - 48 weeks of treatment. Approximately 50% of the patients may be eligible for a shortened treatment duration: 24 - 28 weeks.

Muir A J AJ, Gong L L, Johnson S G SG, Lee M T M MT, Williams M S MS, Klein T E TE, Caudle K E KE, Nelson D R DR, . Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for IFNL3 (IL28B) genotype and PEG interferon-α-based regimens., Clin. Pharmacol. Ther. 2014 01;95(2):141-6.

Peginterferon alfa-2b
Pegintron®, Sylatron®

Unfavorable Response to Peginterferon alfa-2b and Ribavirin Based Regimen for Hepatitic C Genotype 1 (IFNL3: Heterozygous for rs12979860 T allele) — **ACTIONABLE**

Pegylated interferon alfa-2b and ribavirin regimen: Hepatitis C genotype 1 patients with this genotype have only a 30% chance of sustained virologic response after 48 weeks of treatment.

Pegylated interferon alfa-2b and ribavirin in combination with protease inhibitor regimen: Hepatitis C genotype 1 patients with this genotype have a 60% chance of sustained virologic response after 24 - 48 weeks of treatment. Approximately 50% of the patients may be eligible for a shortened treatment duration: 24 - 28 weeks.

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Voriconazole
Vfend®

Increased Sensitivity to Voriconazole (CYP2C19: Poor Metabolizer) — **ACTIONABLE**

Voriconazole plasma concentrations are expected to be high if a standard dose is used, which may increase the risk of adverse events (hepatotoxicity, visual disturbances/halucinations and neurologic disorders). Consider an alternative medication that is not dependent on CYP2C19 metabolism, such as isavuconazole, liposomal amphotericin B or posaconazole. If voriconazole is warranted, consider a decreased dose and careful therapeutic drug monitoring.

Moriyama Brad B, Obeng Aniwaa Owusu AO, Barbarino Julia J, Penzak Scott R SR, Henning Stacey A SA, Scott Stuart A SA, Agúndez José A G JA, Wingard John R JR, McLeod Howard L HL, Klein Teri E TE, Cross Shane S, Caudle Kelly E KE, Walsh Thomas J TJ. Clinical Pharmacogenetics Implementation Consortium (CPIC®) Guideline for CYP2C19 and Voriconazole Therapy., Clin. Pharmacol. Ther. 2016 12;():.

Acamprosate
Campral®

Decreased Response to Acamprosate (GRIN2B: Homozygous for rs2058878 T allele) — **INFORMATIVE**

The glutamate receptor, ionotropic, N-methyl D-aspartate 2B (GRIN2B) encodes the subunit N-methyl D-aspartate receptor subtype 2B of the glutamate receptor complex. These receptors are the predominant excitatory neurotransmitter receptors in the brain. The patient is homozygous for T allele of GRIN2B variant rs2058878. Preliminary studies indicate that the patient's genotype may associated with an unfavorable response to acamprosate treatment for alcoholism. Absence of the minor A allele was associated with higher risk of early relapse and shorter abstinence during the first 3 months of acamprosate treatment. Replication of these results in a larger cohort is still needed to validate these findings.

Karpyak V M VM, Biernacka J M JM, Geske J R JR, Jenkins G D GD, Cunningham J M JM, Rüegg J J, Kononenko O O, Leontovich A A AA, Abulseoud O A OA, Hall-Flavin D K DK, Loukianova L L LL, Schneekloth T D TD, Skime M K MK, Frank J J, Nöthen M M MM, Rietschel M M, Kiefer F F, Mann K F KF, Weinshilboum R M RM, Frye M A MA, Choi D S DS. Genetic markers associated with abstinence length in alcohol-dependent subjects treated with acamprosate., Transl Psychiatry 2014 10;4():e462.

Amitriptyline
Elavil®

Increased Sensitivity to Amitriptyline (CYP2C19: Poor Metabolizer) — **ACTIONABLE**

Consider a 50% reduction of recommended amitriptyline starting dose, and monitor the plasma concentrations of amitriptyline and nortriptyline to adjust the dose.

Hicks J K JK, Swen J J JJ, Thorn C F CF, Sangkuhl K K, Kharasch E D ED, Ellingrod V L VL, Skaar T C TC, Müller D J DJ, Gaedigk A A, Stingl J C JC; Clinical Pharmacogenetics Implementation Consortium. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants., Clin Pharmacol Ther 2013 May;93(5):402-8.

Brivaracetam
Briviact®

Possible Sensitivity to Brivaracetam (CYP2C19: Poor Metabolizer) — ACTIONABLE

Brivaracetam is primarily metabolized by hydrolysis and to a minor extent by hydroxylation, which is mediated by CYP2C19. In CYP2C19 poor metabolizers, the plasma concentration of brivaracetam is increased by 42%. Brivaracetam dose reduction may be required. Monitor the patient for any signs of adverse reaction or drug toxicity.

Stockis Armel A, Watanabe Shikiko S, Rouits Elisabeth E, Matsuguma Kyoko K, Irie Shin S. Brivaracetam single and multiple rising oral dose study in healthy Japanese participants: influence of CYP2C19 genotype., Drug Metab. Pharmacokinet. 2014 10;29(5):394-9.
Briviact [package insert]. Smyrna, GA: UCB, Inc.; 2016.

Bupropion
Wellbutrin®, Zyban®, Aplenzin®, Contrave®

Possibly Decreased Response to Bupropion (CYP2B6: Intermediate Metabolizer) — INFORMATIVE

Bupropion is metabolized to its active metabolite hydroxybupropion by CYP2B6. This metabolite contributes to the therapeutic effects of bupropion when used as a smoking cessation agent or as an antidepressant. Individuals who are CYP2B6 intermediate metabolizers may or may not have lower blood levels of hydroxybupropion which may or may not result in a reduced response to bupropion treatment. Bupropion can be prescribed at standard label-recommended dosage with careful monitoring of the patient's response. Therapeutic monitoring of hydroxybupropion levels may be considered to guide dosing adjustment.

Zhu A Z X AZ, Cox L S LS, Nollen N N, Faseru B B, Okuyemi K S KS, Ahluwalia J S JS, Benowitz N L NL, Tyndale R F RF. CYP2B6 and bupropion's smoking-cessation pharmacology: the role of hydroxybupropion., Clin. Pharmacol. Ther. 2012 11;92(6):771-7.
Lee Anna M AM, Jepson Christopher C, Hoffmann Ewa E, Epstein Leonard L, Hawk Larry W LW, Lerman Caryn C, Tyndale Rachel F RF. CYP2B6 genotype alters abstinence rates in a bupropion smoking cessation trial., Biol. Psychiatry 2007 09;62(6):635-41.
Høiseth Gudrun G, Haslemo Tore T, Uthus Linda H LH, Molden Espen E. Effect of CYP2B6*6 on Steady-State Serum Concentrations of Bupropion and Hydroxybupropion in Psychiatric Patients: A Study Based on Therapeutic Drug Monitoring Data., Ther Drug Monit 2015 09;37(5):589-93.

Bupropion
Wellbutrin®, Zyban®, Aplenzin®, Contrave®

Decreased Response to Bupropion for Smoking Cessation (ANKK1: Altered DRD2 function) — INFORMATIVE

Smoking Cessation: The patient's genotype result is associated with a positive response to nicotine replacement therapy and a lesser response to bupropion treatment.

David Sean P SP, Strong David R DR, Munafò Marcus R MR, Brown Richard A RA, Lloyd-Richardson Elizabeth E EE, Wileyto Paul E PE, Evins Eden A AE, Shields Peter G PG, Lerman Caryn C, Niaura Raymond R. Bupropion efficacy for smoking cessation is influenced by the DRD2 Taq1A polymorphism: analysis of pooled data from two clinical trials., Nicotine Tob Res 2007 12;9(12):1251-7.

Carisoprodol
Soma®

Altered Sensitivity to Carisoprodol (CYP2C19: Poor Metabolizer) — INFORMATIVE

CYP2C19 poor metabolizers have a lower capacity to metabolize carisoprodol to meprobamate, and may therefore have an increased risk of developing concentration-dependent side effects such as drowsiness and hypotension when receiving standard doses of carisoprodol. Carisoprodol should be used with caution in patients with reduced CYP2C19 activity. Because there is insufficient data to allow calculation of dose adjustment, consider reducing the dose or using an alternative medication.

Bramness Jørgen G JG, Skurtveit Svetlana S, Fauske Lars L, Grung Merete M, Molven Anders A, Mørland Jørg J, Steen Vidar M VM. Association between blood carisoprodol:meprobamate concentration ratios and CYP2C19 genotype in carisoprodol-drugged drivers: decreased metabolic capacity in heterozygous CYP2C19*1/CYP2C19*2 subjects?, Pharmacogenetics 2003 07;13(7):383-8.

Citalopram
Celexa®

Increased Sensitivity to Citalopram (CYP2C19: Poor Metabolizer) — ACTIONABLE

At standard label-recommended dosage, citalopram plasma concentrations levels are expected to be high and adverse events may occur. Consider a 50% reduction of the recommended starting dose to help prevent concentration-dependent adverse events. Dose escalations over 20 mg/day for CYP2C19 poor metabolizers are not recommended. An alternative medication may also be considered.

Hicks J Kevin JK, Bishop Jeffrey R JR, Sangkuhl Katrin K, Müller Daniel J DJ, Ji Yuan Y, Leckband Susan G SG, Leeder J Steven JS, Graham Rebecca L RL, Chiulli Dana L DL, LLerena Adrián A, Skaar Todd C TC, Scott Stuart A SA, Stingl Julia C JC, Klein Teri E TE, Caudle Kelly E KE, Gaedigk Andrea A. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors., Clin. Pharmacol. Ther. 2015 5;():.

Citalopram
Celexa®

Reduced Response to Citalopram (HTR2A: Heterozygous for the A allele (rs7997012)) — INFORMATIVE

The patient is heterozygous for HTR2A variant rs7997012. Preliminary studies report that heterozygous HTR2A variant rs7997012 may be associated with an unfavorable response to citalopram.

Niitsu T, Fabbri C, Bentini F, Serretti A. Pharmacogenetics in major depression: a comprehensive meta-analysis. Prog Neuropsychopharmacol Biol Psychiatry 2013 Aug;45():183-94.

Clobazam

Onfi®

Increased Sensitivity to Clobazam (CYP2C19: Poor Metabolizer) — ACTIONABLE

In CYP2C19 poor metabolizers, plasma levels of the active metabolite N-desmethylclobazam were 5-fold higher than those found in CYP2C19 normal metabolizers. Therefore, the starting dose should be 5 mg/day and dose titration should proceed slowly according to weight. Patients should be titrated initially to 10 mg /day (≤30 kg body weight) or 20 mg/day (>30 kg body weight). If necessary and based upon clinical response, an additional titration to the maximum doses 20 mg/day (≤30 kg body weight) or 40 mg/day (>30 kg body weight) may be started on day 21.

Onfi [package insert]. Deerfield, IL: Lundbeck Inc.; 2013.

Seo Takayuki T, Nagata Rie R, Ishitsu Takateru T, Murata Tsukasa T, Takaishi Chisato C, Hori Masaharu M, Nakagawa Kazuko K. Impact of CYP2C19 polymorphisms on the efficacy of clobazam therapy., Pharmacogenomics 2008 05;9(5):527-37.

Kosaki Kenjiro K, Tamura Kazuyo K, Sato Reiko R, Samejima Hazuki H, Tanigawara Yusuke Y, Takahashi Takao T. A major influence of CYP2C19 genotype on the steady-state concentration of N-desmethylclobazam., Brain Dev. 2004 11;26(8):530-4.

Clomipramine

Anafranil®

Increased Sensitivity to Clomipramine (CYP2C19: Poor Metabolizer) — ACTIONABLE

Consider a 50% reduction of recommended clomipramine starting dose, and monitor the plasma concentrations of clomipramine and desmethyl-clomipramine to adjust the dose.

Hicks J K JK, Swen J J JJ, Thorn C F CF, Sangkuhl K K, Kharasch E D ED, Ellingrod V L VL, Skaar T C TC, Müller D J DJ, Gaedigk A A, Stingl J C JC; Clinical Pharmacogenetics Implementation Consortium. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants., Clin Pharmacol Ther 2013 May;93(5):402-8.

Clozapine

Clozaril®

Unfavorable Response to Clozapine (HTR2A: Homozygous for the C allele (rs6311)) — INFORMATIVE

The patient does not carry the HTR2A variant rs6311. Preliminary studies suggest that this genotype may be associated with an unfavorable response to clozapine in patients with European ancestry.

Arranz M J MJ, Munro J J, Sham P P, Kirov G G, Murray R M RM, Collier D A DA, Kerwin R W RW. Meta-analysis of studies on genetic variation in 5-HT2A receptors and clozapine response., Schizophr. Res. 1998 10;32(2):93-9.

Melkersson Kristina I KI, Gunes Arzu A, Dahl Marja-Liisa ML. Impact of serotonin receptor 2A gene haplotypes on C-peptide levels in clozapine- and olanzapine-treated patients., Hum Psychopharmacol 2010 09;25(4):347-52.

Clozapine

Clozaril®

Risk of Metabolic Syndrome with Clozapine (HTR2C: Heterozygous for the C allele (rs1414334)) — INFORMATIVE

Genetic variation in the Serotonin 2C Receptor (HTR2C) gene is known to be partially involved in the adverse effects to atypical antipsychotic medications. The patient is heterozygous for HTR2C variant rs1414334. The patient may have an increased risk of developing metabolic syndrome when treated with clozapine.

Risselada A J AJ, Vehof J J, Bruggeman R R, Wilffert B B, Cohen D D, Al Hadithy A F AF, Arends J J, Mulder H H. Association between HTR2C gene polymorphisms and the metabolic syndrome in patients using antipsychotics: a replication study., Pharmacogenomics J. 2012 01;12(1):62-7.

Mulder Hans H, Franke Barbara B, van der-Beek van der Annemarie Aart AA, Arends Johan J, Wilmink Frederik W FW, Scheffer Hans H, Egberts Antoine C G AC. The association between HTR2C gene polymorphisms and the metabolic syndrome in patients with schizophrenia., J Clin Psychopharmacol 2007 07;27(4):338-43.

Diazepam

Valium®

Increased Sensitivity to Diazepam (CYP2C19: Poor Metabolizer) — INFORMATIVE

CYP2C19 poor metabolizers have a lower capacity to metabolize diazepam and its active metabolite nordiazepam. Therefore, they may experience more concentration-dependent side effects, such as increased or prolonged sedation, if treated with standard doses of diazepam. Diazepam should be used with caution in these patients, and a reduced dose or longer dosing interval may be needed.

Inomata Shinichi S, Nagashima Atsushi A, Itagaki Fumio F, Homma Masato M, Nishimura Masuhiro M, Osaka Yoshiko Y, Okuyama Kazuhiko K, Tanaka Einosuke E, Nakamura Takako T, Kohda Yukinao Y, Naito Shinsaku S, Miyabe Masayuki M, Toyooka Hidenori H. CYP2C19 genotype affects diazepam pharmacokinetics and emergence from general anesthesia., Clin. Pharmacol. Ther. 2005 12;78(6):647-55.

Wan J J, Xia H H, He N N, Lu Y Q YQ, Zhou H H HH. The elimination of diazepam in Chinese subjects is dependent on the mephenytoin oxidation phenotype., Br J Clin Pharmacol 1997 02;42(4):471-4.

Disulfiram

Antabuse®

Increased Sensitivity to Disulfiram (DBH: Reduced Dopamine Beta-Hydroxylase Activity) — INFORMATIVE

Dopamine β-hydroxylase (DBH) is the final enzyme in norepinephrine biosynthesis, catalyzing the oxidative hydroxylation of dopamine to norepinephrine. The patient carries one copy of the T allele of the DBH rs1611115 which is significantly associated with low DBH activity. Preliminary studies in alcohol-dependent patients indicate that this genotype is associated with increased side effects following disulfiram therapy. Replication of these results in a larger cohort is still needed to validate these findings.

Major L F LF, Lerner P P, Ballenger J C JC, Brown G L GL, Goodwin F K FK, Lovenberg W W. Dopamine-beta-hydroxylase in the cerebrospinal fluid: relationship to disulfiram-induced psychosis., Biol. Psychiatry 1979 11;14(2):337-44.

Ewing J A JA, Rouse B A BA, Mueller R A RA, Silver D D. Can dopamine beta-hydroxylase levels predict adverse reactions to disulfiram?, Alcohol. Clin. Exp. Res. 1978 05;2(1):93-4.

PATIENT INFORMATION

NAME: Sample
ACC #: 0000000000
DOB: DD/MM/YYYY
SEX:

Doxepin
Silenor®

Increased Sensitivity to Doxepin (CYP2C19: Poor Metabolizer) — **ACTIONABLE**

Consider a 50% reduction of recommended doxepin starting dose, and monitor plasma concentrations of doxepin and desmethyl-doxepin to adjust the dose.

Hicks J K JK, Swen J J JJ, Thorn C F CF, Sangkuhl K K, Kharasch E D ED, Ellingrod V L VL, Skaar T C TC, Müller D J DJ, Gaedigk A A, Stingl J C JC; Clinical Pharmacogenetics Implementation Consortium. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants., Clin Pharmacol Ther 2013 May;93(5):402-8.

Escitalopram
Lexapro®

Increased Sensitivity to Escitalopram (CYP2C19: Poor Metabolizer) — **ACTIONABLE**

At standard label-recommended dosage, escitalopram plasma concentrations levels are expected to be high and adverse events may occur. Consider a 50% reduction of the recommended starting dose to help prevent concentration-dependent adverse events. An alternative medication may also be considered.

Hicks J Kevin JK, Bishop Jeffrey R JR, Sangkuhl Katrin K, Müller Daniel J DJ, Ji Yuan Y, Leckband Susan G SG, Leeder J Steven JS, Graham Rebecca L RL, Chiulli Dana L DL, LLerena Adrián A, Skaar Todd C TC, Scott Stuart A SA, Stingl Julia C JC, Klein Teri E TE, Caudle Kelly E KE, Gaedigk Andrea A. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors., Clin. Pharmacol. Ther. 2015 5;():.

Flibanserin
Addyi®

Increased Exposure to Flibanserin (CYP2C19: Poor Metabolizer) — **ACTIONABLE**

For treating premenopausal women with acquired, generalized hypoactive sexual desire disorder (HSDD): Flibanserin is primarily metabolized by CYP3A4 and, to a lesser extent, by CYP2C19. CYP2C19 poor metabolizers have increased flibanserin exposure compared to CYP2C19 normal metabolizers. As this change in exposure may increase the risk of hypotension, syncope, and CNS depression, advise and monitor patient more closely for serious adverse effects.

Addyi [package insert]. Raleigh, NC: Sprout Pharmaceuticals, Inc.; 2015.

Imipramine
Tofranil®

Increased Sensitivity to Imipramine (CYP2C19: Poor Metabolizer) — **ACTIONABLE**

Consider a 50% reduction of the recommended imipramine starting dose, and monitor the plasma concentrations of imipramine and desipramine to adjust the dose.

Hicks J K JK, Swen J J JJ, Thorn C F CF, Sangkuhl K K, Kharasch E D ED, Ellingrod V L VL, Skaar T C TC, Müller D J DJ, Gaedigk A A, Stingl J C JC; Clinical Pharmacogenetics Implementation Consortium. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants., Clin Pharmacol Ther 2013 May;93(5):402-8.

Leflunomide
Arava®

Increased Sensitivity to Leflunomide (CYP2C19: Poor Metabolizer) — **INFORMATIVE**

Leflunomide is metabolized by CYP2C19 and CYP1A2 to its active metabolite teriflunomide. Preliminary studies indicate that patients with decreased CYP2C19 activity have a higher risk of developing gastrointestinal side effects and hepatotoxicity. There is insufficient data to calculate dose adjustment. If leflunomide is prescribed at standard dosing, monitor closely the patient's response and be alert to increased side effects. Full blood cell count (CBC) and liver function parameters should be checked no more than 6 months before beginning treatment, and every month for the initial 6 months of therapy. Blood pressure should be checked before beginning treatment and periodically thereafter.

Wiese Michael D MD, Schnabl Matthew M, O'Doherty Catherine C, Spargo Llewellyn D LD, Sorich Michael J MJ, Cleland Leslie G LG, Proudman Susanna M SM. Polymorphisms in cytochrome P450 2C19 enzyme and cessation of leflunomide in patients with rheumatoid arthritis., Arthritis Res. Ther. 2014 07;14(4):R163.
Bohanec Grabar Petra P, Grabnar Iztok I, Rozman Blaz B, Logar Dusan D, Tomsic Matija M, Suput Dasa D, Trdan Tina T, Peterlin Masic Lucija L, Mrhar Ales A, Dolzan Vita V. Investigation of the influence of CYP1A2 and CYP2C19 genetic polymorphism on 2-Cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]-2-butenamide (A77 1726) pharmacokinetics in leflunomide-treated patients with rheumatoid arthritis., Drug Metab. Dispos. 2009 09;37(10):2061-8.

Lithium
Eskalith®, Lithobid®

Decreased Response to Lithium (BDNF: Homozygous for rs6265 C Allele) — **INFORMATIVE**

BDNF encodes the brain-derived neurotrophic factor involved in neuroprotection and neuroplasticity. The patient is homozygous for the C allele of BDNF variant rs6265. This genotype is associated with a poor response to lithium treatment for bipolar disorder.

Rybakowski J K JK, Suwalska A A, Skibinska M M, Szczepankiewicz A A, Leszczynska-Rodziewicz A A, Permoda A A, Czerski P M PM, Hauser J J. Prophylactic lithium response and polymorphism of the brain-derived neurotrophic factor gene., Pharmacopsychiatry 2005 07;38(4):166-70.
Rybakowski Janusz K JK, Suwalska Aleksandra A, Skibinska Maria M, Dmitrzak-Weglarz Monika M, Leszczynska-Rodziewicz Anna A, Hauser Joanna J. Response to lithium prophylaxis: interaction between serotonin transporter and BDNF genes., Am. J. Med. Genet. B Neuropsychiatr. Genet. 2007 10;144B(6):820-3.

Metformin
Glucophage®

Increased Risk of Unresponsiveness to Metformin (C11orf65 rs11212617 A/A; SLC47A2 -130G>A A/A) — **INFORMATIVE**

The patient carries genotype AA for rs11212617 and AA for rs12943590. The genotype results indicate that the patient has increased renal and secretory clearance of metformin and decreased response to metformin treatment for type 2 diabetes.

Chung Jae-Yong JY, Cho Sung Kweon SK, Kim Tae Hee TH, Kim Kyoung Hee KH, Jang Geun Hye GH, Kim Choon Ok CO, Park Eun-Mi EM, Cho Joo-Youn JY, Jang In-Jin IJ, Choi Ji Ha JH. Functional characterization of MATE2-K genetic variants and their effects on metformin pharmacokinetics., Pharmacogenet. Genomics 2013 06;23(7):365-73.
Choi J H JH, Yee S W SW, Ramirez A H AH, Morrissey K M KM, Jang G H GH, Joski P J PJ, Mefford J A JA, Hesselson S E SE, Schlessinger A A, Jenkins G G, Castro R A RA, Johns S J SJ, Stryke D D, Sali A A, Ferrin T E TE, Witte J S JS, Kwok P-Y PY, Roden D M DM, Wilke R A RA, McCarty C A CA, Davis R L RL, Giacomini K M KM. A common 5'-UTR variant in MATE2-K is associated with poor response to metformin., Clin. Pharmacol. Ther. 2011 10;90(5):674-84.
Stocker S L SL, Morrissey K M KM, Yee S W SW, Castro R A RA, Xu L L, Dahlin A A, Ramirez A H AH, Roden D M DM, Wilke R A RA, McCarty C A CA, Davis R L RL, Brett C M CM, Giacomini K M KM. The effect of novel promoter variants in MATE1 and MATE2 on the pharmacokinetics and pharmacodynamics of metformin., Clin. Pharmacol. Ther. 2013 01;93(2):186-94.

Methadone
Dolophine®

Possible Sensitivity to Methadone (CYP2B6: Intermediate Metabolizer) — INFORMATIVE

Based on currently available evidence, S-methadone plasma concentrations may increase, resulting in higher risk of cardiac arrhythmias and QTc prolongation. Consider lower starting doses of methadone, and adjust dosing based on the clinical response.

Dobrinas Maria M, Crettol Séverine S, Oneda Beatrice B, Lahyani Rachel R, Rotger Margalida M, Choong Eva E, Lubomirov Rubin R, Csajka Chantal C, Eap Chin B CB. Contribution of CYP2B6 alleles in explaining extreme (S)-methadone plasma levels: a CYP2B6 gene resequencing study., Pharmacogenet Genomics 2013 01;23(2):84-93.
Kharasch Evan D ED, Regina Karen J KJ, Blood Jane J, Friedel Christina C. Methadone Pharmacogenetics: CYP2B6 Polymorphisms Determine Plasma Concentrations, Clearance, and Metabolism., Anesthesiology 2015 10;123(5):1142-53.
Kringen Marianne K MK, Chalabianloo Fatemeh F, Bernard Jean-Paul JP, Bramness Jørgen G JG, Molden Espen E, Høiseth Gudrun G. The combined effect of CYP2B6 genotype and other candidate genes on a steady-state serum concentration of methadone in opioid maintenance treatment., Ther Drug Monit 2017 07;():.

Methotrexate
Trexall®

Increased risk for methotrexate toxicity (MTHFR: Reduced MTHFR Activity) — INFORMATIVE

The patient carries the MTHFR 677 T allele resulting in a reduced MTHFR activity. **Malignancy:** Leukemia or lymphoma patients who are treated with methotrexate standard regimens might have an increased likelihood of treatment interruptions due to methotrexate toxicity. Consider at least a 25% reduction in methotrexate starting dose, followed by titration based on toxicity. Other genetic and clinical factors may also influence the patient's risk for toxicity and response to methotrexate treatment. **Nonmalignant conditions:** a limited number of studies found an association between the MTHFR 677 T allele and methotrexate-induced toxicity in rheumatoid arthritis patients. However, there is insufficient data to calculate dose adjustment. Monitor patient closely for increased side effects and adjust the dose accordingly. Other genetic and clinical factors may also influence the patient's risk for toxicity and response to methotrexate treatment.

De Mattia Elena E, Toffoli Giuseppe G. C677T and A1298C MTHFR polymorphisms, a challenge for antifolate and fluoropyrimidine-based therapy personalisation., Eur J Cancer 2009 04;45(8):1333-51.
Choi Yun Jung YJ, Park Hyangmin H, Lee Ji Sung JS, Lee Ju-Yeon JY, Kim Shin S, Kim Tae Won TW, Park Jung Sun JS, Kim Jeong Eun JE, Yoon Dok Hyun DH, Suh Cheolwon C. Methotrexate elimination and toxicity: MTHFR 677C>T polymorphism in patients with primary CNS lymphoma treated with high-dose methotrexate., Hematol Oncol 2016 10;():.
Zhao Ming M, Liang Liang L, Ji Liwei L, Chen Di D, Zhang Yatong Y, Zhu Yuanchao Y, Ongaro Alessia A. MTHFR gene polymorphisms and methotrexate toxicity in adult patients with hematological malignancies: a meta-analysis., Pharmacogenomics 2016 7;17(9):1005-17.

Morphine
MS Contin®

Altered Response to Morphine (COMT: High/Normal COMT Activity) — INFORMATIVE

The patient does not carry the COMT Val158Met variant. The patient may require higher doses of morphine for adequate pain control. The dosing regimen needs to be individualized for each patient, taking into account the patient's prior analgesic treatment experience.

Rakvåg Trude T TT, Ross Joy R JR, Sato Hiroe H, Skorpen Frank F, Kaasa Stein S, Klepstad Pål P. Genetic variation in the catechol-O-methyltransferase (COMT) gene and morphine requirements in cancer patients with pain., Mol Pain 2008 02 18;4:64.
Rakvåg Trude Teoline TT, Klepstad Pål P, Baar Cecilie C, Kvam Tor-Morten TM, Dale Ola O, Kaasa Stein S, Krokan Hans Einar HE, Skorpen Frank F. The Val158Met polymorphism of the human catechol-O-methyltransferase (COMT) gene may influence morphine requirements in cancer pain patients., Pain 2005 06;116(1-2):73-8.
Matic Maja M, Simons Sinno H P SH, van Lingen Richard A RA, van Rosmalen Joost J, Elens Laure L, de Wildt Saskia N SN, Tibboel Dick D, van Schaik Ron H N RH. Rescue morphine in mechanically ventilated newborns associated with combined OPRM1 and COMT genotype., Pharmacogenomics 2014 08;15(10):1287-95.

Naltrexone
Vivitrol®, Contrave®

Altered Response to Naltrexone (OPRM1: Normal OPRM1 Function) — INFORMATIVE

Treatment of alcohol dependence: the patient has the OPRM1 118AA wild-type genotype that is associated with a poorer outcome with naltrexone therapy. Naltrexone-treated patients not carrying the OPRM1 118A>G G allele are less likely to respond to this drug, and may have higher relapse rates than those who are carriers of this allele. This association has not been reported consistently across studies.

Kranzler Henry R HR, Armeli Stephen S, Covault Jonathan J, Tennen Howard H. Variation in OPRM1 moderates the effect of desire to drink on subsequent drinking and its attenuation by naltrexone treatment., Addict Biol 2013 01;18(1):193-201.
Chamorro Antonio-Javier AJ, Marcos Miguel M, Mirón-Canelo José-Antonio JA, Pastor Isabel I, González-Sarmiento Rogelio R, Laso Francisco-Javier FJ. Association of μ-opioid receptor (OPRM1) gene polymorphism with response to naltrexone in alcohol dependence: a systematic review and meta-analysis., Addict Biol 2012 04;17(3):505-12.
Coller Janet K JK, Cahill Sharon S, Edmonds Carolyn C, Farquharson Aaron L AL, Longo Marie M, Minniti Rinaldo R, Sullivan Thomas T, Somogyi Andrew A AA, White Jason M JM. OPRM1 A118G genotype fails to predict the effectiveness of naltrexone treatment for alcohol dependence., Pharmacogenet. Genomics 2011 11;21(12):902-5.

PATIENT INFORMATION

NAME: Sample
ACC #: 0000000000
DOB: DD/MM/YYYY
SEX:

Olanzapine

Zyprexa®

Increased Risk of Weight Gain with Olanzapine (HTR2C: Homozygous for the C allele (rs3813929)) — **INFORMATIVE**

Genetic variations in the Serotonin 2C Receptor (HTR2C) gene in known to be partially involved in the adverse effects associated with atypical antipsychotic medications. The patient is homozygous for C allele of HTR2C variant rs3813929. Patients with this genotype may have an increased risk of weight gain when treated with olanzapine.

Godlewska B R BR, Olajossy-Hilkesberger L L, Ciwoniuk M M, Olajossy M M, Marmurowska-Michałowska H H, Limon J J, Landowski J J. Olanzapine-induced weight gain is associated with the -759C/T and -697G/C polymorphisms of the HTR2C gene., Pharmacogenomics J. 2009 07;9(4):234-41.
Ellingrod Vicki L VL, Perry Paul J PJ, Ringold John C JC, Lund Brian C BC, Bever-Stille Kristy K, Fleming Frank F, Holman Timothy L TL, Miller Del D. Weight gain associated with the -759C/T polymorphism of the 5HT2C receptor and olanzapine., Am. J. Med. Genet. B Neuropsychiatr. Genet. 2005 03;134B(1):76-8.
Daray Federico Manuel FM, Rodante Demián D, Carosella Laura G LG, Silva María Elena ME, Martínez Melina M, Fernández Busch María V MV, Faccone Diego F DF, Rothlin Rodolfo P RP, Maffía Paulo C PC. -759C>T Polymorphism of the HTR2C Gene is Associated with Second Generation Antipsychotic-Induced Weight Gain in Female Patients with Schizophrenia., Pharmacopsychiatry 2017 03;50(1):14-18.

Phenobarbital

Luminal®

Possible Sensitivity to Phenobarbital (CYP2C19: Poor Metabolizer) — **INFORMATIVE**

CYP2C19 is partly involved in the metabolism of phenobarbital, and although CYP2C19 poor metabolizers have a 20% lower clearance of phenobarbital than normal metabolizers, no significant changes in clinical outcome has been reported with this antiepileptic drug. Therefore, phenobarbital can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

Lee Soon Min SM, Chung Jae Yong JY, Lee Young Mock YM, Park Min Soo MS, Namgung Ran R, Park Kook In KI, Lee Chul C. Effects of cytochrome P450 (CYP) 2C19 polymorphisms on pharmacokinetics of phenobarbital in neonates and infants with seizures., Arch. Dis. Child. 2012 05;97(6):569-72.
Mamiya K K, Hadama A A, Yukawa E E, Ieiri I I, Otsubo K K, Ninomiya H H, Tashiro N N, Higuchi S S. CYP2C19 polymorphism effect on phenobarbitone. Pharmacokinetics in Japanese patients with epilepsy: analysis by population pharmacokinetics., Eur. J. Clin. Pharmacol. 2000 07;55(11-12):821-5.
Yukawa E E, Mamiya K K. Effect of CYP2C19 genetic polymorphism on pharmacokinetics of phenytoin and phenobarbital in Japanese epileptic patients using Non-linear Mixed Effects Model approach., J Clin Pharm Ther 2006 06;31(3):275-82.
Anderson, Gail D. "Chemisry, Biotransformation, and Pharmacokinetics." Antiepileptic Drugs. 5th ed. Philadelphia: Lippincott Williams & Wilkins, 2002. 496-03. Print.

Primidone

Mysoline®

Possible Sensitivity to Primidone (CYP2C19: Poor Metabolizer) — **INFORMATIVE**

CYP2C19 is partly involved in the metabolism of primidone and although CYP2C19 poor metabolizers have a 20% lower clearance of phenobarbital (active metabolite) than normal metabolizers, no significant changes in clinical outcome has been reported with this antiepileptic drug. Therefore, primidone can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

Fincham, Richard W., and Dorothy D. Schottelius. "Primidone." Antiepileptic Drugs. 5th ed. Philadelphia: Lippincott Williams & Wilkins, 2002. 621-36. Print.

Propofol

Diprivan®

Possible Altered Propofol Response (CYP2B6: Intermediate Metabolizer) — **INFORMATIVE**

Preliminary studies indicate that the patient's genotype may be associated with higher propofol exposure at standard dosing. This CYP2B6 genotype along with other factors such as old age (>65 years) and associated comorbidities may contribute to delayed emergence from anesthesia. There is insufficient data to allow calculation of dose adjustment; careful monitoring during post-surgery is recommended. The dosing regimen needs to be individualized for each patient, considering the patient's prior propofol dose requirements, age and comorbidities.

Mastrogianni Orthodoxia O, Gbandi Emma E, Orphanidis Amvrosios A, Raikos Nikolaos N, Goutziomitrou Evangelia E, Kolibianakis Efstratios M EM, Tarlatzis Basil C BC, Goulas Antonis A. Association of the CYP2B6 c.516G>T polymorphism with high blood propofol concentrations in women from northern Greece., Drug Metab. Pharmacokinet. 2014 04;29(2):215-8.
Murayama N N, Minoshima M M, Shimizu M M, Guengerich F P FP, Yamazaki H H. Involvement of human cytochrome P450 2B6 in the omega- and 4-hydroxylation of the anesthetic agent propofol., Xenobiotica 2007 07;37(7):717-24.
Court M H MH, Duan S X SX, Hesse L M LM, Venkatakrishnan K K, Greenblatt D J DJ. Cytochrome P-450 2B6 is responsible for interindividual variability of propofol hydroxylation by human liver microsomes., Anesthesiology 2001 01;94(1):110-9.

Risperidone

Risperdal®

Risk of Metabolic Syndrome with Risperidone (HTR2C: Heterozygous for the C allele (rs1414334)) — **INFORMATIVE**

Genetic variations in the Serotonin 2C Receptor (HTR2C) gene in known to be partially involved in the adverse effects associated with atypical antipsychotic medications. The patient is heterozygous for HTR2C variant rs1414334. The patient may have an increased risk of developing metabolic syndrome when treated with risperidone.

Risselada A J AJ, Vehof J J, Bruggeman R R, Wilffert B B, Cohen D D, Al Hadithy A F AF, Arends J J, Mulder H H. Association between HTR2C gene polymorphisms and the metabolic syndrome in patients using antipsychotics: a replication study., Pharmacogenomics J. 2012 01;12(1):62-7.

Sertraline

Zoloft®

Increased Sensitivity to Sertraline (CYP2C19: Poor Metabolizer) — **INFORMATIVE**

At standard label-recommended dosage, sertraline levels are expected to be high, and adverse events may occur. **Consider a 50% decrease of the initial dose and titrate based on the clinical response and tolerability.** An alternative medication may also be considered.

Hicks J Kevin JK, Bishop Jeffrey R JR, Sangkuhl Katrin K, Müller Daniel J DJ, Ji Yuan Y, Leckband Susan G SG, Leeder J Steven JS, Graham Rebecca L RL, Chiulli Dana L DL, LLerena Adrián A, Skaar Todd C TC, Scott Stuart A SA, Stingl Julia C JC, Klein Teri E TE, Caudle Kelly E KE, Gaedigk Andrea A. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors., Clin. Pharmacol. Ther. 2015 5;():.

Sulfasalazine

Azulfidine®, Sulfazine®

Decreased Response to Sulfasalazine For the Treatment of Rheumatoid Arthritis (ABCG2: Normal Function) — INFORMATIVE

Rheumatoid Arthritis: The patient carries two copies of ABCG2 rs2231142 C allele. Preliminary data suggests that this genotype may be associated with decreased plasma levels of sulfasalazine which may decrease the likelihood of response to this drug.

Wiese M D MD, Alotaibi N N, O'Doherty C C, Sorich M J MJ, Suppiah V V, Cleland L G LG, Proudman S M SM. Pharmacogenomics of NAT2 and ABCG2 influence the toxicity and efficacy of sulphasalazine containing DMARD regimens in early rheumatoid arthritis., Pharmacogenomics J. 2014 07;14(4):350-5.
Gotanda Keisuke K, Tokumoto Tomoko T, Hirota Takeshi T, Fukae Masato M, Ieiri Ichiro I. Sulfasalazine disposition in a subject with 376C>T (nonsense mutation) and 421C>A variants in the ABCG2 gene., Br J Clin Pharmacol 2015 10;80(5):1236-7.

Tetrabenazine

Xenazine®

Normal Sensitivity to Tetrabenazine (CYP2D6: Normal Metabolizer) — ACTIONABLE

For treating chorea associated with Huntington's disease: Individualization of dose with careful weekly titration is required. The first week's starting dose is 12.5 mg daily; second week, 25 mg (12.5 mg twice daily); then slowly titrate at weekly intervals by 12.5 mg to a tolerated dose. **The maximum daily dose in CYP2D6 normal metabolizers is 100 mg, with a maximum single dose of 37.5 mg**. If serious adverse events occur, titration should be stopped and the dose of tetrabenazine should be reduced. If the adverse event(s) do not resolve, consider withdrawal of tetrabenazine.

Xenazine [package insert]. Deerfield, IL: Lundbeck Inc.; 2011.

Tofacitinib

Xeljanz®

Increased Sensitivity to Tofacitinib when coadministered with CYP3A4 Inhibitors (CYP2C19: Poor Metabolizer) — INFORMATIVE

Tofacitinib is metabolized primarily by CYP3A4 with some contribution from CYP2C19. Genetic variations in the CYP2C19 gene do not significantly influence tofacitinib exposure. In absence of coadministered CYP3A4 inhibitors, tofacitinib can be prescribed according to standard label-recommended dosage and administration (i.e 5 mg twice daily). **However, tofacitinib dose should be reduced to 5 mg once daily if a patient who is a CYP2C19 poor metabolizer is also prescribed a CYP3A4 inhibitor such as ketoconazole, erythromycin, diltiazem, troleandomycin, nefazodone, fluconazole, verapamil and HIV protease inhibitors.**

Xeljanz [package insert]. New York, NY: Pfizer Inc.; 2014.

Trimipramine

Surmontil®

Increased Sensitivity to Trimipramine (CYP2C19: Poor Metabolizer) — ACTIONABLE

Consider a 50% reduction of recommended trimipramine starting dose, and monitor the plasma concentrations of trimipramine and desmethyl-trimipramine to adjust the dose.

Hicks J K JK, Swen J J JJ, Thorn C F CF, Sangkuhl K K, Kharasch E D ED, Ellingrod V L VL, Skaar T C TC, Müller D J DJ, Gaedigk A A, Stingl J C JC; Clinical Pharmacogenetics Implementation Consortium. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants., Clin Pharmacol Ther 2013 May;93(5):402-8.

Zonisamide

Zonegran®

Possible Sensitivity to Zonisamide (CYP2C19: Poor Metabolizer) — INFORMATIVE

CYP2C19 is partly involved in the metabolism of zonisamide, and although preliminary studies show that CYP2C19 poor metabolizers have a slightly lower (30%) zonisamide clearance than normal metabolizers, no significant change in the clinical outcome has been reported with this antiepileptic drug. Therefore, zonisamide can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

Okada Yusuke Y, Seo Takayuki T, Ishitsu Takateru T, Wanibuchi Atsuko A, Hashimoto Nami N, Higa Yoko Y, Nakagawa Kazuko K. Population estimation regarding the effects of cytochrome P450 2C19 and 3A5 polymorphisms on zonisamide clearance., Ther Drug Monit 2008 08;30(4):540-3.

PATIENT INFORMATION

NAME: Sample
ACC #: 0000000000
DOB: DD/MM/YYYY
SEX:

Test Details

Gene	Genotype	Phenotype	Clinical Consequences
12q15	rs7297610 C/C	Homozygous for the C allele (rs7297610)	Favorable response to hydrochlorothiazide in African Americans
4q25	rs2200733 C/C	Wild-type for rs2200733	The patient is non carrier of 4q25 variants and are not associated increased risk atrial fibrillation unless other cardiovascular risk factors are present.
9p21	rs10757278 G/A rs1333049 C/G	Slightly increased risk for coronary artery disease	The patient carries one mutation in each of the two variants of 9p21. There is a heterozygous mutation in 9p21 variant rs1333049 and a heterozygous mutation in 9p21 variant rs10757278. The patient's genotype is associated with a 25 - 50% increased risk of coronary artery disease as compared to non-carriers of the 9p21 variants.
ABCB1	2677G>T G/G	Variant Allele Not Present	Consistent with high transporter expression.
ABCB1	1236T>C C/C	Homozygous Mutant - Variant Allele Present	Consistent with decreased transporter expression.
ABCB1	2677G>A G/G	Variant Allele Not Present	Consistent with high transporter expression.
ABCB1	1000-44G>A A/A	Homozygous Mutant - Variant Allele Present	Consistent with decreased transporter expression.
ABCG2	421C>A C/C	Normal Function	Consistent with a normal ABCG2 transporter function. The patient's risk for statin-induced adverse events is normal.
ADRA2A	5749G>A G/G	Wild Type for rs1800545	
ALDH2 ADH1B	1369G>A G/G 706A>G C/C	Normal Alcohol and Acetaldehyde Metabolism After Alcohol Ingestion	East Asians: ALDH2 rs671 A allele or the ADH1B rs1229984 T allele associated with increased risk of alcohol related co-morbidities are absent.
ANKK1/DRD2	DRD2:Taq1A A/G	Altered DRD2 function	Consistent with a reduced dopamine receptor D2 function.
Apolipoprotein E	ε3/ε3	Normal APOE function	Not associated with type III hyperlipoproteinemia - No increased risk of cardiovascular disease
BDNF	434C>T C/C	Homozygous for rs6265 C Allele	Consistent with normal activity-dependent secretion of BDNF from neurons and normal BDNF signaling.
C11orf65	rs11212617 A/A	Homozygous for the A allele (rs11212617)	Normal glycemic response to metformin
CACNA1C	5361G>A G/A	Heterozygous for rs1051375 A allele	Possible intermediate function of the L-type calcium channel.
CACNA1C	270344G>A G/A 5361G>A G/A	Risk of Bipolar Disorder: Caucasians - Increased; Asians - Normal	The patient carries a variant in the gene coding for the voltage-dependent calcium channel L-type, alpha 1C subunit (CACNA1C). This genotype is associated with an altered calcium gating, excessive neuronal depolarization and an altered mood regulation function. This genotype has been associated with higher rates of mood disorder recurrence and an increased risk of bipolar disorder in Caucasians. The patient carries one copy of the risk allele for bipolar disorder in Asians. A single copy of this variant is associated with normal risk of bipolar disorder in patients of Asian origin and the exact functional significance of this variant remains unknown.
COMT	Val158Met G/G	High/Normal COMT Activity	Consistent with a normal catechol O-methyltransferase (COMT) function.
CYP2B6	*1/*9	Intermediate Metabolizer	Consistent with a moderate deficiency in CYP2B6 activity. Potential risk for side effects or loss of efficacy with drug substrates.

CYP2C	g.96405502G>A A/A	**High Sensitivity**	
CYP2C19	*2/*2	**Poor Metabolizer**	Consistent with a significant deficiency in CYP2C19 activity. Increased risk for side effects or loss of efficacy with drug substrates.
CYP2C9	*1/*1	**Normal Metabolizer**	Consistent with a typical CYP2C9 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP2D6	*1/*41	**Normal Metabolizer**	Consistent with a typical CYP2D6 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP3A4	*1/*1	**Normal Metabolizer**	Consistent with a typical CYP3A4 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
CYP3A5	*3/*3	**Poor Metabolizer**	Consistent with a poor CYP3A5 activity. This phenotype is the most common in the general population. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
CYP4F2	1347G>A G/G	**Homozygous for the G allele (rs2108622)**	
DBH	-1021C>T C/T	**Reduced Dopamine Beta-Hydroxylase Activity**	Consistent with a low dopamine beta-hydroxylase activity and a reduced conversion of dopamine to norepinephrine.
DRD2	rs2283265 C/A	**Heterozygous for rs2283265 A allele**	The patient carries one copy of the rs2283265 A allele.
DRD2	-241A>G T/T	**Homozygous for rs1799978 T Allele**	Associated with a favorable response to Risperidone.
FKBP5	rs1360780 C/C	**Homozygous for rs1360780 C allele**	Genotype may be associated with less frequent depressive episodes.
GRIK1	rs2832407 C/C	**Homozygous for rs2832407 C allele**	Glutamate receptor, ionotropic, kainate 1 (GRIK1) belongs to the kainate family of glutamate receptors, which are the predominant excitatory neurotransmitter receptors in the brain. The patient carries two copies of the GRIK1 rs2832407 C allele.
GRIN2B	rs2058878 T/T	**Homozygous for rs2058878 T allele**	Increased risk of early relapse and shorter abstinence in alcoholics when treated with Acamprosate.
HTR2A	-1438G>A C/C	**Homozygous for the C allele (rs6311)**	The patient does not carry the variant allele at rs6311 which may be associated with greater serotonin 2A receptor gene expression.
HTR2A	rs7997012 A/G	**Heterozygous for the A allele (rs7997012)**	Reduced response to citalopram and escitalopram
HTR2C	114138144C>G G/C	**Heterozygous for the C allele (rs1414334)**	This genotype is associated with risperidone- and clozapine-induced metabolic syndrome.
HTR2C	-759C>T C/C	**Homozygous for the C allele (rs3813929)**	Consistent with altered satiety signaling mediated by the serotonin receptor 2C (HTR2C). Increased incidence of metabolic side effects (weight gain, hyperglycemia, hyperlipidemia) with atypical antipsychotic medications.
IFNL3	rs12979860 C/T	**Heterozygous for rs12979860 T allele**	Unfavorable Response to Peginterferon alfa-2a and alfa-2b and Ribavirin Based Regimen for Hepatitic C Genotype 1
ITGB3	176T>C T/C	**Increased Platelet Reactivity**	The patient carries the 176T>C mutation of the integrin β3 gene which is associated with an increased platelet reactivity.

LPA	rs10455872 A/A rs3798220 T/T	**No increased risk of cardiovascular disease**	The patient is a non carrier of the risk alleles of LPA (rs3798220 and rs 10455872). The patient's genotype is associated with normal lipoprotein levels. The patient has no increased risk of atherosclerosis and cardiovascular disease as compared to the general population unless other risk factors are present.
MTHFR	677C>T CT	**Reduced MTHFR Activity**	The patient carries one MTHFR C677T mutation (heterozygous) and the patient's MTHFR activity is reduced slightly. This is not associated with an increased risk of hyperhomocysteinemia.
MTHFR	1298A>C AA 677C>T CT	**No Increased Risk of Hyperhomocysteinemia**	The patient MTHFR function is reduced slightly. This is not associated with an increased risk for venous thromboembolism.
NOS3	G894T G/G	**Normal Basal Nitric Oxide Production**	The G/G genotype is not associated with an increased risk of developing coronary artery disease, hypertension and ischemic stroke.
OPRM1	A118G A/A	**Normal OPRM1 Function**	Consistent with a normal OPRM1 receptor signaling efficiency induced by exogenous opioids. This is associated with a good analgesia following standard opioid doses and a poor response to naltrexone.
SLC47A2	-130G>A A/A	**Increased Function**	Increased renal and secretion clearance of metformin
SLCO1B1	521T>C T/T	**Normal Function**	Consistent with a typical SLCO1B1 transporter function. The patient's risk for statin-induced myopathy is not increased.
VKORC1	-1639G>A G/G	**Low Warfarin Sensitivity**	VKORC1 is the site of action of warfarin. The patient may require an increase in warfarin dose.

Alleles Tested: 12q15 rs7297610; **4q25** rs2200733, rs10033464; **9p21** rs10757278, rs1333049, rs2383206; **ABCB1** 1236T>C, 1678A>G, 2677G>A, 2677G>T, 1000-44G>A; **ABCG2** 421C>A, 376C>T; **ADH1B** 706A>G; **ADRA2A** 5749G>A; **ALDH2** 1369G>A; **ANKK1/DRD2** DRD2:Taq1A; **Apolipoprotein E** ε2, ε4, (ε3 is reference); **BDNF** 434C>T; **C11orf65** rs11212617; **CACNA1C** 270344G>A, 5361G>A; **COMT** Val158Met, 36C>T, 447G>A, c.1-98A>G; **CYP2B6** *16, *2, *3, *4, *6, *9, *12, *18, *19, *20, *21, *22, *27, *28; **CYP2C** g.96405502G>A; **CYP2C19** *2, *24, *3, *35, *4, *4B, *5, *6, *7, *8, *9, *10, *13, *17; **CYP2C9** *2, *3, *31, *35, *4, *5, *6, *8, *9, *10, *11, *12, *13, *14, *15, *16, *27; **CYP2D6** *2, *3, *33, *4, *4M, *42, *49, *50, *53, *54, *55, *7, *8, *9, *10, *11, *12, *14A, *14B, *17, *19, *20, *29, *35, *38, *41, *44, *56A, *56B, *5 (gene deletion), XN (gene duplication); **CYP3A4** *1G, *1B, *2, *3, *5, *6, *7, *8, *11, *12, *13, *14, *15, *16A, *16B, *17, *18A, *18B, *19, *20, *22; **CYP3A5** *1D, *3, *3C, *6, *7, *8, *9; **CYP4F2** 1347G>A; **DBH** -1021C>T; **DRD2** rs1124493, rs2283265, 957C>T, 811-83G>T, -241A>G; **FKBP5** rs1360780; **GRIK1** rs2832407; **GRIN2B** rs2058878; **HTR2A** -1438G>A, rs7997012, 102C>T; **HTR2C** -759C>T, 114138144C>G; **IFNL3** rs12979860; **ITGB3** 176T>C; **LPA** rs3798220, rs10455872; **MTHFR** 1298A>C, 677C>T; **NOS3** G894T; **OPRM1** A118G, rs9479757; **SLC47A2** -130G>A; **SLCO1B1** 521T>C, , -11187G>A, , , , 1865+248G>A; **VKORC1** Asp36Tyr, 1173C>T, -1639G>A

Limitation: This test will not detect all the known alleles that result in altered or inactive tested genes. This test does not account for all individual variations in the individual tested. Absence of a detectable gene mutation does not rule out the possibility that a patient has different phenotypes due to the presence of an undetected polymorphism or due to other factors such as drug-drug interactions, comorbidities, and lifestyle habits.

Methodology: Array-based assays detect listed alleles, including all common and most rare variants with known clinical significance at analytical sensitivity and specificity >99%.

Lab Disclaimer: Diagnomics is a CLIA-certified, CAP-accredited, and HIPAA-compliant laboratory. The Diagnomics' Clinical Laboratory (CAP# 9050024 / CLIA# 05D2103644) performed the genotyping assay required to generate the input for this pharmacogenetic report. The performance characteristics of this assay were determined by Diagnomics. This assay has not been cleared or approved by the U.S. Food and Drug Administration.

Translational Software Disclaimer: The information presented on this report is provided as general educational health information. The content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Only a physician, pharmacist, or other healthcare professional should advise a patient on the use of the medications prescribed.
The pharmacogenetic assay involves the use of reporting software and genotype-phenotype associations performed by Translational Software (www.translationalsoftware.com). The software has not been evaluated by the Food and Drug Administration. The software, and the report generated by the software, is not intended to diagnose, treat, cure, or prevent any disease. A qualified designee within the lab uses Translational Software to generate and subsequently review the report. The pharmacogenetic report is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. It remains the responsibility of the health-care provider to determine the best course of treatment for a patient. Adherence to dose guidelines does not necessarily assure a successful medical outcome.

Approved by

PATIENT INFORMATION

NAME: Sample
ACC #: 0000000000
DOB: DD/MM/YYYY
SEX:

Patient Information Card

This is a summary genetic report for your patient to share with other healthcare providers. The card can be cut out along the dashed line and carried with the patient.

REPORT DETAILS

Patient: Sample
DOB: 9/30/1950
ACC #: 2018000307617

Pharmacogenetic Test Summary

CYP2C19	*2/*2	Poor Metabolizer
CYP2C9	*1/*1	Normal Metabolizer
CYP2D6	*1/*41	Normal Metabolizer
CYP3A4	*1/*1	Normal Metabolizer
CYP3A5	*3/*3	Poor Metabolizer

MTHFR	677C>T CT	Reduced MTHFR Activity
MTHFR	1298A>C AA 677C>T CT	No Increased Risk of Hyperhomocysteinemia
VKORC1	-1639G>A G/G	Low Warfarin Sensitivity

For a complete report contact Diagnomics, Inc.
www.genovive.com.mx