



PATIENT INFORMATION

NAME: BRL SAMPLE
SAMPLE ID:
DOB: 1/20/1930
SEX: Male

SPECIMEN DETAILS

SPECIMEN TYPE: Buccal Swab
COLLECTION DATE: 11/8/20xx
RECEIVED DATE: 11/9/20xx
REPORT DATE: 11/11/20xx

PROVIDER INFORMATION

Physician Name: BRL SAMPLE
Clinic Name: BLUE RIDGE LABORATORIES

Comprehensive Pharmacogenetic Report

Current Patient Medications

Alendronate, Atrac-Tain, Buspirone, Eliquis, Omeprazole, Quetiapine, Vitamin D2, Vitamin B 12, Lantus, Simvastatin, Tamsulosin, Acetaminophen, Albuterol, Glucagon, Lorazepam, Polyethylene Glycols, Torsemide

Simvastatin | ZOCOR®
Increased Simvastatin Exposure (SLCO1B1: Decreased Function)
ACTIONABLE

The patient's genotype is associated with possible increased simvastatin exposure. Patients may be at an increased myopathy risk with doses >20 mg.

Consider an alternative statin. If simvastatin use is warranted, consider limiting dose to <20 mg.

Lorazepam | ATIVAN®
Possible Altered Response to Lorazepam (UGT2B15: Intermediate Metabolizer)
INFORMATIVE

Lorazepam clearance may be reduced in this patient. However, there is insufficient evidence whether this change results in a significant clinical effect. Consider monitoring the patient for increased sedation and adjust dosing accordingly.

Omeprazole | PRILOSEC®
Slightly Decreased to Normal Exposure to Omeprazole (CYP2C19: Rapid Metabolizer)
ACTIONABLE

The patient's genotype may be associated with a slightly decreased omeprazole exposure following standard dosing. Be alert for insufficient response, consider prescribing omeprazole at standard label-recommended dosage and administration. May consider increasing the recommended dose for certain indications by 50-100% to optimize therapeutic efficacy.

Eliquis | APIXABAN
Normal Response to Apixaban
INFORMATIVE

Pharmacogenetic guidance: Apixaban is not extensively metabolized and only ~20% of the dose is metabolized primarily by CYP3A4 and CYP3A5, with minor contributions from CYP1A2 and CYP2J2. This drug is a substrate for the efflux transport proteins P-gp (ABCB1) and BCRP (ABCG2). While these enzymes and transporters are polymorphic, genetic variations are unlikely to have a clinically significant impact on apixaban exposure, and no genotype-based dosing adjustments are recommended. Polypharmacy guidance: Exposure to apixaban increases by 100% when co-administered with ketoconazole, a strong CYP3A/P-gp inhibitor. This translates into an increased bleeding risk (70% increase). Hence, for patients receiving 5 mg twice daily, apixaban dose should be decreased to 2.5 mg twice daily when it is coadministered with drugs that are strong dual inhibitors of CYP3A4 and P-gp (e.g., ketoconazole, itraconazole, ritonavir, and clarithromycin). In patients already taking 2.5 mg twice daily, coadministration of apixaban with strong dual inhibitors of CYP3A4 and P-gp should be avoided. No dose adjustment is recommended when co-administered with moderate inhibitors. Co-administration with rifampin, a strong CYP3A/P-gp inducer, results in halving of exposure to apixaban. There is no clinical experience at these reduced exposures. Hence, concomitant administration of strong CYP3A/P-gp inducers should be avoided.

Quetiapine | SEROQUEL®
Normal Response to Quetiapine
INFORMATIVE

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ADRA2A	C-1291G C/G	Heterozygous for the G Allele	Carriers of the G allele of ADRA2A C-1291G variant, show greater reduction of inattentive symptoms when administered Methylphenidate or Dexmethylphenidate.
ANKK1/DRD2	DRD2:Taq1A G/G	Unaltered DRD2 function	Consistent with a normal dopamine receptor D2 function.
APOE	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.
CACNA1C	5361G>A A/A	Homozygous for rs1051375 A allele	Possible reduced function of the L-type calcium channel.
CACNA1C	270344G>A G/G 5361G>A A/A	Risk of Bipolar Disorder: Caucasians - Normal; Asians - Normal	The patient does not carry a variant in the gene coding for the voltage-dependent calcium channel L-type, alpha 1C subunit (CACNA1C). This genotype is associated with a normal neuronal depolarization and a normal mood regulation function. This genotype has been associated with lower rates of mood disorder recurrence and a normal risk of bipolar disorder in Caucasians. The patient carries two copies of the risk alleles for bipolar disorder in Asians. Preliminary studies report that this genotype is associated with lower age of onset of bipolar disease in Asians. However, the exact functional significance of this variant remains unknown.
COMT	Val158Met A/A	Low COMT Activity	Consistent with a significantly reduced catechol O-methyltransferase (COMT) function.
CYP1A2	*1A/*1F	Normal Metabolizer - Higher Inducibility	Consistent with a typical CYP1A2 activity in absence of inducing substances. Rapid Metabolism occurs in presence of inducers such as barbiturates, cruciferous vegetables, carbamazepine, rifampin and smoking.
CYP2B6	*1/*6	Intermediate Metabolizer	Consistent with a moderate deficiency in CYP2B6 activity. Potential risk for side effects or loss of efficacy with drug substrates.
CYP2C19	*1/*17	Rapid Metabolizer	Consistent with a moderate increase in CYP2C19 enzyme activity.
CYP2C9	*1/*1	Normal Metabolizer	Consistent with a typical CYP2C9 enzyme activity.
CYP2D6	*1/*2	Normal Metabolizer	Consistent with a typical CYP2D6 enzyme activity.
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	*1/*3	Intermediate Metabolizer	Consistent with an intermediate CYP3A5 activity (Expresser). Exercise caution if CYP3A5 drug substrates are prescribed.
CYP4F2	c.1297G>A A/G	Reduced Activity	Consistent with a deficiency in CYP4F2 protein expression, resulting in reduced vitamin K metabolism.
DBH	-1021C>T C/C	Normal Dopamine Beta-Hydroxylase Activity	Consistent with a normal dopamine beta-hydroxylase activity and a normal conversion of dopamine to norepinephrine.
F2 F5	rs1799963 GG rs6025 CC	Normal Risk of Thrombosis	Unless other genetic or circumstantial risk factors are present, the patient is not expected to have an increased risk for thrombosis.
GRIK4	83-10039T>C T/C	Reduced Response to Citalopram	Consistent with a possible non-response to citalopram.
HTR2A	rs7997012 G/G	Homozygous for G allele (rs7997012)	Reduced response to citalopram and escitalopram
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.

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MTHFR	c.665C>T GG	Normal MTHFR Activity	The patient does not carry the MTHFR c.665C>T variant, and the patient's MTHFR activity is normal. This is not associated with an increased risk of hyperhomocysteinemia.
MTHFR	c.1286A>C TT c.665C>T GG	No Increased Risk of Hyperhomocysteinemia	The patient does not carry the MTHFR c.665C>T or c.1286A>C variant. Therefore, the patient has normal MTHFR function, and no elevation of plasma homocysteine levels is expected.
OPRK1	36G>T C/C	Homozygous for G Allele (36G>T)	
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.
SLC6A3	1215A>G A/A	Wild type for SLC6A3 variant rs6347	Homozygous carrier of A allele of SLC6A3 1215A>G variant.
SLCO1B1	*1/*5	Decreased Function	Consistent with a decreased SLCO1B1 transporter function. Exercise caution when certain SLCO1B1 drug substrates are prescribed.
TPMT	*1/*3A	Intermediate Metabolizer	Consistent with a moderately decreased TPMT activity. Exercise caution if TPMT drug substrates are prescribed.
UGT2B15	*1/*2	Intermediate Metabolizer	Consistent with a moderately decreased UGT2B15 glucuronidation function. Potential risk for side effects with drug substrates.
VKORC1	-1639G>A G/A	Intermediate Warfarin Sensitivity	Consistent with a moderately decreased VKORC1 expression. Exercise caution with coumarin anticoagulants.

Alleles Tested: **ABCB1** 3435C>T, 1236T>C, 2677G>A, 2677G>T; **ABCG2** 421C>A; **ADRA2A** C-1291G, c.216C>A, c.427A>G; **ANKK1/DRD2** DRD2:Taq1A; **APOE** ε2, ε4, (ε3 is reference); **BDNF** 434C>T; **CACNA1C** 270344G>A, 5361G>A; **COMT** Val158Met; **CYP1A2** *1C, *1D, *1E, *1F, *1J, *1K, *1L, *1V, *1W; **CYP2B6** *5, *6, *7, *9, *18, *18.002, *22; **CYP2C19** *2, *3, *4A, *4B, *5, *6, *7, *8, *9, *10, *17; **CYP2C9** *2, *3, *4, *5, *6, *8, *11, *14; **CYP2D6** *2, *3, *4, *4M, *6, *7, *9, *10, *11, *12, *14, *15, *17, *29, *35, *41, *114, *5 (gene deletion), XN (gene duplication); **CYP3A4** *2, *3, *12, *16A, *16B, *17, *22; **CYP3A5** *3, *6, *7, *8, *9; **CYP4F2** c.1297G>A; **DBH** -1021C>T; **F2** rs1799963; **F5** rs6025; **GRIK4** 83-10039T>C; **HTR2A** rs7997012; **HTR2C** -759C>T; **MTHFR** c.1286A>C, c.665C>T; **OPRK1** 36G>T; **OPRM1** A118G; **SLC6A3** 328G>A, 1215A>G; **SLCO1B1** *5; **TPMT** *2, *3A, *3B, *3C; **UGT2B15** *2; **VKORC1** -1639G>A

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Risk Management



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

Increased Risk of Antipsychotic-Induced Tardive Dyskinesia

The patient does not carry the Taq1A variant (homozygous for the A2 allele).

The genotype results predict that the patient has normal dopamine receptor DRD2 density and functioning. The patient has increased risk for tardive dyskinesia when treated with antipsychotics.

Closely monitor the patient for signs of tardive dyskinesia.



Antipsychotic-Induced Hyperprolactinemia

Normal Risk of Antipsychotic-Induced Hyperprolactinemia

The patient does not carry the Taq1A variant (homozygous for the A2 allele).

The genotype results predict that the patient has normal dopamine receptor DRD2 density and functioning. The patient has normal risk of hyperprolactinemia when treated with antipsychotics.

Monitor the patients closely for any signs of hyperprolactinemia.



Antipsychotic-Induced Weight Gain

Low Risk of Antipsychotic-Induced Weight Gain

The patient does not carry the Taq1A variant (homozygous for the A2 allele).

The genotype results predict that the patient has normal dopamine receptor DRD2 density and functioning. The patient has a normal risk for weight gain when treated with antipsychotics.

Monitor the 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.



Hyperhomocysteinemia - Depression

No Increased Risk of Hyperhomocysteinemia

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The patient does not carry the MTHFR c.665C>T variant. MTHFR enzyme activity is normal.

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. With a normal MTHFR activity, this patient can process folate normally and is unlikely to have elevated plasma levels of homocysteine.

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.



Calcium Channels Function and Bipolar Disorder

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

The patient carries two copies of the rs1006737 G allele and two copies of the rs1051375 A allele. Caucasians: Risk allele for CACNA1C rs1006737 is absent. Asians: Risk allele for CACNA1C rs1051375 is absent.

The patient does not carry a variant in the gene coding for the voltage-dependent calcium channel L-type, alpha 1C subunit (CACNA1C). This genotype is associated with a normal neuronal depolarization and a normal mood regulation function. This genotype has been associated with lower rates of mood disorder recurrence and a normal risk of bipolar disorder in Caucasians. The patient does not carry the variant associated with risk of bipolar disorder in Asians.

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.



Thrombophilia

Normal Risk of Thrombosis

The patient does not carry the F5 c.1601G>A variant (also known as Factor V Leiden) or the F2 c.*97G>A variant (also known as Factor II 20210G>A).

The patient's risk of thrombosis is not increased (average risk of clotting is about 1 in 1000 for anyone in a year). However, because this test cannot find all of the inherited reasons for abnormal clotting, other factors may affect this risk assessment.

Assess thrombotic risk based on other genetic and/or circumstantial risk factors such as smoking, obesity, malignancy, prolonged immobilization or surgery.

Estrogen-containing contraceptive and hormone replacement therapy: unless other genetic and/or circumstantial risk factors are present, consider standard prescribing and monitoring practices.



Hyperhomocysteinemia - Thrombosis

No Increased Risk of Hyperhomocysteinemia

The patient does not carry the MTHFR c.665C>T variant or MTHFR c.1286A>C variant. MTHFR enzyme activity is normal.

Based on results for the MTHFR c.665C>T and c.1286A>C variants, the patient has normal MTHFR activity and is unlikely to have elevated plasma levels of homocysteine. Hyperhomocysteinemia is associated with a risk for venous thromboembolism (VTE). Unless other risk factors are present, the patient is not expected to have an increased risk for VTE.

MTHFR enzyme activity is normal.

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Potentially Impacted Medications

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Anticancer Agents	Antifolates	Methotrexate (Trexall®)		
	Angiotensin II Receptor Antagonists	Azilsartan (Edarbi®, Edarbyclor®)		
		Candesartan (Atacand®)		
		Eprosartan (Teveten®)		
		Irbesartan (Avapro®)		
		Losartan (Cozaar®, Hyzaar®)		
		Olmесartan (Benicar®)		
		Telmisartan (Micardis®)		
	Valsartan (Diovan®, Entresto®)			
	Antianginal Agents	Ranolazine (Ranexa®)		
Amiodarone (Nexterone®, Pacerone®)				
		Disopyramide (Norpace®)		
Antiarrhythmics	Flecainide (Tambocor®)			
	Mexiletine (Mexitil®)			
	Propafenone (Rythmol®)			
	Quinidine (Quinidine®)			
	Sotalol (Betapace®, Sorine®, Sotylize®)			
Cardiovascular	Anticoagulants	Apixaban (Eliquis®)		
		Betrixaban (Bevyxxa®)		
		Dabigatran Etxilate (Pradaxa®)	Warfarin (Coumadin®)	
		Edoxaban (Savaysa®)		
		Fondaparinux (Arixtra®)		
	Rivaroxaban (Xarelto®)			
	Antiplatelets	Clopidogrel (Plavix®)		
		Prasugrel (Effient®)		
		Ticagrelor (Brilinta®)		
		Vorapaxar (Zontivity®)		
Beta Blockers	Bisoprolol (Zebeta®)			
	Carvedilol (Coreg®)			
	Labetalol (Normodyne®, Trandate®)			
	Metoprolol (Lopressor®)	Atenolol (Tenormin®)		
	Nebivolol (Bystolic®)			
Calcium Channel Blockers	Propranolol (Inderal®)			
	Timolol (Blocadren®)			
	Verapamil (Covera-HS®, Verelan®, Isoptin®)			
Diuretics	Torsemide (Demadex®)			
Statins				
			Fluvastatin (Lescol®)	Atorvastatin (Lipitor®)
			Pravastatin (Pravachol®)	Lovastatin (Mevacor®, Altoprev®, Advicor®)
			Rosuvastatin (Crestor®)	Pitavastatin (Livalo®) Simvastatin (Zocor®)

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Diabetes	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-IV®) Fosnetupitant / Palonosetron (Akynzeo-IV®) Metoclopramide (Reglan®) Netupitant / Palonosetron (Akynzeo -oral®) Palonosetron (Aloxi®) Rolapitant (Varubi®)	Granisetron (Sancuso®, Sustol®) Ondansetron (Zofran®, Zuplenz®)	
	Proton Pump Inhibitors	Esomeprazole (Nexium®) Rabeprazole (Aciphex®)	Dexlansoprazole (Dexilant®, Kapidex®) Lansoprazole (Prevacid®) Omeprazole (Prilosec®) Pantoprazole (Protonix®)	
	Endocrine-Metabolic Agents	Eliglustat (Cerdelga®) Imiglucerase (Cerezyme®) Miglustat (Zavesca®) Taliglucerase alfa (Elelyso®) Velaglucerase alfa (Vpriv®)		
Gynecology	Endometriosis Pain Agents	Elagolix (Orilissa®)		
Hematology	Hemostatic Agents	Avatrombopag (Doptelet®) Eltrombopag (Promacta®) Lusutrombopag (Mulpleta®)		
Infections	Antifungals	Amphotericin B (AmBisome®, Abelcet®) Anidulafungin (Eraxis®) Caspofungin (Cancidas®) Fluconazole (Diflucan®) Isavuconazonium (Cresemba®) Itraconazole (Sporanox®) Micafungin (Mycamine®) Posaconazole (Noxafil®)		Voriconazole (Vfend®)
	Anti-HIV Agents	Dolutegravir (Tivicay®, Triumeq®) Doravirine (Pifeltro®) Etravirine (Eduvant®) Raltegravir (Isentress®, Dutrebis®) Rilpivirine (Intelence®)	Efavirenz (Sustiva®)	
	Antimalarials	Proguanil (Malarone®)		

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Multiple Sclerosis	Disease-Modifying Agents	Siponimod (Mayzent®)		
	Fibromyalgia Agents	Milnacipran (Savella®)		
Pain	Muscle Relaxants	Cyclobenzaprine (Flexeril®, Amrix®) Metaxalone (Skelaxin®) Methocarbamol (Robaxin®)	Carisoprodol (Soma®) Tizanidine (Zanaflex®)	
	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®) Oliceridine (Olinvyk) Oxycodone (Percocet®, Oxycontin®) Oxymorphone (Opana®, Numorphan®) Sufentanil (Sufenta®) Tapentadol (Nucynta®) Tramadol (Ultram®)	Methadone (Dolophine®) Morphine (MS Contin®)	
	Antiaddictives	Disulfiram (Antabuse®) Lofexidine (Lucemyra®)	Bupropion (Wellbutrin®, Zyban®, Aplenzin®, Contrave®) Levodopa / Carbidopa (Sinemet®) Naltrexone (Vivitrol®, Contrave®)	

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	<p>Anti-ADHD Agents</p>	<p>Clonidine (Kapvay®) Guanfacine (Intuniv®)</p>	<p>Amphetamine (Adderall®, Evekeo®) Atomoxetine (Strattera®) Dexmethylphenidate (Focalin®) Dextroamphetamine (Dexedrine®) Lisdexamfetamine (Vyvanse®) Methylphenidate (Ritalin®, Aptensio XR®, Concerta®, Metadate ER®, Quillivant ER®)</p>	
	<p>Anticonvulsants</p>	<p>Brivaracetam (Briviact®) Cannabidiol (Epidiolex®) Carbamazepine (Tegretol®, Carbatrol®, Eptol®) Eslicarbazepine (Aptiom®) Ethosuximide (Zarontin®) Ezogabine (Potiga®) Felbamate (Felbatol®) Fosphenytoin (Cerebyx®) Gabapentin (Neurontin®) Lacosamide (Vimpat®) Lamotrigine (Lamictal®) Levetiracetam (Keppra®) Oxcarbazepine (Trileptal®, Oxtellar XR®) Perampanel (Fycompa®) Phenobarbital (Luminal®) Phenytoin (Dilantin®) Pregabalin (Lyrica®) Primidone (Mysoline®) Rufinamide (Banzel®) Tiagabine (Gabitril®) Topiramate (Topamax®) Valproic Acid (Depakene®) Vigabatrin (Sabril®) Zonisamide (Zonegran®)</p>		
	<p>Antidementia Agents</p>	<p>Donepezil (Aricept®) Galantamine (Razadyne®) Memantine (Namenda®)</p>		

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Psychotropic	Antidepressants	Amoxapine (Amoxapine®)	Sertraline (Zoloft®)	Amitriptyline (Elavil®) Citalopram (Celexa®) Clomipramine (Anafranil®) Doxepin (Silenor®) Escitalopram (Lexapro®) Imipramine (Tofranil®) Trimipramine (Surmontil®)
		Desipramine (Norpramin®)		
		Desvenlafaxine (Pristiq®)		
		Duloxetine (Cymbalta®)		
		Fluoxetine (Prozac®, Sarafem®)		
		Fluvoxamine (Luvox®)		
		Levomilnacipran (Fetzima®)		
		Maprotiline (Ludiomil®)		
		Mirtazapine (Remeron®)		
		Nefazodone (Serzone®)		
Antipsychotics		Nortriptyline (Pamelor®)	Clozapine (Clozaril®) Olanzapine (Zyprexa®)	
		Paroxetine (Paxil®, Brisdelle®)		
		Protriptyline (Vivactil®)		
		Trazodone (Oleptro®)		
		Venlafaxine (Effexor®)		
		Vilazodone (Viibryd®)		
		Vortioxetine (Trintellix®)		
		Aripiprazole (Abilify®, Aristada®)		
		Asenapine (Saphris®)		
		Brexipiprazole (Rexulti®)		
Benzodiazepines		Cariprazine (Vraylar®)	Diazepam (Valium®) Lorazepam (Ativan®) Oxazepam (Serax®)	
		Chlorpromazine (Thorazine®)		
		Fluphenazine (Prolixin®)		
		Haloperidol (Haldol®)		
		Iloperidone (Fanapt®)		
		Loxapine (Loxitane®, Adasuve®)		
		Lurasidone (Latuda®)		
		Paliperidone (Invega®)		
		Perphenazine (Trilafon®)		
		Pimavanserin (Nuplazid®)		
Mood Stabilizers		Pimozide (Orap®)	Lithium (Eskalith®, Lithobid®)	
		Quetiapine (Seroquel®)		
		Risperidone (Risperdal®)		
Other Neurological Agents		Thioridazine (Mellaril®)	Tetrabenazine (Xenazine®)	
		Thiothixene (Navane®)		
		Trifluoperazine (Stelazine®)		
Anti-Hyperuricemics and Anti-Gout Agents		Ziprasidone (Geodon®)		
		Alprazolam (Xanax®)		
		Clobazam (Onfi®)		
		Clonazepam (Klonopin®)		
		Deutetrabenazine (Austedo®)		
		Dextromethorphan / Quinidine (Nuedexta®)		
		Flibanserin (Addyi®)		
		Valbenazine (Ingrezza®)		
		Allopurinol (Zyloprim®, Lopurin®, Aloprim®)		
		Colchicine (Mitigare®)		
		Febuxostat (Uloric®)		

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Rheumatology	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®)		
Urologicals	Alpha-Blockers for Benign Prostatic Hyperplasia	Alfuzosin (UroXatral®) Doxazosin (Cardura®) Silodosin (Rapaflo®) Tamsulosin (Flomax®) Terazosin (Hytrin®)		
	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


<p>⊗ Citalopram Celexa®</p>	<p>Insufficient Response to Citalopram (CYP2C19: Rapid Metabolizer)</p> <p>At standard label-recommended dosage, citalopram plasma concentrations levels are expected to be low which may result in a loss of efficacy. Consider an alternative medication. If citalopram is warranted, consider increasing the dose to a maximum of 150% and titrate based on the clinical response and tolerability.</p>	<p>ACTIONABLE</p>
<p>⊗ Pitavastatin Livalo®</p>	<p>Increased Pitavastatin Exposure (SLCO1B1: Decreased Function)</p> <p>The patient's genotype is associated with possible increased pitavastatin exposure. Patients may be at an increased myopathy risk with doses >1 mg per day.</p> <p>Consider starting pitavastatin at doses ≤2 mg. If doses >2 mg are needed, consider an alternative statin or combination therapy (e.g., pitavastatin plus a non-statin guideline directed medical therapy).</p>	<p>ACTIONABLE</p>
<p>⊗ Simvastatin Zocor®</p>	<p>Increased Simvastatin Exposure (SLCO1B1: Decreased Function)</p> <p>The patient's genotype is associated with possible increased simvastatin exposure. Patients may be at an increased myopathy risk with doses >20 mg.</p> <p>Consider an alternative statin. If simvastatin use is warranted, consider limiting dose to <20 mg.</p>	<p>ACTIONABLE</p>
<p>⊗ Voriconazole Vfend®</p>	<p>Non-Response to Voriconazole (CYP2C19: Rapid Metabolizer)</p> <p>Voriconazole plasma concentrations are expected to be low if a standard dose is used, increasing the risk of loss of response and effectiveness and subsequent disease progression. Consider an alternative medication that is not dependent on CYP2C19 metabolism, such as isavuconazole, liposomal amphotericin B or posaconazole.</p>	<p>ACTIONABLE</p>
<p>⊗ Lovastatin Mevacor®, Altoprev®, Advicor®</p>	<p>Increased Lovastatin Exposure (SLCO1B1: Decreased Function)</p> <p>The patient's genotype is associated with possible increased lovastatin exposure. Patients may be at an increased myopathy risk.</p> <p>Consider an alternative statin based on disease-specific guidelines. If lovastatin use is warranted, consider limiting dose to ≤20 mg per day.</p>	<p>ACTIONABLE</p>
<p>⊗ Escitalopram Lexapro®</p>	<p>Insufficient Response to Escitalopram (CYP2C19: Rapid Metabolizer)</p> <p>At standard label-recommended dosage, escitalopram plasma concentrations levels are expected to be low which may result in a loss of efficacy. Consider an alternative medication. If escitalopram is warranted, consider increasing the dose to a maximum of 150% and titrate based on the clinical response and tolerability.</p>	<p>ACTIONABLE</p>
<p>⊗ Atorvastatin Lipitor®</p>	<p>Increased Atorvastatin Exposure (SLCO1B1: Decreased Function)</p> <p>The patient's genotype is associated with possible increased atorvastatin exposure. Patients may be at an increased myopathy risk.</p> <p>Consider starting atorvastatin at doses ≤40 mg. If doses >40 mg are needed, consider combination therapy (e.g., atorvastatin plus a non-statin guideline directed therapy).</p>	<p>ACTIONABLE</p>
<p>⊗ Trimipramine Surmontil®</p>	<p>Decreased Trimipramine Exposure (CYP2C19: Rapid Metabolizer)</p> <p>The patient's high CYP2C19 activity is likely to result in a significantly increased metabolism of trimipramine to desmethyl trimipramine and a subsequent decrease in trimipramine exposure leading to therapy failure or increased side effects.</p> <p>Psychiatric Conditions: Consider an alternative medication. If trimipramine is warranted, consider therapeutic drug monitoring to guide dose adjustments.</p>	<p>INFORMATIVE</p>


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 **Clomipramine**
Anafranil® **Decreased Clomipramine Exposure (CYP2C19: Rapid Metabolizer)** **INFORMATIVE**
 The patient's high CYP2C19 activity is likely to result in a significantly increased metabolism of clomipramine to desmethyl clomipramine and a subsequent decrease in clomipramine exposure leading to therapy failure or increased side effects.
Psychiatric Conditions: Consider an alternative medication. If clomipramine is warranted, consider therapeutic drug monitoring to guide dose adjustments.


 **Imipramine**
Tofranil® **Decreased Imipramine Exposure (CYP2C19: Rapid Metabolizer)** **INFORMATIVE**
 The patient's high CYP2C19 activity is likely to result in a significantly increased metabolism of imipramine to desipramine and a subsequent decrease in imipramine exposure leading to therapy failure or increased side effects.
Psychiatric Conditions: Consider an alternative medication. If imipramine is warranted, consider therapeutic drug monitoring to guide dose adjustments.

 **Doxepin**
Silenor® **Decreased Doxepin Exposure (CYP2C19: Rapid Metabolizer)** **INFORMATIVE**
 The patient's high CYP2C19 activity is likely to result in a significantly increased metabolism of doxepin to desmethyl doxepin and a subsequent decrease in doxepin exposure leading to therapy failure or increased side effects.
Psychiatric Conditions: Consider an alternative medication. If doxepin is warranted, consider therapeutic drug monitoring to guide dose adjustments.
Insomnia: Doxepin can be prescribed according to the standard recommended dosage and administration.


 **Amitriptyline**
Elavil® **Decreased Amitriptyline Exposure (CYP2C19: Rapid Metabolizer)** **INFORMATIVE**
 The patient's high CYP2C19 activity is likely to result in a significantly increased metabolism of amitriptyline to nortriptyline and a subsequent decrease in amitriptyline exposure leading to therapy failure or increased side effects.
Psychiatric Conditions: Consider an alternative medication. If amitriptyline is warranted, consider therapeutic drug monitoring to guide dose adjustments.
Neuropathic Pain: Consider an alternative medication. If amitriptyline is warranted titrate dose according to the patient's clinical response and tolerability.


 **Fluvastatin**
Lescol® **Increased Fluvastatin Exposure (SLCO1B1: Decreased Function; CYP2C9: Normal Metabolizer)** **ACTIONABLE**
 The patient's genotype is associated with possible increased fluvastatin exposure. Fluvastatin can be prescribed at standard label-recommended dosage and administration, but patients may be at an increased risk for myopathy with doses >40 mg per day.


 **Omeprazole**
Prilosec® **Slightly Decreased to Normal Exposure to Omeprazole (CYP2C19: Rapid Metabolizer)** **ACTIONABLE**
 The patient's genotype may be associated with a slightly decreased omeprazole exposure following standard dosing. Be alert for insufficient response, consider prescribing omeprazole at standard label-recommended dosage and administration. May consider increasing the recommended dose for certain indications by 50-100% to optimize therapeutic efficacy.


 **Tacrolimus**
Prograf® **Insufficient Response to Tacrolimus (CYP3A5: Intermediate Metabolizer)** **ACTIONABLE**
 The genotype result predicts that the patient expresses the CYP3A5 protein. Therefore, the patient may metabolize tacrolimus more rapidly, resulting in low tacrolimus trough levels. Studies have shown patients with this genotype may be at increased risk for acute transplant rejection while taking a standard dose of tacrolimus. Therefore, increasing starting dose 1.5 to 2 times recommended starting dose with close monitoring is strongly recommended to achieve therapeutic effect. Total starting dose should not exceed 0.3mg/kg/day.


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 <p>Warfarin <i>Coumadin®</i></p>	<p>Dosing Adjustments are Expected (CYP2C9 *1/*1; VKORC1 -1639G>A G/A; CYP4F2 c.1297G>A A/G)</p> <p>When initiating warfarin treatment for indications with a target INR of 2-3, consider one of the following methods to estimate dosing requirements:</p> <p>FDA Label: CYP2C9 and VKORC1 genotype results indicate an expected therapeutic dose of 5-7 mg/day.</p> <p>Pharmacogenomics algorithms/calculators available at www.warfarindosing.org:</p> <p>Caucasians and Asians: Use the patient's demographics and other clinical factors along with CYP2C9 and VKORC1 genotypes to calculate the expected therapeutic dose. Consider an additional 5-10% increase to the calculated dose.</p> <p>Africans and African Americans: Use the patient's demographics and other clinical factors along with CYP2C9 and VKORC1 genotypes to calculate the expected therapeutic dose.</p> <p>The provided recommendations in Africans and African Americans apply only when all the following CYP2C9 alleles are tested: *5, *6, *8, *11.</p>	<p>ACTIONABLE</p>
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 <p>Tetrabenazine <i>Xenazine®</i></p>	<p>Normal Sensitivity to Tetrabenazine (CYP2D6: Normal Metabolizer)</p> <p>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.</p>	<p>ACTIONABLE</p>
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 <p>Pravastatin <i>Pravachol®</i></p>	<p>Increased Pravastatin Exposure (SLCO1B1: Decreased Function)</p> <p>The patient's genotype is associated with possible increased pravastatin exposure. Pravastatin can be prescribed at standard label-recommended dosage and administration, but patients may be at an increased myopathy risk with doses >40 mg per day.</p>	<p>ACTIONABLE</p>
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 <p>Rosuvastatin <i>Crestor®</i></p>	<p>Increased Rosuvastatin Exposure (SLCO1B1: Decreased Function; ABCG2: Normal Function)</p> <p>The patient's genotype is associated with possible increased rosuvastatin exposure. Rosuvastatin can be prescribed at standard label-recommended dosage and administration, but patients may be at an increased myopathy risk with doses >20 mg.</p>	<p>ACTIONABLE</p>
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 <p>Pantoprazole <i>Protonix®</i></p>	<p>Slightly Decreased to Normal Exposure to Pantoprazole (CYP2C19: Rapid Metabolizer)</p> <p>The patient's genotype may be associated with a slightly decreased pantoprazole exposure following standard dosing. Be alert for insufficient response, consider prescribing pantoprazole at standard label-recommended dosage and administration. May consider increasing the recommended dose for certain indications by 50-100% to optimize therapeutic efficacy.</p>	<p>ACTIONABLE</p>
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 <p>Lansoprazole <i>Prevacid®</i></p>	<p>Slightly Decreased to Normal Exposure to Lansoprazole (CYP2C19: Rapid Metabolizer)</p> <p>The patient's genotype may be associated with a slightly decreased lansoprazole exposure following standard dosing. Be alert for insufficient response, consider prescribing lansoprazole at standard label-recommended dosage and administration. May consider increasing the recommended dose for certain indications by 50-100% to optimize therapeutic efficacy.</p>	<p>ACTIONABLE</p>
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 <p>Efavirenz <i>Sustiva®</i></p>	<p>Increased Efavirenz Exposure (CYP2B6: Intermediate Metabolizer)</p> <p>The genotype result indicates that the patient is likely to have higher dose-adjusted trough concentrations of efavirenz following standard dosing. This may result in increased risk of CNS adverse events. Consider initiating efavirenz with a decreased dose of 400 mg/day. If therapeutic drug monitoring is available and a decreased efavirenz dose is prescribed, consider obtaining steady-state plasma efavirenz concentrations to ensure concentrations are in the suggested therapeutic range (~1 to 4 µg/mL).</p>	<p>ACTIONABLE</p>
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 Atomoxetine <i>Strattera®</i>	Possible Atomoxetine Underexposure Leading to Decreased Response (CYP2D6: Normal Metabolizer) The genotype result indicates that the patient is likely to have an insufficient response due to inadequate drug exposure following standard dosing. Consider the following dosing strategy:	ACTIONABLE
<ul style="list-style-type: none"> • Initiate treatment at 40 mg/day, increase to 80 mg/day after 3 days and maintain dose. • If after 2 weeks, optimal clinical response is not observed and adverse events are not present, consider a dose increase to 100 mg/day. • If after 2 weeks, optimal clinical response is not observed and adverse events are not present, consider therapeutic drug monitoring 1-2 hours post dose. If the plasma concentration is less than 200 ng/ml consider a dose increase to a target of 400 ng/ml. Doses greater than 100 mg/day may be needed to achieve a targeted therapeutic concentration. (Therapeutic range: 200-1000 ng/ml). 		
 Dexlansoprazole <i>Dexilant®, Kapidex®</i>	Slightly Decreased to Normal Exposure to Dexlansoprazole (CYP2C19: Rapid Metabolizer) The patient's genotype may be associated with a slightly decreased dexlansoprazole exposure following standard dosing. Be alert for insufficient response, consider prescribing dexlansoprazole at standard label-recommended dosage and administration. May consider increasing the recommended dose for certain indications by 50-100% to optimize therapeutic efficacy.	INFORMATIVE
 Diazepam <i>Valium®</i>	Possible Altered Sensitivity to Diazepam (CYP2C19: Rapid Metabolizer) CYP2C19 rapid and ultra-rapid metabolizers metabolize diazepam and nordiazepam more rapidly than normal metabolizers. However, there is insufficient data to allow calculation of dose adjustment when diazepam is prescribed. Monitor the patient's response and adjust the dose accordingly.	INFORMATIVE
 Dextroamphetamine <i>Dexedrine®</i>	Poor Response to Dextroamphetamine (COMT: Low COMT Activity) The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, dextroamphetamine should be administered at the lowest effective dose, and dosage should be individually adjusted.	INFORMATIVE
 Granisetron <i>Sancuso®, Sustol®</i>	Unfavorable Response to Standard Granisetron Dosing (ABCB1: Variant Allele Not Present) The genotype result predicts that the patient has normal ABCB1 transporter expression. Patients with this genotype may experience decreased efficacy. No dose adjustments are recommended.	INFORMATIVE
 Lorazepam <i>Ativan®</i>	Possible Altered Response to Lorazepam (UGT2B15: Intermediate Metabolizer) Lorazepam clearance may be reduced in this patient. However, there is insufficient evidence whether this change results in a significant clinical effect. Consider monitoring the patient for increased sedation and adjust dosing accordingly.	INFORMATIVE
 Methylphenidate <i>Ritalin®, Aptensio XR®, Concerta®, Metadate ER®, Quillivant ER®</i>	Poor Response to Methylphenidate (COMT: Low COMT Activity) The patient's genotype result predicts a reduced therapeutic response to methylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.	INFORMATIVE
 Morphine <i>MS Contin®</i>	Altered Response to Morphine (COMT: Low COMT Activity) The patient carries two COMT Val158Met variants, which translates to a reduced COMT function. The patient may require lower 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.	INFORMATIVE
 Oxazepam	Possible Altered Response to Oxazepam (UGT2B15: Intermediate Metabolizer)	INFORMATIVE

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Serax®

Oxazepam clearance may be reduced in this patient. However, there is insufficient evidence whether this change results in a significant clinical effect. Consider monitoring the patient for increased sedation and adjust dosing accordingly.



Tizanidine

Possible Non-Response to Tizanidine (CYP1A2: Normal Metabolizer - Higher Inducibility)

INFORMATIVE

Zanaflex®

There is little evidence regarding the impact of CYP1A2 genetic variants on tizanidine response. Smokers may be at risk for non-response and may require higher doses. There is an association between high tizanidine plasma concentrations and the risk of hypotension and excessive sedation. Therefore, careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels, leading to excessive hypotension and sedation. Careful monitoring accompanied by dose reduction may be needed in patients who have quit smoking.



Sulfasalazine

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

INFORMATIVE

Azulfidine®, Sulfazine®

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.



Sertraline

Possible Reduced Response to Sertraline (CYP2C19: Rapid Metabolizer)

INFORMATIVE

Zoloft®

Sertraline can be prescribed at standard label-recommended dosage and administration. If patient does not respond to recommended maintenance dosing, consider an alternative medication.



Ondansetron

Unfavorable Response to Standard Ondansetron Dosing (ABCB1: Variant Allele Not Present)

INFORMATIVE

Zofran®, Zuplenz®

The genotype result predicts that the patient has normal ABCB1 transporter expression. Patients with this genotype may experience decreased efficacy. No dose adjustments are recommended.



Naltrexone

Altered Response to Naltrexone (OPRM1: Normal OPRM1 Function)

INFORMATIVE

Vivitrol®, Contrave®

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.



Olanzapine

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

INFORMATIVE

Zyprexa®

Genetic variations in the Serotonin 2C Receptor (HTR2C) gene is 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.



Olanzapine

Non-Response to Olanzapine (CYP1A2: Normal Metabolizer - Higher Inducibility)

INFORMATIVE

Zyprexa®

There is little evidence regarding the impact of CYP1A2 genetic variants on olanzapine response. Smokers may be at risk for non-response at standard doses. Careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction may be needed in patients who have quit smoking.



Methadone

Increased Methadone Exposure (CYP2B6: Intermediate Metabolizer)

INFORMATIVE

Dolophine®

The patient's genotype may be associated with an increased methadone exposure following standard dosing.

For Addiction Treatment: There is limited evidence indicating that intermediate metabolizers require lower doses, therefore, a dose adjustment cannot be calculated.

For Pain Management: There are no studies documenting the effect of CYP2B6 genetic variations on methadone exposure when this drug is used as an analgesic. Consider standard prescribing and monitoring practices.

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 Lithium <i>Eskalith®</i> , <i>Lithobid®</i>	Decreased Response to Lithium (BDNF: Homozygous for rs6265 C allele) 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.	INFORMATIVE
 Lisdexamfetamine <i>Vyvanse®</i>	Poor Response to Lisdexamfetamine (COMT: Low COMT Activity) The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, lisdexamfetamine should be administered at the lowest effective dose, and dosage should be individually adjusted.	INFORMATIVE
 Levodopa / Carbidopa <i>Sinemet®</i>	Unfavorable Response to Levodopa/Carbidopa Treatment of Cocaine Addiction (DBH: Normal Dopamine Beta-Hydroxylase Activity) Dopamine β-hydroxylase (DBH) is the final enzyme in norepinephrine biosynthesis, catalyzing the oxidative hydroxylation of dopamine to norepinephrine. The patient does not carry the T allele of DBH rs1611115, which is significantly associated with low DBH activity. Preliminary studies indicate that levodopa/carbidopa treatment offers no additional benefit when compared to placebo for treating cocaine addiction in patients with this genotype. Replication of these results in a larger cohort is still needed to validate these findings.	INFORMATIVE
 Dexmethylphenidate <i>Focalin®</i>	Poor Response to Dexmethylphenidate (COMT: Low COMT Activity) The patient's genotype result predicts a reduced therapeutic response to dexmethylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.	INFORMATIVE
 Carisoprodol <i>Soma®</i>	Altered Sensitivity to Carisoprodol (CYP2C19: Rapid Metabolizer) There is insufficient data to allow calculation of dose adjustment. If carisoprodol is prescribed, it is recommended to use a lower dose, and to carefully monitor the patient for side effects.	INFORMATIVE
 Atenolol <i>Tenormin®</i>	Unfavorable Response to Atenolol (CACNA1C: Homozygous for rs1051375 A allele) CACNA1C encodes for an alpha-1 subunit of a voltage-dependent calcium channel. The patient carries two copies of CACNA1C rs1051375 A allele. In hypertensive patients with stable coronary artery disease, the A/A genotype may be associated with a higher risk of adverse outcomes (occurrence of death, nonfatal myocardial infarction, or nonfatal stroke) following treatment with atenolol compared with verapamil.	INFORMATIVE
 Clozapine <i>Clozaril®</i>	Non-Response to Clozapine (CYP1A2: Normal Metabolizer - Higher Inducibility) Smokers have a high risk for non-response at standard doses and may require higher doses. There is an association between high clozapine doses and the risk of seizures, and therefore careful monitoring is recommended during dosing adjustment. Smoking cessation will increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction is recommended in patients who have quit smoking.	INFORMATIVE
 Bupropion <i>Wellbutrin®, Zyban®, Aplenzin®, Contrave®</i>	Altered Bupropion Exposure (CYP2B6: Intermediate Metabolizer)	INFORMATIVE

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The genotype result indicates that the patient is likely to have increased bupropion exposure, but decreased exposure to the active metabolite (hydroxybupropion). This metabolite contributes to the therapeutic effects of bupropion when used as a smoking cessation agent or as an antidepressant. This decrease in exposure of hydroxybupropion may result in decreased therapeutic efficacy.

Smoking Cessation: There is insufficient data to allow calculation of dose adjustment. Consider standard prescribing and closer monitoring.

Major Depressive Disorder and Prevention of Seasonal Affective Disorder: There is insufficient data to allow calculation of dose adjustment. Therapeutic monitoring of bupropion-hydroxybupropion levels may be considered to guide dosing adjustments.

 **Amphetamine**
Adderall®, *Evekeo®*

Poor Response to Amphetamine salts (COMT: Low COMT Activity)

INFORMATIVE

The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, amphetamines should be administered at the lowest effective dose, and dosage should be individually adjusted.

 **Aripiprazole**
Abilify®, *Aristada®*

Normal Exposure to Aripiprazole (CYP2D6: Normal Metabolizer)

ACTIONABLE

The patient's genotype is associated with normal aripiprazole exposure. Consider prescribing aripiprazole at standard label-recommended dosage and administration. Careful titration is recommended until a favorable response is achieved.

Daily dosing (oral): the daily maintenance and maximum recommended doses are 10-15 mg and 30 mg, respectively. Reduce dose by 50% if a strong CYP2D6 inhibitor or a strong CYP3A4 inhibitor is co-administered. Reduce the dose to 25% of the usual dose if both a strong CYP2D6 inhibitor and a strong CYP3A4 inhibitor are co-administered. Double the dose if a strong CYP3A4 inducer is co-administered.

Single dosing (intramuscular): consider one single injection of 675 mg of *Aristada Initio* when initiating treatment with *Aristada*. Avoid using *Aristada Initio* if a strong CYP2D6 inhibitor or a strong CYP3A4 inhibitor or a strong CYP3A4 inducer is co-administered.

Monthly dosing (intramuscular): the starting and maintenance monthly recommended dose is 400 mg for *Abilify Maintena* or 441 mg, 662 mg and 882 mg for *Aristada*. For *Abilify Maintena*, reduce the monthly dose to 300 mg if a strong CYP2D6 inhibitor or a strong CYP3A4 inhibitor is co-administered to patients receiving aripiprazole at 400 mg, and reduce dose to 200 mg in patients receiving aripiprazole at 300 mg. For *Aristada*, reduce the dose to the next lower strength if a strong CYP2D6 inhibitor or a strong CYP3A4 inhibitor is co-administered for more than 14 days. For *Abilify Maintena*, reduce the dose to 200 mg if both a strong CYP2D6 inhibitor and a strong CYP3A4 inhibitor are co-administered to patients receiving aripiprazole at 400 mg, and reduce the dose to 160 mg in patients receiving aripiprazole at 300 mg. For *Aristada*, avoid use for patients at 662 mg or 882 mg dose if both a strong CYP2D6 inhibitor and a strong CYP3A4 inhibitor are co-administered. No dosage adjustment is necessary in patients taking 441 mg *Aristada*, if tolerated. If a strong CYP3A4 inducer is co-administered for more than 14 days, avoid using *Abilify Maintena*. For *Aristada*, if a strong CYP3A4 inducer is co-administered for more than 14 days, increase the 441 mg dose to 662 mg; no dose adjustment is necessary for 662 mg and 882 mg doses.

Every 6 weeks or two months dosing with *Aristada* (intramuscular): depending on individual patient's needs, treatment may be initiated with the 882 mg dose every 6 weeks or 1064 mg dose every two months. Reduce the dose to a lower strength: 441 mg every 4 weeks if a strong CYP2D6 inhibitor or a strong CYP3A4 inhibitor is co-administered for more than 14 days. Reduce the dose to a lower strength: 441 mg every 4 weeks if a strong CYP2D6 inhibitor and a strong CYP3A4 inhibitor are both co-administered for more than 14 days. If a strong CYP3A4 inducer is co-administered for more than 14 days, no dose adjustment is necessary for the 662 mg, 882 mg or 1064 mg doses, whereas 441 mg dose should be increased to 662 mg.

 **Aprepitant**
Emend-oral®

Normal Response to Aprepitant

ACTIONABLE

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Pharmacogenetic guidance: Aprepitant undergoes extensive metabolism via N- and O-dealkylations. These pathways are primarily catalyzed by CYP3A4 with minor involvement from CYP1A2 and CYP2C19. The drug is also glucuronidated by UGT1A4 and UGT1A3. No genetically guided drug selection or dosing recommendations are available.

Polypharmacy Guidance: In presence of moderate and strong CYP3A4 inhibitors, a significantly increased exposure of aprepitant is expected which may lead to adverse reactions. These drugs should be avoided with aprepitant. Strong CYP3A4 inducers can significantly decrease aprepitant exposure resulting in a loss of efficacy. These drugs should also be avoided with aprepitant. Aprepitant is a moderate (dose-dependent) inhibitor, and an inducer of CYP3A4 and an inducer of CYP2C9. Some substrates of these enzymes are contraindicated with aprepitant while others should be closely monitored and their dosing adjusted when coadministered with this antiemetic medication.

✓ **Apremilast**
Otezla®

Normal Response to Apremilast

ACTIONABLE

Pharmacogenetic guidance: Apremilast is primarily eliminated via both hydrolysis and cytochrome P450-mediated oxidative metabolism (with subsequent glucuronidation). Cytochrome P450-metabolism is mediated by CYP3A4, with minor contributions from CYP1A2 and CYP2A6. Genetic polymorphisms of these enzymes are not expected to affect the efficacy or safety profiles of apremilast. **Polypharmacy guidance:** The use of metabolizing enzyme inducers (e.g. rifampin, phenobarbital, carbamazepine, phenytoin) with apremilast is not recommended.

✓ **Anidulafungin**
Eraxis®

Normal Response to Anidulafungin

ACTIONABLE

Pharmacogenetic guidance: Anidulafungin undergoes slow chemical degradation to a peptide that lacks antifungal activity and which is subsequently converted to peptidic degradants and eliminated. Hepatic metabolism of anidulafungin has not been observed. Anidulafungin is not a substrate, inducer, or inhibitor of cytochrome P450 enzymes. No genetically guided drug selection or dosing recommendations are available.

✓ **Avatrombopag**
Doptelet®

Normal Risk of Avatrombopag-Induced Thrombosis (F2 rs1799963 GG; F5 rs6025 CC)

ACTIONABLE

Unless other risk factors are present, avatrombopag can be prescribed and administered according to the FDA recommendations.

✓ **Betrixaban**
Bevyxxa®

Normal Response to Betrixaban

ACTIONABLE

Pharmacogenetic guidance: The predominant metabolic pathway of betrixaban is amide hydrolysis with minor cytochrome P450 enzymes-based metabolism (less than 1% of the drug is metabolized by CYP1A1, CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6 and CYP3A4). The main elimination pathway of the drugs is biliary excretion followed by urinary excretion. Betrixaban is a substrate for the efflux transport protein P-gp (ABCB1) and while this transporter is polymorphic, genetic variations are unlikely to have a clinically significant impact on betrixaban exposure, and no genotype-based dosing adjustments are available. **Polypharmacy guidance:** Concomitant use with P-gp inhibitors such as amiodarone, azithromycin, verapamil, ketoconazole, clarithromycin results in increased plasma levels of betrixaban and increased risk of bleeding. Dosing reduction and close monitoring are recommended in presence of P-gp inhibitors.

✓ **Brexpiprazole**
Lexulti®

Normal Exposure to Brexpiprazole (CYP2D6: Normal Metabolizer)

ACTIONABLE

The patient's genotype is associated with a normal brexpiprazole exposure following standard dosing. Consider prescribing brexpiprazole at standard label-recommended dosage and administration. Careful titration is recommended until a favorable response is achieved.

Adjunctive Treatment of Major Depression Disorder: the recommended starting doses are 0.5 mg or 1 mg once daily. The daily maintenance doses and maximum recommended dose are 1-2 mg and 3 mg, respectively.

Schizophrenia: the recommended starting dose is 1 mg once daily. The daily maintenance doses and maximum recommended dose are 2-4 mg and 4 mg, respectively.

Dose adjustments with co-medications: reduce dose by 50% if a strong CYP2D6 inhibitor or a strong CYP3A4 inhibitor is co-administered. Administer a quarter of the usual dose if both a strong/moderate CYP2D6 inhibitor and a strong/moderate CYP3A4 inhibitor are co-administered. Double the usual dose over 1 to 2 weeks if a strong CYP3A4 inducer is co-administered.

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SEX: Male

<p>✓ Candesartan Atacand®</p>	<p>Normal Sensitivity to Candesartan Cilexetil</p> <p>Pharmacogenetic guidance: Candesartan cilexetil is hydrolyzed to candesartan its active metabolite in the gastrointestinal tract during absorption. Candesartan undergoes minor hepatic metabolism by O-deethylation to an inactive metabolite. Genetic variability of the cytochrome P450 genes is not expected to affect the patient's response to candesartan cilexetil. No genotype-based dosing adjustments are available.</p>	<p>ACTIONABLE</p>
<p>✓ Brivaracetam Briviact®</p>	<p>Normal Sensitivity to Brivaracetam (CYP2C19: Rapid Metabolizer)</p> <p>Brivaracetam is primarily metabolized by hydrolysis and to a minor extent by hydroxylation, which is mediated by CYP2C19. Brivaracetam can be prescribed at the standard label recommended dosage.</p>	<p>ACTIONABLE</p>
<p>✓ Caspofungin Cancidas®</p>	<p>Normal Response to Caspofungin</p> <p>Pharmacogenetic guidance: Caspofungin is cleared slowly and is metabolized by hydrolysis and N-acetylation. The drug undergoes also spontaneous chemical degradation. Distribution, rather than excretion or biotransformation, is the dominant mechanism influencing plasma clearance. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Co-administration of caspofungin with metabolizing enzyme inducers (e.g., rifampin, efavirenz, nevirapine, phenytoin, or carbamazepine) may result in clinically meaningful reductions in caspofungin concentrations which may require dosing adjustment.</p>	<p>ACTIONABLE</p>
<p>✓ Cevimeline Evoxac®</p>	<p>Normal Sensitivity to Cevimeline (CYP2D6: Normal Metabolizer)</p> <p>Cevimeline can be prescribed according to standard label-recommended dosage and administration.</p>	<p>ACTIONABLE</p>
<p>✓ Clobazam Onfi®</p>	<p>Normal Sensitivity to Clobazam (CYP2C19: Rapid Metabolizer)</p> <p>The genotype result predicts a rapid metabolizer phenotype, which translates to an increased CYP2C19 function. Rapid metabolizers have a higher capacity to metabolize N-desmethyloclobazam, the active metabolite of clobazam. However, there is insufficient data to allow calculation of dose adjustment when clobazam is prescribed. Therefore, the dosing recommendation for normal metabolizers is proposed. Clobazam can be prescribed at standard label-recommended dosage and administration. Individualize dosing within each body weight group, based on clinical efficacy and tolerability. Do not proceed with dose escalation more rapidly than weekly, because serum concentrations of clobazam and its active metabolite require 5 and 9 days, respectively, to reach steady state. Recommended daily dosing: ≤30 kg body weight: starting dose 5 mg; day 7: 10 mg and day 14: 20 mg; >30 kg body weight: starting dose 10 mg, day 7: 20 mg and day 14: 40 mg.</p>	<p>ACTIONABLE</p>
<p>✓ Codeine Codeine; Fioricet® with Codeine</p>	<p>Normal Exposure to Codeine Active Metabolite (CYP2D6: Normal Metabolizer)</p> <p>The patient genotype is associated with normal conversion of codeine to its active metabolite (morphine), which may result in standard pharmacological and/or toxic effects.</p> <p>Codeine can be prescribed at standard label-recommended age- or weight-based dosing and monitoring.</p>	<p>ACTIONABLE</p>
<p>✓ Clopidogrel Plavix®</p>	<p>Increased Exposure to Clopidogrel Active Metabolite (CYP2C19: Rapid Metabolizer)</p> <p>ACS and PCI: Clopidogrel can be prescribed at standard label-recommended dosage and administration.</p>	<p>ACTIONABLE</p>
<p>✓ Darifenacin Enablex®</p>	<p>Normal Response to Darifenacin (CYP2D6: Normal Metabolizer)</p> <p>Darifenacin can be prescribed at standard label-recommended dosage and administration.</p>	<p>ACTIONABLE</p>
<p>✓ Dextromethorphan / Quinidine</p>	<p>Normal Sensitivity to Dextromethorphan-Quinidine (CYP2D6: Normal Metabolizer)</p>	<p>ACTIONABLE</p>

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Nuedexta®

Patients with Pseudobulbar Affect: quinidine is a specific inhibitor of CYP2D6-dependent oxidative metabolism used in the dextromethorphan-quinidine combination to increase the systemic bioavailability of dextromethorphan. Dextromethorphan-quinidine can be prescribed according to standard label-recommended dosage and administration.

✓ **Desvenlafaxine**
 Pristiq®

Normal Sensitivity to Desvenlafaxine (CYP2D6: Normal Metabolizer)

ACTIONABLE

Desvenlafaxine can be prescribed at standard label-recommended dosage and administration.

✓ **Dolutegravir**
 Tivicay®, Triumeq®

Normal Response to Dolutegravir

ACTIONABLE

Pharmacogenetic guidance: Dolutegravir is eliminated mainly through metabolism by UGT1A1 and a minor contribution from CYP3A. Although UGT1A1 poor metabolizers or patients taking inhibitors of UGT1A1 activity have increased plasma levels of dolutegravir, these changes are not clinically significant. No dosing adjustments are required for dolutegravir due to genetic variations in UGT1A1. **Polypharmacy guidance:** Coadministration of dolutegravir with drugs that are strong enzyme inducers, such as rifampin, may result in reduced plasma concentrations of this drug.

✓ **Doravirine**
 Pifeltro®

Normal Exposure to Doravirine

ACTIONABLE

Pharmacogenetic guidance: Doravirine is primarily metabolized by CYP3A. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Doravirine is contraindicated when co-administered with drugs that are strong CYP3A enzyme inducers as significant decreases in doravirine plasma concentrations may occur, which may decrease the effectiveness of doravirine. Co-administration of doravirine with drugs that are inhibitors of CYP3A may result in increased plasma concentrations of doravirine.

✓ **Duloxetine**
 Cymbalta®

Normal Exposure to Duloxetine

ACTIONABLE

Pharmacogenetic guidance: Duloxetine is primarily metabolized by CYP1A2 and to a lesser extent by CYP2D6. While these clearance pathways are diminished in subjects with reduced enzyme activity, these changes have not been shown to be clinically significant. No genetically guided drug selection or dosing recommendations are recommended. **Polypharmacy guidance:** Co-administration of duloxetine with a CYP1A2 inhibitor should be avoided. Co-administration of duloxetine with CYP2D6 inhibitors may result in higher duloxetine concentrations. Duloxetine is a moderate inhibitor of CYP2D6.

✓ **Elagolix**
 Orilissa®

Possible Increased Elagolix Exposure (SLCO1B1: Decreased Function)

ACTIONABLE

Elagolix can be prescribed at standard label-recommended dosage and administration.

✓ **Eltrombopag**
 Promacta®

Normal Risk of Eltrombopag-Induced Thrombosis (F5: Normal Thrombosis Risk)

ACTIONABLE

Venous and arterial thromboses have been reported in adult patients being treated with eltrombopag, more frequently in patients with hepatitis C and chronic liver disease. Other risk factors that can potentially increase the risk of thrombosis include but are not limited to splenectomy, immobilization, surgery, anti-phospholipid antibody syndrome and use of estrogen-containing contraceptives. The absence of the F5 c.1601G>A variant (also known as Factor V Leiden) in this patient indicates that the patient has a typical risk for thrombosis. Use eltrombopag as recommended.

✓ **Eprosartan**
 Teveten®

Normal Sensitivity to Eprosartan

ACTIONABLE

Pharmacogenetic guidance: Eprosartan is eliminated by biliary and renal excretion, primarily as unchanged compound. Eprosartan is not metabolized by the cytochrome P450 enzymes. Genetic variability of the cytochrome P450 genes is not expected to affect the patient's response to eprosartan. No genotype-based dosing adjustments are available.

✓ **Etravirine**
 Edurant®

Normal Exposure to Etravirine

ACTIONABLE

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Pharmacogenetic guidance: Etravirine is primarily eliminated by metabolism via CYP3A4, CYP2C9 and CYP2C19. The metabolites are subsequently glucuronidated by uridine diphosphate glucuronosyltransferase. Renal elimination of etravirine is negligible. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Co-administration of etravirine with drugs that inhibit or induce CYP3A4, CYP2C9, and/or CYP2C19 may alter the therapeutic effect or adverse reaction profile of etravirine. Etravirine is an inducer of CYP3A and a weak inhibitor of CYP2C9, CYP2C19 and P-glycoprotein.

<p>✓ Eliglustat Cerdelga®</p>	<p>Normal Exposure to Eliglustat (CYP2D6: Normal Metabolizer)</p> <p>The genotype result indicates that the patient is likely to have a normal eliglustat exposure. Consider prescribing eliglustat at standard label-recommended dosage and administration (84 mg orally twice daily).</p> <p>Dose adjustments with co-medications: Reduce the dosage of eliglustat to 84 mg once daily if the patient is also taking a strong/moderate CYP2D6 inhibitor or a strong/moderate CYP3A inhibitor. Eliglustat is contraindicated if a strong/moderate CYP2D6 inhibitor AND a strong/moderate CYP3A inhibitor are co-administered. Eliglustat should be avoided if the patient is also taking a CYP3A inducer.</p>	<p>ACTIONABLE</p>
<p>✓ Dronabinol Marinol®</p>	<p>Normal Dronabinol Exposure (CYP2C9: Normal Metabolizer)</p> <p>The patient's genotype predicts a normal CYP2C9 metabolic activity. Dronabinol can be prescribed at standard label-recommended dosage and administration.</p>	<p>ACTIONABLE</p>
<p>✓ Fesoterodine Toviaz®</p>	<p>Normal Sensitivity to Fesoterodine (CYP2D6: Normal Metabolizer)</p> <p>Fesoterodine can be prescribed at standard label-recommended dosage and administration.</p>	<p>ACTIONABLE</p>
<p>✓ Flibanserin Addyi®</p>	<p>Normal Exposure to Flibanserin (CYP2C19: Rapid Metabolizer)</p> <p>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. The genotype results predict that the patient is expected to have a normal clearance and a typical exposure to flibanserin. Use label-recommended dosage and follow standard precautions.</p>	<p>ACTIONABLE</p>
<p>✓ Fluconazole Diflucan®</p>	<p>Normal Response to Fluconazole</p> <p>Pharmacogenetic guidance: Fluconazole not extensively metabolized and is eliminated primarily by renal excretion, with approximately 80% of the administered dose appearing in the urine as unchanged drug and 11% as metabolites. The pharmacokinetics of fluconazole is markedly affected by reduction in renal function. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Fluconazole is a moderate inhibitor of CYP3A4, CYP2C9 and CYP2C19 enzymes. Fluconazole treated patients who are concomitantly treated with drugs with a narrow therapeutic window metabolized by CYP2C9, CYP2C19 or CYP3A4 should be monitored. The enzyme inhibiting effect of fluconazole persists 4-5 days after discontinuation of the drug due to its long half-life.</p>	<p>ACTIONABLE</p>
<p>✓ Fluvoxamine Luvox®</p>	<p>Normal Sensitivity to Fluvoxamine (CYP2D6: Normal Metabolizer)</p> <p>Fluvoxamine can be prescribed at standard label recommended-dosage and administration. Careful titration is recommended until a favorable response is achieved.</p>	<p>ACTIONABLE</p>
<p>✓ Fosaprepitant Emend-IV®</p>	<p>Normal Response to Fosaprepitant</p>	<p>ACTIONABLE</p>

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Pharmacogenetic guidance: Fosaprepitant is a prodrug of aprepitant which is rapidly converted to aprepitant following intravenous administration. Its antiemetic effects are attributable to aprepitant. Aprepitant undergoes extensive metabolism via N- and O-dealkylations. These pathways are primarily catalyzed by CYP3A4 with minor involvement from CYP1A2 and CYP2C19. The drug is also glucuronidated by UGT1A4 and UGT1A3. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy Guidance:** In presence of moderate and strong CYP3A4 inhibitors, a significantly increased exposure of aprepitant is expected which may lead to adverse reactions. These drugs should be avoided with fosaprepitant. Strong CYP3A4 inducers can significantly decrease aprepitant exposure resulting in a loss of efficacy. These drugs should also be avoided with fosaprepitant. Aprepitant is a moderate (dose-dependent) inhibitor, and an inducer of CYP3A4 and an inducer of CYP2C9. Some substrates of these enzymes are contraindicated with fosaprepitant while others should be closely monitored and their dosing adjusted when coadministered with this antiemetic medication.

✓ **Fosphenytoin** **Normal Phenytoin (Fosphenytoin Active Metabolite) Exposure (CYP2C9: Normal Metabolizer)** **ACTIONABLE**
Cerebyx®
 Fosphenytoin is a prodrug of phenytoin. The genotype results indicate that the patient is expected to have a normal CYP2C9 enzyme activity. Fosphenytoin can be prescribed at a standard loading dose and a standard maintenance dose. Consider therapeutic drug monitoring and evaluate the patient's response to optimize the maintenance dosage.

✓ **Flurbiprofen** **Normal Flurbiprofen Exposure (CYP2C9: Normal Metabolizer)** **ACTIONABLE**
Ansaid®
Rheumatoid Arthritis and Osteoarthritis: Flurbiprofen therapy can be initiated at standard label-recommended dosage and administration. Consider using the lowest effective dosage for the shortest duration consistent with the patient treatment goals.
 Consider initiating treatment at the lowest end of the dosing range in geriatric patients. A dosage adjustment may be warranted when flurbiprofen is administered with CYP2C9 inhibitors or inducers.

✓ **Glimepiride** **Normal Exposure to Glimepiride** **ACTIONABLE**
Amaryl®
Pharmacogenetic guidance: Glimepiride is metabolized by CYP2C9. While this clearance pathway is diminished in subjects with reduced CYP2C9 activity, such a change has not been shown to be clinically significant. No genetically guided drug selection or dosing adjustments are recommended. **Polypharmacy guidance:** Co-administration of glimepiride with a strong CYP2C9 inhibitor may result in higher glimepiride concentrations possibly leading to hypoglycemia. Co-administration with a strong CYP2C9 inducer may result in lower glimepiride concentrations and a lack of efficacy.

✓ **Haloperidol** **Normal Exposure to Haloperidol (CYP2D6: Normal Metabolizer)** **ACTIONABLE**
Haldol®
 The patient's genotype is associated with a normal haloperidol exposure following standard dosing. Consider prescribing haloperidol at standard label-recommended dosage and administration. Careful titration is recommended until a favorable response is achieved.

✓ **Hydrocodone** **Normal Exposure to Hydrocodone Active Metabolite (CYP2D6: Normal Metabolizer)** **ACTIONABLE**
Vicodin®
 The patient genotype is associated with normal hydrocodone and active metabolite (hydromorphone) exposure following standard dosing.
 Hydrocodone can be prescribed at standard label-recommended age- or weight-based dosing and monitoring.

✓ **Ibuprofen** **Normal Ibuprofen Exposure (CYP2C9: Normal Metabolizer)** **ACTIONABLE**
Advil®, Motrin®
Pain, Dysmenorrhea, Rheumatoid Arthritis, Osteoarthritis, Fever and Other Anti-Inflammatory Uses: Ibuprofen therapy can be initiated at standard label-recommended dosage and administration. Consider using the lowest effective dosage for the shortest duration consistent with the patient treatment goals.
 Consider initiating treatment at the lowest end of the dosing range in geriatric patients. A dosage adjustment may be warranted when ibuprofen is administered with CYP2C9 inhibitors or inducers.

Imiglucerase **Normal Response to Imiglucerase** **ACTIONABLE**

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<p>✓ Cerezyme®</p>	<p>Pharmacogenetic guidance: Imiglucerase is a monomeric glycoprotein enzyme produced by recombinant DNA technology. Imiglucerase dosage should be individualized to each patient. Individual patient dosage may require increase or decrease based on therapeutic goals. Imiglucerase is not metabolized by the CYP450 enzymes. No genetically-guided drug selection or dosing recommendations are available.</p>
<p>✓ Isavuconazonium Cresemba®</p>	<p>Normal Response to Isavuconazonium ACTIONABLE Pharmacogenetic guidance: Isavuconazonium sulfate is a prodrug that is rapidly hydrolyzed in plasma by butylcholinesterase into its active moiety isavuconazole. Isavuconazole is extensively metabolized CYP3A4 and CYP3A5 and Common genetic polymorphism of these metabolizing enzymes gene are not expected to affect isavuconazole exposure. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Isavuconazole is a sensitive CYP3A4 substrate and its use with strong CYP3A4 inhibitors or inducers contraindicated.</p>
<p>✓ Itraconazole Sporanox®</p>	<p>Normal Response to Itraconazole ACTIONABLE Pharmacogenetic guidance: Itraconazole is extensively metabolized to several metabolites by CYP3A4. The main metabolite is hydroxy-itraconazole, which has in vitro antifungal activity comparable to itraconazole; trough plasma concentrations of this metabolite are about twice those of itraconazole. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Coadministration of itraconazole with potent CYP3A4 inducers may decrease the bioavailability of itraconazole and hydroxy-itraconazole to such an extent that efficacy may be reduced. Therefore, administration of potent CYP3A4 inducers with itraconazole is not recommended and the use of these drugs should be avoided 2 weeks before and during treatment with itraconazole. Potent CYP3A4 inhibitors may increase the bioavailability of itraconazole and these drugs should be used with caution when coadministered with this antifungal. Itraconazole inhibit the metabolism of drugs metabolized by CYP3A4 or transported by P-glycoprotein, which may result in increased plasma concentrations of these drugs and/or their active metabolite(s) when they are coadministered. These elevated plasma concentrations may increase or prolong both therapeutic and adverse effects of these drugs. When using concomitant medication, it is recommended that the corresponding label be consulted for information on possible contraindications or need for dose adjustments.</p>
<p>✓ Iloperidone Fanapt®</p>	<p>Normal Sensitivity to Iloperidone (CYP2D6: Normal Metabolizer) ACTIONABLE Iloperidone can be prescribed at standard label-recommended dosage and administration. Iloperidone must be titrated slowly from a low starting dose to avoid orthostatic hypotension. If patients taking iloperidone experience symptoms that could indicate the occurrence of cardiac arrhythmias (e.g., dizziness, palpitations, or syncope), the prescriber should initiate further evaluation, including cardiac monitoring.</p>
<p>✓ Lacosamide Vimpat®</p>	<p>Normal Exposure to Lacosamide ACTIONABLE Pharmacogenetic guidance: Lacosamide is primarily cleared by renal excretion and metabolized by CYP3A4, CYP2C9 and CYP2C19. While these clearance pathways are diminished in subjects with reduced enzyme activity, these changes have not been shown to be clinically significant. No genetically guided drug selection or dosing adjustments are recommended. Polypharmacy guidance: Co-administration of lacosamide, in patients with reduced renal function, with strong CYP2C9 and/or CYP3A4 inhibitors may result in higher lacosamide concentrations.</p>
<p>✓ Lurasidone Latuda®</p>	<p>Normal Response to Lurasidone ACTIONABLE Pharmacogenetic guidance: Lurasidone is metabolized by CYP3A4. No genotype-based dosing adjustments are available. Polypharmacy guidance: The concomitant use of lurasidone with all CYP3A4 inhibitors may result in an increase in lurasidone plasma concentrations, which could increase or prolong adverse drug effects. Lurasidone should not be administered with strong CYP3A4 inhibitors. Lurasidone dose should not exceed 40 mg when administered with moderate CYP3A4 inhibitors. Monitor patients receiving lurasidone and any CYP3A4 inhibitor. Rifampin or other strong inducers of CYP3A should not be administered with lurasidone. If lurasidone is used concomitantly with a moderate CYP3A4 inducer, it may be necessary to increase lurasidone dose after chronic treatment (7 days or more) with the CYP3A4 inducer.</p>
<p>✓ Lusutrombopag Mulpleta®</p>	<p>Normal Risk of Lusutrombopag-Induced Thrombosis (F2 rs1799963 GG; F5 rs6025 CC) ACTIONABLE Unless other risk factors are present, lusutrombopag can be prescribed and administered according to the FDA recommendations.</p>

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<p>✓ Meloxicam Mobic®</p>	<p>Normal Meloxicam Exposure (CYP2C9: Normal Metabolizer)</p> <p>Pain, Rheumatoid Arthritis and Osteoarthritis: Meloxicam therapy can be initiated at standard label-recommended dosage and administration. Consider using the lowest effective dosage for the shortest duration consistent with the patient treatment goals.</p> <p>Consider initiating treatment at the lowest end of the dosing range in geriatric patients. A dosage adjustment may be warranted when meloxicam is administered with CYP2C9 inhibitors or inducers.</p>	<p>ACTIONABLE</p>
<p>✓ Lofexidine Lucemyra®</p>	<p>Normal Exposure to Lofexidine (CYP2D6: Normal Metabolizer)</p> <p>Lofexidine is metabolized by CYP2D6 with contributions from CYP2C19 and CYP1A2. The genotype results predict that the patient is expected to have a normal clearance and a typical exposure to this drug. Use label-recommended dosage and follow standard precautions.</p>	<p>ACTIONABLE</p>
<p>✓ Metoprolol Lopressor®</p>	<p>Normal Exposure to Metoprolol (CYP2D6: Normal Metabolizer)</p> <p>The patient's genotype is associated with a normal metoprolol exposure following standard dosing. Consider prescribing metoprolol at standard label-recommended dosage and administration. Selection of proper dosage requires individual titration.</p>	<p>ACTIONABLE</p>
<p>✓ Micafungin Mycamine®</p>	<p>Normal Response to Micafungin</p> <p>Pharmacogenetic guidance: Micafungin is metabolized by arylsulfatase, catechol-O-methyltransferase and cytochrome P450 enzymes. Even though micafungin is a substrate for and a weak inhibitor of CYP3A in vitro, hydroxylation by CYP3A is not a major pathway for micafungin metabolism in vivo. No genetically guided drug selection or dosing recommendations are available.</p>	<p>ACTIONABLE</p>
<p>✓ Miglustat Zavesca®</p>	<p>Normal Response to Miglustat</p> <p>Pharmacogenetic guidance: Miglustat is not metabolized by human CYP450 enzymes and the drug is mainly eliminated by renal excretion. No genetically-guided drug selection or dosing recommendations are available.</p>	<p>ACTIONABLE</p>
<p>✓ Mirtazapine Remeron®</p>	<p>Normal Exposure to Mirtazapine</p> <p>Pharmacogenetic guidance: Mirtazapine is metabolized by CYP2D6 as well as CYP1A2 and CYP3A4. While these clearance pathways are diminished in subjects with reduced enzyme activity, these changes have not been shown to be clinically significant. No genetically guided drug selection or dosing recommendations are recommended.</p> <p>Polypharmacy guidance: Co-administration of mirtazapine with CYP inhibitors did not result in clinically relevant pharmacokinetics changes. While co-administration with strong CYP inducers (ex. phenytoin, carbamazepine, rifampicin) may result in lower mirtazapine concentrations and a lack of efficacy.</p>	<p>ACTIONABLE</p>
<p>✓ Mirabegron Myrbetriq®</p>	<p>Normal Sensitivity to Mirabegron (CYP2D6: Normal Metabolizer)</p> <p>Mirabegron can be prescribed at standard label-recommended dosage and administration.</p>	<p>ACTIONABLE</p>
<p>✓ Nebivolol Bystolic®</p>	<p>Normal Sensitivity to Nebivolol (CYP2D6: Normal Metabolizer)</p> <p>Nebivolol can be prescribed at standard label-recommended dosage and administration. Caution is recommended during up-titration until a favorable response is achieved.</p>	<p>ACTIONABLE</p>
<p>✓ Oxycodone Percocet®, Oxycontin®</p>	<p>Normal Exposure to Oxycodone Active Metabolite (CYP2D6: Normal Metabolizer)</p> <p>The patient genotype is associated with normal oxycodone and active metabolite (oxymorphone) exposure following standard dosing.</p> <p>Oxycodone can be prescribed at standard label-recommended age- or weight-based dosing and monitoring.</p>	<p>ACTIONABLE</p>

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<p>✓ Paliperidone <i>Invega®</i></p>	<p>Normal Sensitivity to Paliperidone (CYP2D6: Normal Metabolizer)</p> <p>Paliperidone can be prescribed at standard label-recommended dosage and administration.</p>	<p>ACTIONABLE</p>
<p>✓ Paroxetine <i>Paxil®, Brisdelle®</i></p>	<p>Normal Sensitivity to Paroxetine (CYP2D6: Normal Metabolizer)</p> <p>Paroxetine can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended until a favorable response is achieved.</p>	<p>ACTIONABLE</p>
<p>✓ Perphenazine <i>Trilafon®</i></p>	<p>Normal Sensitivity to Perphenazine (CYP2D6: Normal Metabolizer)</p> <p>Perphenazine can be prescribed at standard label-recommended dosage and administration.</p>	<p>ACTIONABLE</p>
<p>✓ Phenytoin <i>Dilantin®</i></p>	<p>Normal Phenytoin Exposure (CYP2C9: Normal Metabolizer)</p> <p>The genotype results indicate that the patient is expected to have a normal CYP2C9 enzyme activity. Phenytoin can be prescribed at a standard loading dose and a standard maintenance dose. Consider therapeutic drug monitoring and evaluate the patient's response to optimize the maintenance dosage.</p>	<p>ACTIONABLE</p>
<p>✓ Posaconazole <i>Noxafil®</i></p>	<p>Normal Response to Posaconazole</p> <p>Pharmacogenetic guidance: Posaconazole is cleared primarily as unchanged drug. The excreted metabolites in urine and feces account for approximately 17% of the administered dose. The metabolic pathways for posaconazole include direct glucuronidation, minor oxidation and dealkylation. CYP3A4 (and possibly CYP1A1 and CYP3A5), UGT1A4, and P-glycoprotein are enzymes and transporters that play a role in the elimination of this antifungal. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: UGT and P-glycoprotein inhibitors or inducers may affect posaconazole plasma concentrations. Concomitant use of posaconazole and these agents should be avoided unless the benefit to the patient outweighs the risk.</p>	<p>ACTIONABLE</p>
<p>✓ Prasugrel <i>Effient®</i></p>	<p>Normal Response to Prasugrel</p> <p>Pharmacogenetic guidance: Prasugrel is a prodrug that is hydrolyzed in the intestine to a thiolactone, which is then converted to the active metabolite primarily by CYP3A4 and CYP2B6, and to a lesser extent by CYP2C9 and CYP2C19. Prasugrel active metabolite exposure and platelet reactivity are not affected by CYP2C19 genetic variants. Prasugrel efficacy or safety profile are also unaffected by CYP2B6, CYP3A5, and CYP2C9 genetic variants. No genetically-guided drug selection or dosing recommendations are available. Polypharmacy guidance: Prasugrel can be administered with drugs that are inducers or inhibitors of cytochrome P450 enzymes.</p>	<p>ACTIONABLE</p>
<p>✓ Propafenone <i>Rythmol®</i></p>	<p>Normal Exposure to Propafenone (CYP2D6: Normal Metabolizer)</p> <p>The patient's genotype is associated with a normal propafenone exposure following standard dosing. Consider prescribing propafenone at standard label-recommended dosage and administration. Careful titration is recommended with ECG monitoring until a favorable response is achieved.</p> <p>Dose adjustments with co-medications: concurrent use of propafenone along with CYP3A4 inhibitors and CYP2D6 inhibitors may significantly increase the plasma concentration of propafenone increasing the risk of proarrhythmia and other adverse events. Therefore, avoid simultaneous use of propafenone with both a CYP2D6 inhibitor and a CYP3A4 inhibitor.</p>	<p>ACTIONABLE</p>
<p>✓ Propranolol <i>Inderal®</i></p>	<p>Normal Sensitivity to Propranolol (CYP2D6: Normal Metabolizer)</p> <p>Propranolol can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended with monitoring until a favorable response is achieved.</p>	<p>ACTIONABLE</p>
<p>✓ Piroxicam</p>	<p>Normal Piroxicam Exposure (CYP2C9: Normal Metabolizer)</p>	<p>ACTIONABLE</p>

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Feldene®

Rheumatoid Arthritis and Osteoarthritis: Piroxicam therapy can be initiated at standard label-recommended dosage and administration. Consider using the lowest effective dosage for the shortest duration consistent with the patient treatment goals.

Consider initiating treatment at the lowest end of the dosing range in geriatric patients. A dosage adjustment may be warranted when piroxicam is administered with CYP2C9 inhibitors or inducers.



Raltegravir

Isentress®, Dutrebis®

Normal Response to Raltegravir

ACTIONABLE

Pharmacogenetic guidance: Raltegravir is eliminated mainly through metabolism by UGT1A1. Although UGT1A1 poor metabolizers or patients taking inhibitors of UGT1A1 activity have increased plasma levels of raltegravir, these changes are not clinically significant. No dosing adjustments are required for raltegravir in patients who carry genetic variants of UGT1A1. **Polypharmacy guidance:** Coadministration of raltegravir with drugs that are strong inducers of UGT1A1, such as rifampin, may result in reduced plasma concentrations of this drug.



Ranolazine

Ranexa®

Normal Sensitivity to Ranolazine (CYP2D6: Normal Metabolizer)

ACTIONABLE

Ranolazine is metabolized mainly by CYP3A4, and to a lesser extent by CYP2D6. This drug can be prescribed at standard label-recommended dosage and administration. The recommended initial dose is 375 mg twice daily. After 2–4 weeks, the dose should be titrated to 500 mg twice daily, and according to the patient’s response, further titrated to a recommended maximum dose of 1000 mg twice daily.

If patient experiences treatment-related adverse events (e.g. dizziness, nausea, vomiting, or syncope), down titration of ranolazine to 500 or 375 mg twice daily may be required. If symptoms do not resolve after dose reduction, treatment should be discontinued.

Ranolazine is a QTc prolonging drug. Caution should be observed when treating: 1- patients with a history of congenital or a family history of long QT syndrome, 2- patients with known acquired QT interval prolongation, and 3- patients treated with drugs affecting the QTc interval. Administration of CYP3A4 inhibitors increases the exposure of ranolazine significantly. As a consequence, the QTc prolongation by ranolazine in the presence of potent CYP3A4 inhibitors is significantly elevated relative to when the drug is administered alone.



Risperidone

Risperdal®

Normal Exposure to Risperidone (CYP2D6: Normal Metabolizer)

ACTIONABLE

The patient’s genotype is associated with a normal risperidone exposure and normal active metabolite (paliperidone) exposure following standard dosing. Consider prescribing risperidone according to standard label-recommended dosage and administration. Dosing is individualized based on the patient’s tolerability and clinical response.



Rolapitant

Varubi®

Normal Response to Rolapitant

ACTIONABLE

Pharmacogenetic guidance: Rolapitant is metabolized primarily by CYP3A4 to a major active metabolite, (C4pyrrolidine-hydroxylated rolapitant). Rolapitant is eliminated primarily through the hepatic/biliary route. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy Guidance:** Strong CYP3A4 inducers can significantly decrease rolapitant exposure resulting in a loss of efficacy. These drugs should be avoided with rolapitant. Rolapitant is a moderate CYP2D6 inhibitor and some CYP2D6 substrates (e.g. thioridazine, pimozide) are contraindicated with rolapitant while others should be closely monitored and their doing adjusted when coadministered with this antiemetic medication. Rolapitant is an inhibitor two major drug efflux transporters: breast-cancer-resistance protein (BCRP) and P-glycoprotein (P-gp). Increased plasma concentrations of BCRP or P-gp substrates may result in potential adverse reactions when coadministered with rolapitant.



Siponimod

Mayzent®

Normal Exposure to Siponimod (CYP2C9: Normal Metabolizer)

ACTIONABLE

NAME: BRL SAMPLE
SAMPLE ID:
DOB: 1/20/1930
SEX: Male

The patient's genotype is associated with a normal siponimod clearance. Consider the following standard daily dosing regimen:

- Initiation and up-titration: days 1-2: 0.25 mg - day 3: 0.50 mg - day 4: 0.75 mg - day 5: 1.25 mg
- Maintenance dose starting day 6 and after: 2 mg

Concomitant use of CYP2C9/3A4 dual inhibitor (e.g. fluconazole) or moderate CYP2C9 inhibitor concomitantly with a strong or moderate CYP3A4 inhibitor are not recommended. Caution should be exercised for concomitant use of moderate CYP2C9 inhibitors.

Concomitant use of strong CYP3A4/moderate CYP2C9 inducers (e.g. rifampicin or carbamazepine) is not recommended.

✓ **Rilpivirine** ACTIONABLE
Intence®
Normal Exposure to Rilpivirine
Pharmacogenetic guidance: Rilpivirine is primarily eliminated by metabolism via CYP3A4. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Co-administration of rilpivirine with drugs that induce or inhibit CYP3A4 may affect the plasma concentrations of rilpivirine.

✓ **Tamsulosin** ACTIONABLE
Flomax®
Normal Response to Tamsulosin (CYP2D6: Normal Metabolizer)
Tamsulosin can be prescribed at standard label-recommended dosage and administration.

✓ **Telmisartan** ACTIONABLE
Micardis®
Normal Sensitivity to Telmisartan
Pharmacogenetic guidance: Telmisartan is metabolized by conjugation to form a pharmacologically inactive acyl glucuronide. Telmisartan is not metabolized by the cytochrome P450 isoenzymes. Genetic variability of the cytochrome P450 genes is not expected to affect the patient's response to telmisartan. No genotype-based dosing adjustments are available.

✓ **Thioridazine** ACTIONABLE
Mellaril®
Normal Sensitivity to Thioridazine (CYP2D6: Normal Metabolizer)
Thioridazine can be prescribed at standard label-recommended dosage and administration.

✓ **Taliglucerase alfa** ACTIONABLE
Elelyso®
Normal Response to Taliglucerase alfa
Pharmacogenetic guidance: Taliglucerase alfa is a recombinant analog of human lysosomal glucocerebrosidase that catalyzes the hydrolysis of glucocerebroside to glucose and ceramide, reducing the amount of accumulated glucocerebroside. Taliglucerase alfa dosage should be individualized to each patient. Individual patient dosage may require increase or decrease based on therapeutic goals. Taliglucerase alfa is not metabolized by the CYP450 enzymes. No genetically-guided drug selection or dosing recommendations are available.

✓ **Tolbutamide** ACTIONABLE
Orinase®
Normal Exposure to Tolbutamide
Pharmacogenetic guidance: Tolbutamide is extensively metabolized by CYP2C9. While this clearance pathway is diminished in subjects with reduced CYP2C9 activity, such a change has not been shown to be clinically significant. No genetically guided drug selection or dosing adjustments are recommended. **Polypharmacy guidance:** Co-administration of tolbutamide with a strong CYP2C9 inhibitor may result in higher tolbutamide concentrations possibly leading to hypoglycemia. Co-administration with a strong CYP2C9 inducer may result in lower tolbutamide concentrations and a lack of efficacy.

✓ **Pimozide** ACTIONABLE
Orap®
Normal Exposure to Pimozide (CYP2D6: Normal Metabolizer)
Consider prescribing pimozide at standard label-recommended dosage and administration. Standard starting dose: 1 to 2 mg/day. Doses may be increased to a maximum of 10 mg/day.
Concomitant use of pimozide with strong CYP2D6 or strong CYP3A inhibitors is contraindicated. Cautions should be taken when pimozide is administered with other drugs that prolong QT.

NAME: BRL SAMPLE
SAMPLE ID:
DOB: 1/20/1930
SEX: Male

<p>✓ Tramadol <i>Ultram®</i></p>	<p>Normal Exposure to Tramadol Active Metabolite (CYP2D6: Normal Metabolizer)</p> <p>The patient genotype is associated with normal conversion of tramadol to its active metabolite (O-desmethyltramadol), which may result in standard pharmacological and/or toxic effects.</p> <p>Tramadol can be prescribed at standard label-recommended age- or weight-based dosing and monitoring.</p>	<p>ACTIONABLE</p>
<p>✓ Olmесartan <i>Benicar®</i></p>	<p>Normal Sensitivity to Olmesartan Medoxomil</p> <p>Pharmacogenetic guidance: Olmesartan medoxomil is hydrolyzed to olmesartan its active metabolite in the gastrointestinal tract during absorption. There is virtually no further metabolism of olmesartan. Genetic variability of the cytochrome P450 genes is not expected to affect the patient's response to olmesartan medoxomil. No genotype-based dosing adjustments are available.</p>	<p>ACTIONABLE</p>
<p>✓ Valbenazine <i>Ingrezza®</i></p>	<p>Normal Sensitivity to Valbenazine (CYP2D6: Normal Metabolizer)</p> <p>Valbenazine can be prescribed at standard label-recommended dosage and administration. The initial dose is 40 mg once daily which can be increased after a week of therapy to the recommended dose of 80 mg once daily.</p> <p><u>Dose adjustments with comedications:</u> reduce the daily recommended dose to 40 mg if a strong CYP3A4 inhibitor is coadministered. In presence of a CYP2D6 inhibitor, the daily recommended dose may be reduced based on tolerability. Concomitant use with CYP3A4 inducers should be avoided.</p>	<p>ACTIONABLE</p>
<p>✓ Vardenafil <i>Levitra®</i></p>	<p>Normal Response to Vardenafil</p> <p>Pharmacogenetic guidance: Preliminary findings indicate that vardenafil exposure is 3 times higher in individuals with CYP3A5*3/*3 genotype compared to those with CYP3A5*1/*1 genotype. The clinical impact of this change is unknown.</p> <p>Polypharmacy guidance: The dosage of vardenafil may require adjustment in patients receiving strong CYP3A4 inhibitors such as ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, atazanavir, or clarithromycin, as well as in patients receiving moderate CYP3A4 inhibitors such as erythromycin. For ritonavir, a single dose of 2.5 mg vardenafil should not be exceeded in a 72-hour period. For indinavir, saquinavir, atazanavir, or ketoconazole: 400 mg daily. For itraconazole: 400 mg daily. For clarithromycin: a single dose of 2.5 mg vardenafil should not be exceeded in a 24-hour period. For ketoconazole: 200 mg daily. For itraconazole: 200 mg daily. For erythromycin: a single dose of 5 mg vardenafil should not be exceeded in a 24-hour period. Inducers of CYP3A4 may decrease the concentrations of vardenafil.</p>	<p>ACTIONABLE</p>
<p>✓ Venlafaxine <i>Effexor®</i></p>	<p>Normal Exposure to Venlafaxine (CYP2D6: Normal Metabolizer)</p> <p>Consider prescribing venlafaxine at standard label-recommended dosage and administration. Careful titration is recommended until a favorable response is achieved.</p> <p>If therapeutic drug monitoring is utilized, the sum of venlafaxine and O-desmethylvenlafaxine (an active metabolite) plasma concentrations should be used for efficacy. While the sum of the parent and the active metabolite are informative for efficacy, a higher parent (venlafaxine) concentration may be associated with higher side effects, including QT prolongation.</p>	<p>ACTIONABLE</p>
<p>✓ Velaglugerase alfa <i>Vpriv®</i></p>	<p>Normal Response to Velaglugerase alfa</p> <p>Pharmacogenetic guidance: Velaglugerase alfa is a hydrolytic lysosomal glucocerebrosidase-specific enzyme produced in human fibroblasts. Velaglugerase alfa dosage should be individualized to each patient. Individual patient dosage may require increase or decrease based on therapeutic goals. Velaglugerase alfa is not metabolized by the CYP450 enzymes. No genetically-guided drug selection or dosing recommendations are available.</p>	<p>ACTIONABLE</p>
<p>✓ Vortioxetine <i>Trintellix®</i></p>	<p>Normal Sensitivity to Vortioxetine (CYP2D6: Normal Metabolizer)</p> <p>Vortioxetine can be prescribed at standard label-recommended dosage and administration. The recommended starting dose is 10 mg/day, which can then be increased to 20 mg/day, as tolerated.</p>	<p>ACTIONABLE</p>
<p>Vorapaxar</p>	<p>Normal Response to Vorapaxar</p>	<p>ACTIONABLE</p>

NAME: BRL SAMPLE
SAMPLE ID:
DOB: 1/20/1930
SEX: Male

<p>✓ Zontivity®</p>	<p>Pharmacogenetic guidance: vorapaxar is metabolized primarily by CYP3A4, with contribution from CYP2J2. Genetic polymorphisms of these genes are not expected to affect the efficacy or safety profiles of this drug. Vorapaxar is contraindicated in people who have had a stroke, transient ischemic attack (TIA), or intracranial hemorrhage, (ICH) because of the increased bleeding risk. Polypharmacy guidance: Avoid concomitant use of vorapaxar with strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, lopinavir/ritonavir, ritonavir, indinavir, and conivaptan). Significant increases in vorapaxar exposure may increase bleeding risk. Avoid concomitant use with drugs that are strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, rifampin, and St. John's wort).</p>
<p>✓ Valsartan Diovan®, Entresto®</p>	<p>Normal Sensitivity to Valsartan ACTIONABLE</p> <p>Pharmacogenetic guidance: Valsartan is excreted largely as unchanged compound. CYP2C9 is responsible for the formation of a minor metabolite, valeryl 4-hydroxy valsartan, which accounts for about 9% of a dose. Given the limited contribution of CYP2C9 in the overall disposition of valsartan, genetic variability of the CYP2C9 gene is not expected to affect the patient's response to valsartan. No genotype-based dosing adjustments are available.</p>
<p>✓ Nortriptyline Pamelor®</p>	<p>Normal Nortriptyline Exposure (CYP2D6: Normal Metabolizer) ACTIONABLE</p> <p>The patient is predicted to be a normal CYP2D6 metabolizer which is likely to result in normal metabolism of nortriptyline to less active compounds.</p> <p>Psychiatric Conditions: Nortriptyline therapy can be prescribed according to standard recommended dosage and administration.</p>
<p>✓ Mexiletine Mexitil®</p>	<p>Normal Sensitivity to Mexiletine (CYP2D6: Normal Metabolizer) ACTIONABLE</p> <p>Mexiletine can be prescribed at standard label-recommended dosage. A careful titration with ECG recording and monitoring of mexiletine plasma concentrations are recommended until a favorable clinical response is achieved.</p>
<p>✓ Metoclopramide Reglan®</p>	<p>Normal Response to Metoclopramide (CYP2D6: Normal Metabolizer) ACTIONABLE</p> <p>Metoclopramide can be prescribed at standard label-recommended dosage and administration.</p>
<p>✓ Glyburide Micronase®</p>	<p>Normal Exposure to Glyburide ACTIONABLE</p> <p>Pharmacogenetic guidance: Glyburide is partially metabolized by CYP2C9 and to a lesser extent by CYP3A4. While these clearance pathways are diminished in subjects with reduced enzyme activity, these changes have not been shown to be clinically significant. No genetically guided drug selection or dosing recommendations are recommended.</p> <p>Polypharmacy guidance: Co-administration of glyburide with strong CYP2C9 and/or CYP3A4 inhibitors may result in higher glyburide concentrations, leading to possible hypoglycemia. Co-administration with strong CYP2C9 and/or CYP3A4 inducers may result in lower glyburide concentrations and a lack of efficacy.</p>
<p>✓ Flecainide Tambacor®</p>	<p>Normal Exposure to Flecainide (CYP2D6: Normal Metabolizer) ACTIONABLE</p> <p>The patient's genotype is associated with a normal flecainide exposure following standard dosing. Consider prescribing flecainide at standard label-recommended dosage and administration. No action is needed besides the standard precautions.</p>
<p>✓ Deutetrabenazine Austedo®</p>	<p>Normal Sensitivity to Deutetrabenazine (CYP2D6: Normal Metabolizer) ACTIONABLE</p> <p>For treating chorea associated with Huntington's disease: Individualization of dose with careful weekly titration is required. The first week's starting dose is 6 mg once daily then slowly titrate at weekly intervals by 6 mg per day to a tolerated dose up to a maximum recommended daily dosage of 48 mg (24 mg twice daily).</p>
<p>✓ Desipramine Norpramin®</p>	<p>Normal Desipramine Exposure (CYP2D6: Normal Metabolizer) ACTIONABLE</p>

NAME: BRL SAMPLE
SAMPLE ID:
DOB: 1/20/1930
SEX: Male

The patient is predicted to be a normal CYP2D6 metabolizer which is likely to result in normal metabolism of desipramine to less active compounds.

Psychiatric Conditions: Desipramine therapy can be prescribed according to standard recommended dosage and administration.

 **Celecoxib**
Celebrex®

Normal Celecoxib Exposure (CYP2C9: Normal Metabolizer) ACTIONABLE
 Celecoxib therapy can be initiated at standard label-recommended dosage and administration.

Consider initiating treatment at the lowest end of the dosing range in geriatric patients. A dosage adjustment may be warranted when celecoxib is administered with CYP2C9 inhibitors or inducers.

Osteoarthritis, Rheumatoid Arthritis, Ankylosing Spondylitis, Acute Pain, Primary Dysmenorrhea: Consider using the lowest effective dosage for the shortest duration consistent with the patient treatment goals.

Acute Migraine: Consider using for the fewest number of days per month, as needed.

Osteoarthritis and Hypertension (co-formulation with amlodipine): Consider using the lowest effective dosage for the shortest duration consistent with the patient treatment goals.

 **Cariprazine**
Vraylar®

Normal Response to Cariprazine ACTIONABLE

Pharmacogenetic guidance: Cariprazine is extensively metabolized by CYP3A4 and, to a lesser extent, by CYP2D6. Genetic variants of CYP2D6 do not have clinically relevant effect on pharmacokinetics of cariprazine and its metabolites. No genetically guided dosing recommendations are available. **Polypharmacy guidance:** CYP3A4 inhibitors or inducers may affect cariprazine plasma concentrations. Cariprazine dose may have to be reduced to half if cariprazine and a strong CYP3A4 inhibitor are used concomitantly. Concomitant use of Cariprazine and a CYP3A4 inducer has not been evaluated and is not recommended.

 **Amphotericin B**
AmBisome®, Abelcet®


Normal Response to Amphotericin B ACTIONABLE

Pharmacogenetic guidance: Amphotericin B is excreted very slowly (over weeks to months) by the kidneys with 2 to 5% of a given dose being excreted in the biologically active form. Details of possible metabolic pathways are unknown. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Nephrotoxic medications such as aminoglycosides, cyclosporine, and pentamidine may enhance the potential for amphotericin B-induced renal toxicity, and should be used concomitantly only with great caution. Intensive monitoring of renal function is recommended in patients requiring any combination of nephrotoxic medications.

 **Apixaban**
Eliquis®

Normal Response to Apixaban INFORMATIVE

Pharmacogenetic guidance: Apixaban is not extensively metabolized and only ~20% of the dose is metabolized primarily by CYP3A4 and CYP3A5, with minor contributions from CYP1A2 and CYP2J2. This drug is a substrate for the efflux transport proteins P-gp (ABCB1) and BCRP (ABCG2). While these enzymes and transporters are polymorphic, genetic variations are unlikely to have a clinically significant impact on apixaban exposure, and no genotype-based dosing adjustments are recommended. **Polypharmacy guidance:** Exposure to apixaban increases by 100% when co-administered with ketoconazole, a strong CYP3A/P-gp inhibitor. This translates into an increased bleeding risk (70% increase). Hence, for patients receiving 5 mg twice daily, apixaban dose should be decreased to 2.5 mg twice daily when it is coadministered with drugs that are strong dual inhibitors of CYP3A4 and P-gp (e.g., ketoconazole, itraconazole, ritonavir, and clarithromycin). In patients already taking 2.5 mg twice daily, coadministration of apixaban with strong dual inhibitors of CYP3A4 and P-gp should be avoided. No dose adjustment is recommended when co-administered with moderate inhibitors. Co-administration with rifampin, a strong CYP3A/P-gp inducer, results in halving of exposure to apixaban. There is no clinical experience at these reduced exposures. Hence, concomitant administration of strong CYP3A/P-gp inducers should be avoided.

 **Allopurinol**
Zyloprim®, Lopurin®, Alopurin®

Normal Response to Allopurinol (ABCG2: Normal Function) INFORMATIVE

The patient carries two copies of rs2231142 C allele. Unless other genetic risk factors are present, this genotype result indicates a normal response to allopurinol. Follow label-recommended standard dosage and administration. This genotype result cannot be used to identify patients at risk for severe cutaneous adverse reactions.

NAME: BRL SAMPLE
SAMPLE ID:
DOB: 1/20/1930
SEX: Male

<p>✓ Amoxapine Amoxapine®</p>	<p>Normal Amoxapine Exposure (CYP2D6: Normal Metabolizer)</p>	<p>INFORMATIVE</p>
<p>Amoxapine can be prescribed at standard label recommended-dosage and administration.</p>		
<p>✓ Azilsartan Edarbi®, Edarbyclor®</p>	<p>Normal Azilsartan Exposure (CYP2C9: Normal Metabolizer)</p>	<p>INFORMATIVE</p>
<p>Azilsartan medoxomil is hydrolyzed to azilsartan, its active metabolite, in the gastrointestinal tract during absorption. Azilsartan is further metabolized to inactive metabolites by CYP2C9. Consider standard label-recommended dosage and administration.</p>		
<p>✓ Benzhydrocodone Apadaz®</p>	<p>Normal Response to Benzhydrocodone (CYP2D6: Normal Metabolizer)</p>	<p>INFORMATIVE</p>
<p>Benzhydrocodone is a prodrug of hydrocodone and is converted to active hydrocodone by intestinal enzymes. Benzhydrocodone can be prescribed at standard label-recommended dosage and administration.</p>		
<p>✓ Cannabidiol Epidiolex®</p>	<p>Normal Response to Cannabidiol</p>	<p>INFORMATIVE</p>
<p>Pharmacogenetic guidance: Cannabidiol is metabolized to oxidative metabolites by CYP3A4 and CYP2C19 and by direct glucuronidation. There are insufficient studies documenting the impact of genetic polymorphisms of these metabolizing enzymes on cannabidiol response. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Enzyme-inducing drugs increase cannabidiol clearance significantly, and careful titration is recommended when the drug is prescribed with enzyme-inducing-antiepileptic drugs. Coadministration of CYP3A4 inhibitors increase cannabidiol exposure by 2-fold, and a dose reduction should be considered in presence of CYP3A inhibitors.</p>		
<p>✓ Chlorpromazine Thorazine®</p>	<p>Normal Sensitivity to Chlorpromazine (CYP2D6: Normal Metabolizer)</p>	<p>INFORMATIVE</p>
<p>Chlorpromazine is metabolized by CYP2D6, CYP3A4 and flavin-containing monooxygenases. This drug can be prescribed at standard label recommended-dosage and administration. Careful titration is recommended until a favorable response is achieved.</p>		
<p>✓ Clonazepam Klonopin®</p>	<p>Normal Response to Clonazepam</p>	<p>INFORMATIVE</p>
<p>Pharmacogenetic guidance: No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: clonazepam is extensively metabolized by CYP3A4 to an amino metabolite that is further acetylated by N-acetyltransferases. This drug should be used with caution when prescribed with CYP3A4 inhibitors or inducers.</p>		
<p>✓ Dihydrocodeine Synalgos-DC®</p>	<p>Normal Response to Dihydrocodeine (CYP2D6: Normal Metabolizer)</p>	<p>INFORMATIVE</p>
<p>Dihydrocodeine can be prescribed at standard label-recommended dosage and administration.</p>		
<p>✓ Disopyramide Norpace®</p>	<p>Normal Exposure to Disopyramide</p>	<p>INFORMATIVE</p>
<p>Pharmacogenetic guidance: Disopyramide is metabolized mainly by CYP3A4 and to a lesser extent by CYP2D6. About 50% of the dose is excreted in urine as unchanged disopyramide and 30% as metabolites. Genetic polymorphisms of CYP2D6 have not been found to affect patient response to disopyramide. No genetically guided drug selection or dosing adjustments are recommended. Polypharmacy guidance: Co-administration of disopyramide with inhibitors of CYP3A4 may cause an increase in disopyramide plasma concentrations, which could result in a fatal interaction. Co-administration with CYP3A4 inducers may cause a decrease in disopyramide plasma concentrations. Caution should be used when co-administering drugs that can affect renal function.</p>		
<p>✓ Disulfiram Antabuse®</p>	<p>Normal Sensitivity to Disulfiram (DBH: Normal Dopamine Beta-Hydroxylase Activity)</p>	<p>INFORMATIVE</p>

NAME: BRL SAMPLE
SAMPLE ID:
DOB: 1/20/1930
SEX: Male

Dopamine β -hydroxylase (DBH) is the final enzyme in norepinephrine biosynthesis, catalyzing the oxidative hydroxylation of dopamine to norepinephrine. The patient does not carry 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 not associated with increased side effects following disulfiram therapy. Replication of these results in a larger cohort is still needed to validate these findings.

<p>✓ Donepezil Aricept®</p>	<p>Normal Response to Donepezil (CYP2D6: Normal Metabolizer)</p> <p>Donepezil can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended until a favorable response is achieved.</p>	<p>INFORMATIVE</p>
<p>✓ Esomeprazole Nexium®</p>	<p>Slightly Decreased Exposure to Esomeprazole (CYP2C19: Rapid Metabolizer)</p> <p>The patient's genotype may be associated with a slightly decreased esomeprazole exposure following standard dosing. Consider prescribing esomeprazole at standard label-recommended dosage and administration.</p>	<p>INFORMATIVE</p>
<p>✓ Ethosuximide Zarontin®</p>	<p>Normal Response to Ethosuximide</p> <p>Pharmacogenetic guidance: No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: ethosuximide is extensively metabolized by CYP3A4, and therefore this drug should be used with caution when prescribed with CYP3A4 inhibitors. Inducers of CYP3A4 increase ethosuximide clearance, and higher doses may be needed when the drug is coadministered with enzyme-inducing drugs.</p>	<p>INFORMATIVE</p>
<p>✓ Febuxostat Uloric®</p>	<p>Normal Response to Febuxostat</p> <p>Pharmacogenetic guidance: Febuxostat is eliminated by both hepatic metabolism and renal excretion. The drug is metabolized both by glucuronidation (40%) and oxidative pathways (35%). The oxidative metabolism involves several cytochrome P450 enzymes (CYPs): CYP1A2, CYP2C8 and CYP2C9 as well as other non-CYP enzymes. Febuxostat is also glucuronidated primarily by UGT1A1 and UGT1A3. Preliminary studies indicate that febuxostat clearance is increased in subjects with UGT1A1*28 allele-UGT1A3*2a allele and decreased in those with the UGT1A1*6 allele. The clinical relevance of these changes is not known. Although serious skin and hypersensitivity reactions have been reported in patients taking febuxostat, there are no genetic biomarkers for predicting such reactions; no genotype-based recommendations are available. Polypharmacy guidance: Concomitant administration of febuxostat, a xanthine oxidase inhibitor, with substrate drugs such as theophylline, azathioprine or mercaptopurine could increase plasma concentrations of these drugs resulting in severe toxicity.</p>	<p>INFORMATIVE</p>
<p>✓ Felbamate Felbatol®</p>	<p>Normal Response to Felbamate</p> <p>Pharmacogenetic guidance: No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: About 40-50% of absorbed felbamate dose appears unchanged in urine, and an additional 50% is present as metabolites and conjugates. Felbamate is a substrate of CYP3A4 and CYP2E1, but these pathways are minor for drug elimination when the drug is given as a monotherapy. This pathway is enhanced by concomitant use of enzyme-inducing antiepileptic drugs, which results in a 30-50% decrease in felbamate plasma concentrations. Felbamate should be titrated slowly, and dose adjustment must be considered in presence of inducers.</p>	<p>INFORMATIVE</p>
<p>✓ Fluoxetine Prozac®, Sarafem®</p>	<p>Normal Sensitivity to Fluoxetine (CYP2D6: Normal Metabolizer)</p> <p>Fluoxetine is metabolized to its active metabolite norfluoxetine and to other metabolites by multiple enzymes including CYP2D6, CYP2C19, CYP2C9, and CYP3A4. Fluoxetine can be prescribed at standard label-recommended dosage and administration.</p>	<p>INFORMATIVE</p>
<p>✓ Fondaparinux Arixtra®</p>	<p>Normal Response to Fondaparinux</p> <p>Pharmacogenetic guidance: Fondaparinux is eliminated unchanged through renal excretion and is not metabolized by CYPs, and therefore genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: The concomitant use of fondaparinux with aspirin or NSAIDs may enhance the risk of hemorrhage. Discontinue agents that may enhance the risk of hemorrhage prior to initiation of therapy with fondaparinux unless essential. If co-administration is necessary, monitor patients closely for hemorrhage.</p>	<p>INFORMATIVE</p>

NAME: BRL SAMPLE
SAMPLE ID:
DOB: 1/20/1930
SEX: Male

✓ **Gabapentin** INFORMATIVE
Neurontin®
Normal Response to Gabapentin
Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available.
Polypharmacy guidance: Gabapentin is eliminated primarily through renal excretion and is not metabolized by CYPs. Genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Gabapentin can be prescribed at standard label-recommended dosage and administration.

✓ **Glipizide** INFORMATIVE
Glucotrol®
Normal Exposure to Glipizide
Pharmacogenetic guidance: Glipizide is metabolized by CYP2C9. While this clearance pathway is diminished in subjects with reduced CYP2C9 activity, such a change has not been shown to be clinically significant. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Co-administration of glipizide with a strong CYP2C9 inhibitor may result in higher glipizide concentrations possibly leading to hypoglycemia. Co-administration with a strong CYP2C9 inducer may result in lower glipizide concentrations and a lack of efficacy.

✓ **Indomethacin** INFORMATIVE
Indocin®
Normal Indomethacin Exposure
Pharmacogenetic guidance: Indomethacin is metabolized mainly by O-demethylation to its inactive metabolite O-desmethyl indomethacin, a reaction catalyzed by CYP2C9. Genetic polymorphisms of CYP2C9 have not been found to affect the response to indomethacin. No genetically guided drug selection or dosing recommendations are available.

✓ **Ketoprofen** INFORMATIVE
Orudis®
Normal Response to Ketoprofen
Pharmacogenetic guidance: Ketoprofen is primarily eliminated by glucuronidation (by UGT1A3, UGT1A9 and UGT2B7) and no major implication of CYP2C9 in the metabolism of this drug has been demonstrated. No genetically guided drug selection or dosing recommendations are available.

✓ **Ketorolac** INFORMATIVE
Toradol®
Normal Response to Ketorolac
Pharmacogenetic guidance: Ketorolac is metabolized by glucuronidation (UGT enzymes) and oxidation but the enzymes catalyzing the oxidation are not well characterized. No genetically guided drug selection or dosing recommendations are available.

✓ **Lamotrigine** INFORMATIVE
Lamictal®
Normal Response to Lamotrigine
Pharmacogenetic guidance: Genotype results obtained from the pharmacogenetic test performed in this patient cannot be used to identify patients at risk for severe cutaneous adverse reactions such as anticonvulsant hypersensitivity syndrome, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Lamotrigine is metabolized by glucuronidation, which is mediated primarily by UGT1A4 with some contribution from UGT1A1 and UGT2B7. There are insufficient studies documenting the impact of genetic polymorphisms of these metabolizing enzymes on lamotrigine response. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Enzyme-inducing drugs increase lamotrigine clearance significantly, and higher doses of this drug are required to maintain therapeutic concentrations. Co-administration of valproic acid, an inhibitor of UGT enzymes, increases lamotrigine levels and may result in serious lamotrigine adverse effects (neurological and cutaneous). A low starting dose with a slow titration schedule is recommended when lamotrigine is added to existing valproic acid treatment.

✓ **Leflunomide** INFORMATIVE
Arava®
Normal Exposure to Leflunomide (CYP2C19: Rapid Metabolizer)
Leflunomide can be prescribed according to standard label-recommended dosage and administration.
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.

✓ **Levomilnacipran** INFORMATIVE
Fetzima®
Normal Response to Levomilnacipran

NAME: BRL SAMPLE
SAMPLE ID:
DOB: 1/20/1930
SEX: Male

Pharmacogenetic guidance: Levomilnacipran is moderately metabolized by desethylation, which is catalyzed primarily by CYP3A4, with minor contributions by CYP2C8, CYP2C19, CYP2D6, and CYP2J2. More than 58% of the dose is excreted in urine as unchanged levomilnacipran, and 18% as N-desethyl levomilnacipran. Genetic polymorphisms of CYPs are not expected to have a significant impact on levomilnacipran exposure. no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** the daily levomilnacipran dose should not exceed 80 mg when coadministered with strong CYP3A4 inhibitors, such as ketoconazole, itraconazole, and ritonavir.

✓ **Maprotiline** Normal Maprotiline Exposure (CYP2D6: Normal Metabolizer) **INFORMATIVE**
Ludiomil®

Maprotiline can be prescribed at standard label recommended-dosage and administration.

✓ **Memantine** Normal Response to Memantine **INFORMATIVE**
Namenda®

Pharmacogenetic Guidance: Memantine is excreted predominantly unchanged in the urine. This drug undergoes partial hepatic metabolism to three inactive metabolites (N-glucuronide, 6--hydroxy metabolite, and 1-nitroso-deaminated metabolite). CYP450 enzymes do not play a significant role in the metabolism of memantine. There are no studies documenting the effects of genetic variability in metabolizing enzymes or organic cationic transporters on memantine response. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy Guidance:** Memantine is predominantly renally eliminated, and drugs that are substrates and/or inhibitors of the CYP450 system are not expected to interact with memantine. Because memantine is eliminated in part by tubular secretion, coadministration of drugs that use the same renal cationic system, including hydrochlorothiazide, triamterene, metformin, cimetidine, ranitidine, quinidine, and nicotine, could potentially result in altered plasma levels of both agents.

✓ **Metaxalone** Normal Response to Metaxalone **INFORMATIVE**
Skelaxin®

Pharmacogenetic guidance: Metaxalone is extensively metabolized by multiple CYP enzymes, including CYP1A2, CYP2D6, CYP2E1, and CYP3A4. Genetic polymorphisms of these enzymes are unlikely to affect its exposure to a significant extent. no genetically guided drug selection or dosing recommendations are available.

✓ **Naproxen** Normal Sensitivity to Naproxen **INFORMATIVE**
Aleve®

Pharmacogenetic guidance: UGT2B7 is responsible for hepatic naproxen acyl glucuronidation, which is the primary elimination pathway for this drug (60% of total clearance). CYP2C9 and CYP1A2 are responsible for the formation of O-desmethylnaproxen but this pathway is not the primary pathway for the elimination for naproxen. Genetic polymorphism of CYP2C9 has not been found to affect the response to naproxen. No genetically guided drug selection or dosing recommendations are available.

✓ **Nateglinide** Normal Nateglinide Exposure (CYP2C9: Normal Metabolizer) **INFORMATIVE**
Starlix®

The patient's genotype predicts a normal exposure to nateglinide, and this drug can be prescribed at label-recommended dosage and administration.

✓ **Nefazodone** Normal Sensitivity to Nefazodone (CYP2D6: Normal Metabolizer) **INFORMATIVE**
Serzone®

Nefazodone is metabolized by CYP3A4 to its active metabolite m-chlorophenylpiperazine and other metabolites. The m-chlorophenylpiperazine metabolite which may contribute to adverse events, is further metabolized by CYP2D6. Nefazodone can be prescribed standard label recommended-dosage and administration.

✓ **Oxcarbazepine** Normal Response to Oxcarbazepine **INFORMATIVE**
Trileptal®, Oxtellar XR®

Pharmacogenetic guidance: Genotype results obtained from the pharmacogenetic test performed in this patient cannot be used to identify patients at risk for severe cutaneous adverse reactions such as anticonvulsant hypersensitivity syndrome, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Oxcarbazepine (prodrug) is converted by a reductase to its active monohydroxylated active metabolite: 10-hydroxycarbazepine (MHD). This active metabolite is eliminated by direct renal excretion, glucuronidation, and hydroxylation (minimal). No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** In the presence of enzyme-inducing drugs, the plasma levels of the active metabolite (MHD) are decreased by 30%.

NAME: BRL SAMPLE
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<p>✓ Oxymorphone <i>Opana®</i>, <i>Numorphan®</i></p>	<p>Normal Response to Oxymorphone INFORMATIVE</p> <p>No genetically guided drug selection or dosing recommendations are available. Oxymorphone is not metabolized by CYPs, and genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Oxymorphone can be prescribed at standard label-recommended dosage and administration.</p>
<p>✓ Pregabalin <i>Lyrica®</i></p>	<p>Normal Response to Pregabalin INFORMATIVE</p> <p>Pharmacogenetic guidance: No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Pregabalin is eliminated primarily through renal excretion and is not metabolized by CYPs. Genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Pregabalin can be prescribed at standard label-recommended dosage and administration.</p>
<p>✓ Primidone <i>Mysoline®</i></p>	<p>Normal Sensitivity to Primidone (CYP2C19: Rapid Metabolizer) INFORMATIVE</p> <p>CYP2C19 is partly involved in the metabolism of phenobarbital, the active metabolite of primidone, and this drug can be prescribed at standard label-recommended dosage and administration.</p>
<p>✓ Protriptyline <i>Vivactil®</i></p>	<p>Normal Protriptyline Exposure (CYP2D6: Normal Metabolizer) INFORMATIVE</p> <p>Protriptyline can be prescribed at standard label recommended-dosage and administration.</p>
<p>✓ Quinidine <i>Quinidine®</i></p>	<p>Normal Exposure to Quinidine INFORMATIVE</p> <p>Pharmacogenetic guidance: In vitro studies using human liver microsomes have shown CYP3A as the primary metabolizing enzyme for quinidine. No genetically guided drug selection or dosing adjustments are recommended. Polypharmacy guidance: Co-administration of drugs/herbs that are known to induce or inhibit CYP3A can change plasma concentrations of quinidine. This may result in adverse events or sub- or supra-therapeutic drug concentration modulating the risk of QT prolongation.</p>
<p>✓ Repaglinide <i>Prandin®</i>, <i>Prandimet®</i></p>	<p>Normal Sensitivity to Repaglinide (SLCO1B1: Decreased Function) INFORMATIVE</p> <p>The patient carries one copy of the SLCO1B1 521T>C variant. This genotype is associated with intermediate transporter function. Repaglinide can be prescribed at label-recommended standard dosage and administration.</p>
<p>✓ Sildenafil <i>Viagra®</i></p>	<p>Normal Response to Sildenafil INFORMATIVE</p> <p>Pharmacogenetic guidance: Preliminary findings indicate that sildenafil exposure is 1.5 times higher in individuals with CYP3A5*3/*3 genotype compared to those with CYP3A5*1/*1 genotype. The clinical significance of this change is unknown. Polypharmacy guidance: Sildenafil is metabolized by CYP3A4 (major route) and CYP2C9 (minor route). In patients taking strong CYP3A inhibitors, sildenafil exposure is significantly increased, and it is recommended not to exceed a maximum single dose of 25 mg in a 48-hour period. Inducers of CYP3A may decrease the concentration of the drug.</p>
<p>✓ Solifenacin <i>Vesicare®</i></p>	<p>Normal Response to Solifenacin INFORMATIVE</p> <p>Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Co-administration of a CYP3A4 strong inhibitor increases solifenacin serum concentrations significantly. Therefore, it is recommended not to exceed a 5 mg daily dose of solifenacin when coadministered with strong CYP3A4 inhibitors, as the risk for QTc prolongation induced by this drug is increased at higher concentrations. Although the effects of moderate CYP3A4 inhibitors were not examined, use caution when this drug is administered with moderate CYP3A4 inhibitors.</p>
<p>✓ Sotalol <i>Betapace®</i>, <i>Sorine®</i>, <i>Sotylize®</i></p>	<p>Normal Exposure to Sotalol INFORMATIVE</p>

NAME: BRL SAMPLE
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DOB: 1/20/1930
SEX: Male

Pharmacogenetic guidance: Excretion of sotalol is predominantly via the kidney in the unchanged form, and therefore lower doses are necessary in conditions of renal impairment. No genetically guided drug selection or dosing adjustments are recommended. **Polypharmacy guidance:** Co-administration of sotalol with drugs that can prolong the QT interval can increase the patient's risk for developing drug induced long QT syndrome.

✓ **Sulindac** INFORMATIVE
Clinoril®
Normal Response to Sulindac
Pharmacogenetic guidance: Sulindac is primarily eliminated by glucuronidation which is catalyzed by several isoforms including UGT1A3, UGT1A9 and UGT2B7. The role of CYP2C9 in sulindac metabolism is of minor relevance. No genetically guided drug selection or dosing recommendations are available.

✓ **Tapentadol** INFORMATIVE
Nucynta®
Normal Response to Tapentadol
 No genetically guided drug selection or dosing recommendations are available. Tapentadol is not metabolized by CYPs, and genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Tapentadol can be prescribed at standard label-recommended dosage and administration.

✓ **Thiothixene** INFORMATIVE
Navane®
Normal Response to Thiothixene
Pharmacogenetic guidance: Thiothixene is metabolized by UGTs and by cytochrome P450 enzymes (CYP1A2 and CYP3A4). No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** It is likely that strong enzyme inducers may lead to substantial decreases in thiothixene plasma concentrations with the potential for reduced effectiveness. Consider increasing the dose of thiothixene when concomitantly used with strong CYP3A4 inducers (e.g., carbamazepine).

✓ **Ticagrelor** INFORMATIVE
Brilinta®
Normal Response to Ticagrelor
Pharmacogenetic guidance: Ticagrelor is extensively metabolized by CYP3A4 and CYP3A5 to both active and inactive metabolites, and this drug does not require bioactivation to achieve its antiplatelet effect. The drug is also a substrate of P-glycoprotein, encoded by the ABCB1 gene. Studies have shown that the efficacy and safety profile of ticagrelor do not depend on CYP2C19 or CYP3A5 metabolizer statuses. Moreover, preliminary studies indicate that relevant genetic variants within the ABCB1, SLCO1B1, CYP3A4 and UGT2B7 genes do not affect ticagrelor exposure, efficacy or safety profiles. No genetically-guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** In presence of strong CYP3A4 inhibitors, significantly increased exposure to ticagrelor is expected which may lead to adverse reactions such as dyspnea or bleeding. These drugs should be avoided with ticagrelor. Strong CYP3A4 inducers can significantly decrease ticagrelor exposure (resulting in a loss of efficacy) and these drugs should also be avoided. Ticagrelor is a weak inhibitor of CYP3A4 and P-glycoprotein and some substrates of these proteins should be closely monitored and their dosing adjusted when coadministered with this medication.

✓ **Timolol** INFORMATIVE
Blocadren®
Normal Sensitivity to Timolol (CYP2D6: Normal Metabolizer)
 Timolol can be prescribed at standard label-recommended dosage and administration.

✓ **Tolterodine** INFORMATIVE
Detrol®
Normal Sensitivity to Tolterodine (CYP2D6: Normal Metabolizer)
 Tolterodine can be prescribed at standard label-recommended dosage and administration.

✓ **Topiramate** INFORMATIVE
Topamax®
Normal Response to Topiramate
Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** About 50% of absorbed topiramate dose appears unchanged in urine, and an additional 50% is present as metabolites and conjugates. Topiramate metabolism by cytochrome P450 enzymes is minor for its elimination when the drug is given as a monotherapy. However, this pathway is enhanced by concomitant use of enzyme-inducing antiepileptic drugs, and may result in reduced topiramate plasma concentrations. Thus, this drug should be titrated slowly, and dose adjustment must be considered in presence of inducers. Concomitant administration of valproic acid and topiramate has been associated with hyperammonemia with and without encephalopathy.

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✓ **Trazodone**
Oleptro®

Normal Response to Trazodone INFORMATIVE

Pharmacogenetic guidance: Trazodone is metabolized to its active metabolite m-chlorophenylpiperazine by CYP3A4. This metabolite which may contribute to adverse events, is further metabolized by CYP2D6. The impact of genetic polymorphisms of this enzyme on the clinical response to trazodone is not well documented. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** It is likely that CYP3A4 inhibitors may lead to substantial increases in trazodone plasma concentrations with the potential for adverse effects. If trazodone is used with a potent CYP3A4 inhibitor, the risk of cardiac arrhythmia may be increased. Therefore coadministration of trazodone with drugs that inhibit CYP3A4 should be approached with caution.

✓ **Trospium**
Sanctura®

Normal Response to Trospium INFORMATIVE

Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** CYP enzymes do not contribute significantly to the elimination of trospium. No major drug-drug interactions are expected with CYP inhibitors or inducers.

✓ **Vigabatrin**
Sabril®

Normal Response to Vigabatrin INFORMATIVE

Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Vigabatrin is eliminated primarily through renal excretion and is not metabolized by CYPs. Therefore, genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Vigabatrin can be prescribed at standard label-recommended dosage and administration.

✓ **Ziprasidone**
Geodon®

Normal Response to Ziprasidone INFORMATIVE

Pharmacogenetic guidance: Ziprasidone is primarily cleared following extensive metabolism. CYP3A4 is the major CYP contributing to the oxidative metabolism of ziprasidone with minor involvement from CYP1A2. Less than one-third of ziprasidone metabolic clearance is mediated by cytochrome P450 catalyzed oxidation and approximately two-thirds via reduction involving glutathione as well as aldehyde oxidase. No genetically guided drug selection or dosing recommendations are available. Individualization of ziprasidone dose with careful weekly titration is required. Dosage adjustments should generally occur at intervals of no less than 2 days, as steady-state plasma concentrations are achieved within 1 to 3 days. In order to ensure use of the lowest effective dose, patients should ordinarily be observed for improvement for several weeks before upward dosage adjustment. When deciding among the alternative treatments available, the prescriber should consider the finding of **ziprasidone's greater capacity to prolong the QT/QTc interval** compared to several other antipsychotic drugs. **Polypharmacy guidance:** Although coadministration of strong CYP3A4 inhibitors are expected to result in modest increases in ziprasidone plasma concentrations, a closer monitoring of the patient's response and a dose reduction may be considered. Ziprasidone dose may need to be increased when used in combination with a chronic treatment of a potent CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, St. John's wort etc.).

✓ **Zonisamide**
Zonegran®

Normal Sensitivity to Zonisamide (CYP2C19: Rapid Metabolizer) INFORMATIVE

CYP2C19 is partly involved in the metabolism of zonisamide, and this drug can be prescribed at standard label-recommended dosage and administration.

✓ **Vilazodone**
Viibryd®

Normal Response to Vilazodone INFORMATIVE

Pharmacogenetic guidance: Vilazodone is predominantly metabolized by CYP3A4. CYP2C19, CYP2D6, and CYP2E1 play a minor role in the biotransformation of this drug. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** It is likely that CYP3A4 inhibitors may lead to substantial increases in vilazodone plasma concentrations with the potential for adverse effects. Vilazodone should be reduced to 20 mg if co-administered with a strong inhibitor of CYP3A4 (e.g., ketoconazole). During coadministration with moderate inhibitors of CYP3A4 (e.g., erythromycin), the dose should be reduced to 20 mg for patients with intolerable adverse events. The dose can be readjusted to the original level when the CYP3A4 inhibitor is discontinued. Consider increasing the dose of vilazodone up to 2-fold when concomitantly used with strong CYP3A4 inducers (e.g., carbamazepine). The maximum daily dose should not exceed 80 mg. If CYP3A4 inducers are discontinued, reduce vilazodone dose to the original level.

✓ **Verapamil**

Favorable Response to Verapamil (CACNA1C: Homozygous for rs1051375 A allele) INFORMATIVE

NAME: BRL SAMPLE
SAMPLE ID:
DOB: 1/20/1930
SEX: Male

Covera-HS®, Verelan®, Isoptin®

CACNA1C encodes for an alpha-1 subunit of a voltage-dependent calcium channel. The patient carries two copies of CACNA1C rs1051375 A allele. In hypertensive patients with stable coronary artery disease, the A/A genotype may be associated with a reduced risk of adverse outcomes (occurrence of death, nonfatal myocardial infarction, or nonfatal stroke) following treatment with verapamil compared with atenolol.

✓ **Valproic Acid**
 Depakene®

Normal Response to Valproic acid

INFORMATIVE

Pharmacogenetic guidance: Genotype results obtained from the pharmacogenetic test performed in this patient cannot be used to identify patients carrying mutations in mitochondrial DNA polymerase γ (POLG). Valproic acid is contraindicated in patients known to have mitochondrial disorders caused by mutations in mitochondrial DNA polymerase γ (POLG; e.g., Alpers-Huttenlocher Syndrome) and children under two years of age who are suspected of having a POLG-related disorder.

Valproic acid is extensively metabolized in the liver, which occurs primarily by glucuronidation with probable contributions of UGT1A6, UGT1A9, and UGT2B7. This drug is also metabolized by a minor CYP-dependent oxidation pathway, which includes multiple enzymes such as CYP2A6, CYP2C9, and CYP2C19. There are insufficient studies documenting the impact of genetic polymorphisms of these metabolizing enzymes on valproic acid response, and no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** enzyme-inducing drugs increase valproic acid clearance 2-fold, and higher doses of this drug are required to maintain therapeutic concentrations when added to a therapy regimen containing enzyme-inducing antiepileptic drugs.

✓ **Trifluoperazine**
 Stelazine®

Normal Response to Trifluoperazine

INFORMATIVE

Pharmacogenetic guidance: Thrifluoperazine extensively metabolized by oxidation, sulfoxidation, hydroxylation and direct glucuronidation catalyzed by UGT1A4. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** It is likely that strong enzyme inducers may lead to substantial decreases in trifluoperazine plasma concentrations with the potential for reduced effectiveness.

✓ **Torsemide**
 Demdex®

Normal Torsemide Exposure (CYP2C9: Normal Metabolizer)

INFORMATIVE

The patient's genotype predicts a normal exposure to torsemide and this drug can be prescribed at label-recommended dosage and administration.

✓ **Tofacitinib**
 Xeljanz®

Normal Exposure to Tofacitinib

INFORMATIVE

Pharmacogenetic guidance: Tofacitinib is metabolized primarily by CYP3A4 with some contribution from CYP2C19. Genetic variations in the CYP2C19 gene do not significantly influence tofacitinib exposure. Tofacitinib may be prescribed at standard dosing, but consider a dose reduction if a CYP2C19 poor metabolizer is also prescribed a CYP3A4 inhibitor such as ketoconazole, erythromycin, diltiazem, troleandomycin, nefazodone, fluconazole, verapamil or HIV protease inhibitors. **Polypharmacy guidance:** Tofacitinib dose should be reduced if a patient is taking strong CYP3A4 inhibitors (e.g., ketoconazole), or if a patient is taking a moderate CYP3A4 inhibitor (e.g., alprazolam) with a strong CYP2C19 inhibitor (e.g., fluconazole).

✓ **Tiagabine**
 Gabitril®

Normal Response to Tiagabine

INFORMATIVE

Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Tiagabine is extensively metabolized by CYP3A4, and therefore this drug should be used with caution when prescribed with CYP3A4 inhibitors. Inducers of CYP3A4 increase tiagabine clearance by 2-fold, and the initial dosage of the drug should be considered carefully when added to a stable therapy regimen containing enzyme-inducing antiepileptic drugs.

✓ **Terazosin**
 Hytrin®

Normal Response to Terazosin

INFORMATIVE

Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** The enzymes involved in metabolizing terazosin have not been characterized.

✓ **Tadalafil**
 Cialis®

Normal Response to Tadalafil

INFORMATIVE

NAME: BRL SAMPLE
SAMPLE ID:
DOB: 1/20/1930
SEX: Male

Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available.
Polypharmacy guidance: Tadalafil is extensively metabolized by CYP3A4. **Tadalafil for Use as Needed** — For patients taking concomitant potent inhibitors of CYP3A4, such as ketoconazole or ritonavir, the maximum recommended dose of vardenafil is 10 mg, not to exceed once every 72 hours. **Tadalafil for Once Daily Use** — For patients taking concomitant strong inhibitors of CYP3A4, the maximum recommended dose is 2.5 mg. Although specific interactions have not been studied, other CYP3A4 moderate inhibitors would likely increase tadalafil exposure. The exposure of tadalafil is reduced when coadministered with rifampin or other CYP3A4 inducers. This can be anticipated to decrease the efficacy of tadalafil for once-daily use, though the magnitude of decreased efficacy is unknown.

✓ **Sufentanil** INFORMATIVE
Sufenta®
Normal Response to Sufentanil
Pharmacogenetic guidance: No genetically guided drug selection or dosing recommendations are available.
Polypharmacy guidance: Sufentanil is primarily metabolized by CYP3A4 and so should be used with caution when prescribed with CYP3A4 inhibitors or inducers.

✓ **Silodosin** INFORMATIVE
Rapaflo®
Normal Response to Silodosin
Pharmacogenetic guidance: silodosin is extensively metabolized by CYP3A4 into pharmacologically inactive metabolites. no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** silodosin is contraindicated with potent CYP3A4 inhibitors, as the risk for serious adverse events is increased at higher concentrations. Use caution when this drug is prescribed with CYP3A4 moderate inhibitors, as drug levels may increase.

✓ **Rufinamide** INFORMATIVE
Banzel®
Normal Response to Rufinamide
Pharmacogenetic guidance: No genetically guided drug selection or dosing recommendations are available.
Polypharmacy guidance: Rufinamide is extensively metabolized by carboxylesterases. Cytochrome P450 enzymes are not involved in its metabolism. Therefore, genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Coadministration of enzyme-inducing antiepileptic drugs produce modest decreases in rufinamide plasma levels, while coadministration of valproate increases the drug levels and requires dose adjustment. Patients stabilized on rufinamide should begin valproate therapy at a low dose, and titrate to a clinically effective dose. Similarly, patients on valproate should begin rufinamide at a lower dose.

✓ **Rivaroxaban** INFORMATIVE
Xarelto®
Normal Response to Rivaroxaban
Pharmacogenetic guidance: Rivaroxaban is metabolized by CYP3A4, CYP3A5, and CYP2J2. It is also a substrate for P-gp (ABCB1) and BCRP (ABCG2) transporters. Genetic polymorphisms of these genes are not expected to affect the efficacy or safety profiles of rivaroxaban. **Polypharmacy guidance:** Avoid concomitant use of rivaroxaban with combined P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, lopinavir/ritonavir, ritonavir, indinavir, and conivaptan). Avoid concomitant use of rivaroxaban with drugs that are combined P-gp and strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, rifampin, and St. John's wort). Patients with renal impairment coadministered rivaroxaban with drugs classified as combined P-gp and moderate CYP3A4 inhibitors (e.g., diltiazem, verapamil, dronedarone, and erythromycin) have increased exposure compared with patients with normal renal function and no inhibitor use. Significant increases in rivaroxaban exposure may increase bleeding risk.

✓ **Rabeprazole** INFORMATIVE
Aciphex®
Slightly Decreased Exposure to Rabeprazole (CYP2C19: Rapid Metabolizer)
The patient's genotype may be associated with a slightly decreased rabeprazole exposure following standard dosing. Consider prescribing rabeprazole at standard label-recommended dosage and administration.

✓ **Quetiapine** INFORMATIVE
Seroquel®
Normal Response to Quetiapine

NAME: BRL SAMPLE
SAMPLE ID:
DOB: 1/20/1930
SEX: Male

Pharmacogenetic guidance: Quetiapine is predominantly metabolized to several metabolites by CYP3A4. CYP3A5 and CYP2D6 are also responsible for quetiapine metabolism but their role in the overall metabolism of this drug is minor compared to CYP3A4. N-desalkylquetiapine, a pharmacologically active metabolite (responsible of the antidepressant effect) is further metabolized by CYP2D6 and CYP3A4. Preliminary studies have shown that genetic polymorphisms of CYP3A4, CYP2D6 and CYP3A5 enzymes may be responsible in variable exposures to quetiapine and to its active metabolite N-desalkylquetiapine. However, the clinical significance of these changes is not established yet and no genetically guided drug selection or dosing recommendations are available. Quetiapine dose should be titrated based on the clinical response and tolerability of the individual patient. **Polypharmacy guidance:** Quetiapine dose should be reduced to **one sixth of original dose** when co-medicated with a potent CYP3A4 inhibitor (e.g., ketoconazole, itraconazole, indinavir, ritonavir, nefazodone). When the CYP3A4 inhibitor is discontinued, the dose should be increased by 6 fold. Quetiapine dose should be increased up to 5 fold of the original dose when used in combination with a chronic treatment (e.g. > 7-14 days) of a potent CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, St. John's wort etc.). When the CYP3A4 inducer is discontinued, the dose should be reduced to the original level within 7-14 days.

<p>✓ Proguanil Malarone®</p>	<p>Normal Exposure to Proguanil</p> <p>Pharmacogenetic guidance: Proguanil is a pro-drug that is primarily metabolized by CYP2C19 to its active metabolite, cycloguanil. Preliminary studies indicate that individuals with reduced CYP2C19 function, have reduced cycloguanil exposure compared to subjects with normal CYP2C19 function, but there is considerable overlap of cycloguanil and proguanil metabolic ratios across CYP2C19 metabolizer status. The clinical relevance of this change is not well understood and there is insufficient data to calculate dose adjustments. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Co-administration of proguanil with a strong CYP2C19 inhibitor may result in lower cycloguanil (higher proguanil) exposure.</p>	<p>INFORMATIVE</p>
<p>✓ Phenobarbital Luminal®</p>	<p>Normal Sensitivity to Phenobarbital (CYP2C19: Rapid Metabolizer)</p> <p>CYP2C19 is partly involved in the metabolism of phenobarbital, and this drug can be prescribed at standard label-recommended dosage and administration.</p>	<p>INFORMATIVE</p>
<p>✓ Pimavanserin Nuplazid®</p>	<p>Normal Response to Pimavanserin</p> <p>Pharmacogenetic guidance: Pimavanserin is predominantly metabolized by CYP3A4 and CYP3A5 and to a lesser extent by CYP2J2, CYP2D6, and other CYP and FMO enzymes. CYP3A4 is the major enzyme responsible for the formation of its major active metabolite (AC-279). There are no available genetically-guided drug selection or dosing recommendations. Polypharmacy guidance: Pimavanserin prolongs the QT interval and its use should be avoided in patients with known QT prolongation or in combination with other drugs known to prolong QT interval including Class 1A antiarrhythmics (e.g., quinidine, procainamide) or Class 3 antiarrhythmics (e.g., amiodarone, sotalol), certain antipsychotic medications (e.g., ziprasidone, chlorpromazine, thioridazine), and certain antibiotics (e.g., gatifloxacin, moxifloxacin). Concomitant use of pimavanserin with CYP3A4 inhibitor increases pimavanserin exposure and a dose reduction of 50% is needed when this drug is coadministered with strong CYP3A inhibitors. Coadministration of pimavanserin with strong CYP3A inducers may result in reduced efficacy and a dose increase may be needed.</p>	<p>INFORMATIVE</p>
<p>✓ Perampanel Fycompa®</p>	<p>Normal Response to Perampanel</p> <p>Pharmacogenetic guidance: Perampanel is eliminated either unchanged or following oxidative metabolism by CYP3A4 and CYP3A5. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Enzyme-inducing drugs decrease perampanel plasma concentrations by 50-60%, and the initial dosage of the drug should be increased when it is added to a stable therapy regimen containing enzyme-inducing antiepileptic drugs. Coadministration with strong enzyme-inducers others than antiepileptic drugs (e.g., rifampin) should be avoided. Coadministration with perampanel with strong CYP3A4 inhibitors such as ketoconazole increases perampanel exposure by 20%.</p>	<p>INFORMATIVE</p>
<p>✓ Palonosetron Aloxi®</p>	<p>Normal response to Palonosetron (CYP2D6: Normal Metabolizer)</p> <p>Palonosetron can be prescribed at standard label-recommended dosage and administration.</p>	<p>INFORMATIVE</p>
<p>✓ Oxybutynin</p>	<p>Normal Response to Oxybutynin</p>	<p>INFORMATIVE</p>

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Ditropan®

Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available.
Polypharmacy guidance: Oxybutynin is extensively metabolized in humans by CYP3A4, and coadministration of a CYP3A4 strong inhibitor (itraconazole) increases oxybutynin serum concentrations. Therefore, use caution when prescribing this drug to patients taking CYP3A4 enzyme inhibitors.

✓ **Oliceridine** INFORMATIVE
Olinvyk
Normal Exposure to Oliceridine (CYP2D6: Normal Metabolizer)
 Oliceridine can be prescribed at standard label-recommended dosage and administration.

✓ **Netupitant / Palonosetron** INFORMATIVE
Akynzeo-oral®
Normal Response to Netupitant-Palonosetron (CYP2D6: Normal Metabolizer)
Netupitant: Netupitant is extensively metabolized to three major metabolites (desmethyl, N-oxide and a hydroxy-methyl derivatives). Metabolism is mediated primarily by CYP3A4 and to a lesser extent by CYP2C9 and CYP2D6. No genetically guided drug selection or dosing recommendations are available for this drug. Netupitant can be prescribed at standard label-recommended dosage and administration.
Palonosetron: Palonosetron can be prescribed at standard label-recommended dosage and administration.

✓ **Nateglinide** INFORMATIVE
Starlix®
Normal Sensitivity to Nateglinide (SLCO1B1: Decreased Function)
 The patient carries one copy of the SLCO1B1 521T>C variant, which is associated with intermediate transporter function. Nateglinide can be prescribed at label-recommended standard dosage and administration.

✓ **Nabumetone** INFORMATIVE
Relafen®
Normal Response to Nabumetone
Pharmacogenetic guidance: Nabumetone is a prodrug, which is converted by CYP1A2 to an active metabolite (6-MNA) that is further metabolized by CYP2C9 to an inactive metabolite. Theoretically, individuals with reduced CYP2C9 activity (i.e CYP2C9 poor metabolizers) may have higher levels of the active metabolite, but it is unknown whether this results in altered drug response. No genetically guided drug selection or dosing recommendations are available.
Polypharmacy Guidance: CYP1A2 inhibitors may inhibit the activation of nabumetone to its active metabolite resulting in a reduction in the therapeutic effects of this drug. On the other hand, CYP1A2 inducers (i.e smoking) may result in higher levels of nabumetone active metabolite, which may affect the response to this drug.

✓ **Milnacipran** INFORMATIVE
Savella®
Normal Response to Milnacipran
Pharmacogenetic guidance: milnacipran is minimally metabolized by UGT enzymes and primarily excreted unchanged in urine. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** coadministration of drugs that inhibit or induce CYP or UGT enzymes are unlikely to affect the exposure of milnacipran.

✓ **Methocarbamol** INFORMATIVE
Robaxin®
Normal Response to Methocarbamol
Pharmacogenetic guidance: Methocarbamol is metabolized via dealkylation and hydroxylation. The enzymes responsible for the metabolism of this drug have not been characterized. No genetically guided drug selection or dosing recommendations are available.

✓ **Methotrexate** INFORMATIVE
Trexall®
Normal Risk for Methotrexate Toxicity (MTHFR: Normal MTHFR Activity)
 The patient does not carry the MTHFR c.665C>T variant, and unless other risk factors are present, the patient is not expected to have an increased risk for methotrexate toxicity. Consider using label-recommended dosage and administration.

✓ **Meperidine** INFORMATIVE
Demerol®
Normal Response to Meperidine

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Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. Meperidine is metabolized to normeperidine by multiple CYPs, including CYP2B6, CYP3A4, and CYP2C19. The effects of genetic variants in these enzymes have not been studied. **Polypharmacy guidance:** In patients taking **strong CYP inducers**, meperidine metabolism is increased resulting in higher levels of its neurotoxic metabolite normeperidine. In presence of ritonavir, meperidine's exposure is significantly reduced while normeperidine concentrations are increased. Based on these findings, the risk of narcotic-related adverse effects from this combination appears to be minimal. However, increased concentrations of normeperidine suggest a potential for toxicity with increased dosages or long-term therapy. This combination should be avoided is possible.

<p>✓ Loxapine <i>Loxitane®</i>, <i>Adasuve®</i></p>	<p>Normal Response to Loxapine</p> <p>Pharmacogenetic guidance: Loxapine is metabolized extensively in the liver following oral administration, with multiple metabolites formed. Loxapine metabolism occurs via hydroxylation and oxidation catalyzed by CYP1A2 along with contributions from CYP3A4, CYP2D6 and FMO. There are no studies documenting the effect of genetic polymorphisms of these metabolizing enzymes on Loxapine disposition and there are no available genetically-guided drug selection or dosing recommendations. Polypharmacy guidance: Loxapine is a central nervous system (CNS) depressant. The concurrent use of Loxapine with other CNS depressants (<i>e.g.</i>, alcohol, opioid analgesics, benzodiazepines, tricyclic antidepressants, general anesthetics, phenothiazines, sedative/hypnotics, muscle relaxants, and/or illicit CNS depressants) can increase the risk of respiratory depression, hypotension, profound sedation, and syncope. Therefore, consider dose reduction/modification of CNS depressants if used concomitantly with Loxapine. Loxapine has anticholinergic activity and concomitant use with other anticholinergic drugs can increase the risk of adverse reactions, including exacerbation of glaucoma and urinary retention.</p>	<p>INFORMATIVE</p>
<p>✓ Losartan <i>Cozaar®</i>, <i>Hyzaar®</i></p>	<p>Normal Response to Losartan (CYP2C9: Normal Metabolizer)</p> <p>Losartan is metabolized to its active metabolite by CYP2C9 and CYP3A4. The patient's genotype predicts a normal exposure to losartan and its active metabolite. Losartan can be prescribed at label-recommended dosage and administration.</p>	<p>INFORMATIVE</p>
<p>✓ Levorphanol <i>Levo Dromoran®</i></p>	<p>Normal Response to Levorphanol</p> <p>Pharmacogenetic guidance: Levorphanol is metabolized by glucuronidation which is mediated by UGT2B7. There are no studies documenting the impact of genetic polymorphisms of this metabolizing enzyme on levorphanol response. And no genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Enzyme inducing drugs are expected to increase levorphanol clearance significantly.</p>	<p>INFORMATIVE</p>
<p>✓ Levetiracetam <i>Keppra®</i></p>	<p>Normal Response to Levetiracetam</p> <p>Pharmacogenetic guidance: No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Levetiracetam is minimally metabolized by non-CYP enzymes (esterases) and is primarily excreted unchanged in urine. Coadministration of enzyme-inducing antiepileptic drugs produce modest decreases in levetiracetam plasma levels.</p>	<p>INFORMATIVE</p>
<p>✓ Labetalol <i>Normodyne®</i>, <i>Trandate®</i></p>	<p>Normal Response to Labetalol</p> <p>Pharmacogenetic guidance: Labetalol is extensively metabolized by UGT2B7, UGT1A1, and CYP2C19 to inactive metabolites. Preliminary studies indicate that following a single 200-mg oral dose, labetalol plasma concentrations are 2.9-fold higher in Chinese individuals with the CYP2C19 *2/*2 genotype than those with the CYP2C19 *1/*1 genotype. The clinical impact of this change is unknown. Polypharmacy guidance: Cimetidine increases the bioavailability of labetalol, and clinical monitoring is advised when both drugs are coadministered.</p>	<p>INFORMATIVE</p>
<p>✓ Irbesartan <i>Avapro®</i></p>	<p>Normal Irbesartan Exposure (CYP2C9: Normal Metabolizer)</p> <p>Irbesartan can be prescribed at standard label-recommended dosage and administration.</p>	<p>INFORMATIVE</p>
<p>✓ Hydrocodone <i>Vicodin®</i></p>	<p>Good Response to Hydrocodone (OPRM1: Normal OPRM1 Function)</p>	<p>INFORMATIVE</p>

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The patient does not carry the OPRM1 118A>G variant. Acute postoperative and cancer pain: the patient is expected to experience good analgesia with standard or increased hydrocodone doses, without an increase in side effects.

✓ **Hydromorphone** INFORMATIVE
Dilaudid®, *Exalgo®*
Normal Response to Hydromorphone
 No genetically guided drug selection or dosing recommendations are available. Hydromorphone is not metabolized by CYPs, and genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Hydromorphone can be prescribed at standard label-recommended dosage and administration.

✓ **Guanfacine** INFORMATIVE
Intuniv®
Normal Response to Guanfacine
Pharmacogenetic guidance: Guanfacine is predominantly metabolized by CYP3A4. No genetically guided drug selection or dosing recommendations are available and guanfacine extended-release should be titrated based on the clinical response and tolerability of the individual patient. **Polypharmacy guidance:** The dose of guanfacine extended-release should be reduced to **one half of the standard dose** when co-medicated with a strong CYP3A4 inhibitor (e.g., ketoconazole, itraconazole, indinavir, ritonavir, nefazodone). When the strong CYP3A4 inhibitor is discontinued, the dose should be increased to the standard recommended dose. Guanfacine dose should be increased up to double the recommended dose when used in combination with a strong CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, St. John's wort etc.). When the CYP3A4 inducer is discontinued, the dose should be reduced to the standard recommended dose within 7-14 days.

✓ **Galantamine** INFORMATIVE
Razadyne®
Normal Sensitivity to Galantamine (CYP2D6: Normal Metabolizer)
 Galantamine can be prescribed at standard label-recommended dosage and administration. Individualization of dose with weekly titration is recommended.

✓ **Fosnetupitant / Palonosetron** INFORMATIVE
Akynzeo-IV®
Normal Response to Fosnetupitant-Palonosetron (CYP2D6: Normal Metabolizer)
Fosnetupitant: Fosnetupitant is converted to netupitant via metabolic hydrolysis. Netupitant is extensively metabolized to three major metabolites (desmethyl, N-oxide and a hydroxy-methyl derivatives). Metabolism is mediated primarily by CYP3A4 and to a lesser extent by CYP2C9 and CYP2D6. No genetically guided drug selection or dosing recommendations are available for this drug. Fosnetupitant can be prescribed at standard label-recommended dosage and administration.
Palonosetron: Palonosetron can be prescribed at standard label-recommended dosage and administration.

✓ **Fluphenazine** INFORMATIVE
Prolixin®
Normal Exposure to Fluphenazine
Pharmacogenetic guidance: Fluphenazine is metabolized by CYP2D6, CYP2C19, CYP3A4 and other enzymes. Genetic polymorphisms of CYP2D6 have not been found to affect patient response to fluphenazine. No genetically guided drug selection or dosing adjustments are recommended. **Polypharmacy guidance:** Co-administration of fluphenazine with inhibitors of CYP3A4 may cause an increase in fluphenazine plasma concentrations while the co-administration with CYP3A4 inducers may cause a decrease in fluphenazine plasma concentrations. The co-administration of fluphenazine with a potent inhibitor of CYP2D6 (e.g. fluoxetine) did not increase fluphenazine exposure to a clinically relevant extent.

✓ **Finasteride** INFORMATIVE
Proscar®
Normal Response to Finasteride
Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available.
Polypharmacy guidance: Finasteride is extensively metabolized in humans by CYP3A4. The effects of potent or moderate CYP3A4 inhibitors on finasteride have not been studied. Because of the potential for drug-drug interactions, use caution when prescribing this drug to patients taking CYP3A4 enzyme inhibitors.

✓ **Fentanyl** INFORMATIVE
Actiq®
Good Response to Fentanyl (OPRM1: Normal OPRM1 Function)
 The patient does not carry the OPRM1 118A>G variant. Acute postoperative and cancer pain: the patient is expected to experience good analgesia at standard fentanyl doses. Because fentanyl has a narrow therapeutic window, it is advised to carefully titrate this drug to a tolerable dose that provides adequate analgesia with minimal side effects.

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 Ezogabine <i>Potiga</i> ®	<p>Normal Response to Ezogabine</p> <p>Pharmacogenetic guidance: although NAT2 rapid acetylators have a 30% increase in the exposure of ezogabine active metabolite, no dose adjustment is necessary in these individuals. Polypharmacy guidance: Ezogabine is extensively metabolized primarily via glucuronidation (by UGT1A4 and UGT1A1) and acetylation (by NAT2). There is no evidence of oxidative metabolism of ezogabine by cytochrome P450 enzymes, and genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Enzyme-inducing drugs such as carbamazepine and phenytoin increase ezogabine clearance by 30%, and dose increase should be considered when this drug is coadministered with enzyme-inducing antiepileptic drugs.</p>	INFORMATIVE
 Eslicarbazepine <i>Aptiom</i> ®	<p>Normal Response to Eslicarbazepine</p> <p>Pharmacogenetic guidance: Genotype results obtained from the pharmacogenetic test performed in this patient cannot be used to identify patients at risk for severe cutaneous adverse reactions such as anticonvulsant hypersensitivity syndrome, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Eslicarbazepine acetate (prodrug) is converted by a reductase to its active metabolite, eslicarbazepine. Eslicarbazepine is eliminated primarily by renal excretion unchanged and as a glucuronide conjugate. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: In the presence of enzyme-inducing drugs, eslicarbazepine plasma levels are significantly decreased, and higher doses of the drug may be needed.</p>	INFORMATIVE
 Edoxaban <i>Savaysa</i> ®	<p>Normal Response to Edoxaban</p> <p>Pharmacogenetic guidance: Edoxaban is eliminated primarily as unchanged drug in urine. There is minimal metabolism via hydrolysis (mediated by carboxylesterase 1; CES1), conjugation, and oxidation by CYP3A4. Edoxaban is a substrate of the efflux transporter P-gp and its active metabolite (formed by CES1) is a substrate of the uptake transporter SLCO1B1. Studies indicate that the two common variants SLCO1B1 rs4149056 and ABCB1 rs1045642 do not affect the exposure to edoxaban or its active metabolite. There are no genotype-based dosing recommendations. Polypharmacy guidance: Avoid the concomitant use of edoxaban with rifampin. No dose reduction is recommended for concomitant P-gp inhibitor use.</p>	INFORMATIVE
 Dutasteride <i>Avodart</i> ®	<p>Normal Response to Dutasteride</p> <p>Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Dutasteride is extensively metabolized in humans by CYP3A4 and CYP3A5. The effect of potent CYP3A4 inhibitors on dutasteride has not been studied. Because of the potential for drug-drug interactions, use caution when prescribing this drug to patients taking potent, chronic CYP3A4 enzyme inhibitors.</p>	INFORMATIVE
 Doxazosin <i>Cardura</i> ®	<p>Normal Response to Doxazosin</p> <p>Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: doxazosin is metabolized by multiple enzymes. There is limited data on the effects of drugs known to influence the metabolism of doxazosin.</p>	INFORMATIVE
 Dolasetron <i>Anzemet</i> ®	<p>Normal Response to Dolasetron (CYP2D6: Normal Metabolizer)</p> <p>Dolasetron can be prescribed at standard label-recommended dosage and administration.</p>	INFORMATIVE
 Diclofenac <i>Voltaren</i> ®	<p>Normal Diclofenac Exposure</p> <p>Pharmacogenetic guidance: Diclofenac is extensively metabolized by hydroxylation and direct glucuronidation. About 50% of diclofenac is eliminated as a 4-hydroxymetabolite, a reaction mediated by CYP2C9. Other CYP enzymes including CYP2C8, CYP2C19 and CYP3A4 are also involved in the formation of a 5-hydroxymetabolite. A substantial portion of the drug is also directly glucuronidated by UGT2B7 and UGT2B4. Genetic polymorphisms of CYP2C9 have not been found to affect the response to diclofenac. No dosing recommendations or genetically guided drug selection are recommended. Polypharmacy guidance: Co-administration of diclofenac with CYP2C9 inhibitors may enhance the drug exposure and toxicity of whereas co-administration with CYP2C9 inducers may lead to compromised efficacy of diclofenac. A dosage adjustment may be warranted when diclofenac is administered with CYP2C9 inhibitors or inducers.</p>	INFORMATIVE

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✓ **Cyclobenzaprine** Normal Response to Cyclobenzaprine INFORMATIVE
Flexeril®, *Amrix®*
Pharmacogenetic guidance: No genetically guided drug selection or dosing recommendations are available. Cyclobenzaprine is excreted primarily as a glucuronide via the kidneys, and as an N-demethylated metabolite by CYP3A4, CYP1A2, and to a lesser extent CYP2D6. Due to the minor involvement of CYP2D6 in the metabolism of cyclobenzaprine, the polymorphism of this enzyme is not of concern in its the clinical use.

✓ **Dabigatran Etexilate** Normal Response to Dabigatran INFORMATIVE
Pradaxa®
Pharmacogenetic guidance: Dabigatran is eliminated primarily unchanged by the kidneys. After oral administration, dabigatran etexilate is converted to its active form dabigatran by esterases. A small portion (20%) of dabigatran dose is also conjugated to form pharmacologically active acyl glucuronides. Dabigatran is not a substrate, inhibitor, or inducer of CYP450 enzymes. Dabigatran etexilate is a substrate of the efflux transporter P-gp (ABCB1). Common genetic polymorphism of the ABCB1 gene (2677G>T/A and 3435 C>T) do not appear to affect dabigatran exposure.
Polypharmacy guidance: *1-Reduction in Risk of Stroke and Systemic Embolism in Non-valvular AF:* In patients with moderate renal impairment (CrCl 30-50 mL/min), concomitant use of the P-gp inhibitor dronedarone or systemic ketoconazole can be expected to produce dabigatran exposure similar to that observed in severe renal impairment. Consider reducing the dose of dabigatran to 75 mg twice daily. Dose adjustment is not necessary when coadministered with other P-gp inhibitors. In patients with CrCl<30 mL/min, avoid use of concomitant P-gp inhibitors with dabigatran. *2-Treatment of DVT and PE Reduction in the Risk of Recurrence of DVT and PE:* Avoid use of concomitant P-gp inhibitors with dabigatran in patients with CrCl <50 mL/min.

✓ **Colchicine** Normal Response to Colchicine INFORMATIVE
Mitigare®
Pharmacogenetic guidance: Colchicine is eliminated both by renal excretion and metabolism. While 50% of the absorbed dose is eliminated unchanged in urine, less than 20% is metabolized by CYP3A4. Glucuronidation is also a metabolic pathway for colchicine. Colchicine is a substrate of P-glycoprotein (encoded by ABCB1 gene) and its efflux by this transporter is important in its disposition. Colchicine has a narrow therapeutic index. Preliminary and limited studies indicate a lack of an effect of CYP3A4 or ABCB1 genetic polymorphisms on clinical response to colchicine in individuals with familial Mediterranean fever (FMF). There are no available genetically-guided drug selection or dosing recommendations. **Polypharmacy guidance:** Because colchicine is a substrate for both the CYP3A4 metabolizing enzyme and the P-glycoprotein efflux transporter, inhibition of either of these pathways may lead to colchicine-related toxicity. Inhibition of both CYP3A4 and P-gp by dual inhibitors such as clarithromycin has been reported to produce life-threatening or fatal colchicine toxicity due to significant increases in systemic colchicine levels. Therefore, concomitant use of colchicine and inhibitors of CYP3A4 or P-glycoprotein should be avoided.

✓ **Clonidine** Normal Exposure to Clonidine INFORMATIVE
Kapvay®
Pharmacogenetic guidance: Clonidine is metabolized by CYP2D6 along with CYP3A4 and CYP1A2. About 40-60% of the dose is excreted in urine as unchanged drug. Preliminary studies indicate that individuals lacking CYP2D6 activity, have increased clonidine exposure compared to subjects with normal CYP2D6 activity. The clinical relevance of this changed is not well understood and there is insufficient data to calculate dose adjustments. Other preliminary studies indicate that individuals with high CYP2D6 activity (pregnant women), have decreased clonidine exposure and may require higher doses to reach target therapeutic plasma concentrations and respond to therapy. No genetically guided drug selection or dosing adjustments are recommended. **Polypharmacy guidance:** Co-administration of clonidine with inhibitors of CYP2D6 or CYP3A4 may cause an increase in clonidine plasma concentrations while the co-administration with CYP3A4 inducers may cause a decrease in clonidine plasma concentrations. Caution should be used when co-administering drugs that can affect renal function.

✓ **Chlorpropamide** Normal Exposure to Chlorpropamide INFORMATIVE
Diabinese®
Pharmacogenetic guidance: Chlorpropamide is metabolized mainly by CYP2C9 and to a lesser extent by CYP2C19. While this clearance pathway is diminished in subjects with reduced CYP2C9 activity, such a change has not been shown to be clinically significant. No genetically guided drug selection or dosing recommendations are available.
Polypharmacy guidance: Co-administration of chlorpropamide with a strong CYP2C9 and/or CYP2C19 inhibitors may result in higher chlorpropamide concentrations possibly leading to hypoglycemia. Co-administration with a strong CYP2C9 and/or CYP2C19 inducers may result in lower chlorpropamide concentrations and a lack of efficacy.

✓ **Carvedilol** Normal Exposure to Carvedilol (CYP2D6: Normal Metabolizer) INFORMATIVE

NAME: BRL SAMPLE
SAMPLE ID:
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SEX: Male

Coreg®

Carvedilol can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended with monitoring until a favorable response is achieved.



Carbamazepine

Tegretol®, Carbatrol®, Epitol®

Normal Response to Carbamazepine

INFORMATIVE

Pharmacogenetic guidance: Genotype results obtained from the pharmacogenetic test performed in this patient cannot be used to identify patients at risk for severe cutaneous adverse reactions such as anticonvulsant hypersensitivity syndrome, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Carbamazepine, a drug with a narrow therapeutic window, is extensively metabolized by CYP3A4/5 to its active epoxide metabolite, which is further metabolized by epoxide hydrolase (EPHX1) to an inactive metabolite. Preliminary studies indicate that carbamazepine plasma concentrations are 30% higher in individuals with the CYP3A5*3/*3 genotype compared to those with CYP3A5*1/*1 or *1/*3 genotypes. The clinical impact of this change is poorly documented. **Polypharmacy guidance:** The dosage of carbamazepine should be decreased in patients receiving CYP3A4 inhibitors. Enzyme-inducing drugs significantly decrease carbamazepine levels, and dose adjustments are recommended when the drug is used with other inducers.



Buprenorphine

Butrans®, Buprenex®

Normal Response to Buprenorphine

INFORMATIVE

Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. Buprenorphine is primarily metabolized by CYP3A4 to norbuprenorphine and by UGT enzymes (mainly UGT1A1 and 2B7). The effects of genetic variants in these enzymes on its response have not been studied. **Polypharmacy guidance:** The concomitant use of buprenorphine with all CYP3A4 inhibitors may result in an increase in the drug levels, which could increase or prolong adverse drug effects. Monitor patients receiving buprenorphine with a CYP3A4 inhibitor. CYP and UGT inducers may decrease buprenorphine levels.



Bisoprolol

Zebeta®

Normal Response to Bisoprolol

INFORMATIVE

Pharmacogenetic guidance: Bisoprolol is eliminated by renal and non-renal pathways with 50% of the total dose being metabolized in the liver and 50% being excreted via the kidneys unchanged. Bisoprolol is predominantly metabolized by CYP3A4 with smaller contribution from CYP2D6. Limited studies suggest that bisoprolol plasma concentrations and its beta-adrenergic inhibition are not affected by CYP2D6 genetic variability. No genetically-guided drug selection or dosing recommendations are available.



Avanafil

Stendra®

Normal Response to Avanafil

INFORMATIVE

Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Avanafil is extensively metabolized by CYP3A4, therefore **Avanafil should not be used with strong CYP3A4 inhibitors** such as ketoconazole, itraconazole, voriconazole, ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, and telithromycin. If taking a moderate CYP3A4 inhibitor, such as erythromycin, amprenavir, aprepitant, diltiazem, fluconazole, fosamprenavir, or verapamil, the dose should be no more than 50 mg in a 24-hour period. Inducers of CYP3A4 may decrease the concentrations of avanafil.



Asenapine

Saphris®

Normal Response to Asenapine

INFORMATIVE

Pharmacogenetic Guidance: Asenapine is extensively metabolized to more than 38 inactive metabolites. The primary metabolism route occurs via direct glucuronidation catalyzed by UGT1A4. Also important but less pronounced is the demethylation pathway as well as the oxidative reactions catalyzed by CYP1A2 with contributions from CYP3A4 and CYP2D6. There are no studies documenting the effect of genetic polymorphisms of these metabolizing enzymes on asenapine disposition and there are no available genetically guided drug selection or dosing recommendations. Asenapine should be prescribed based on the clinical response and tolerability of the individual patient. **Polypharmacy guidance:** Coadministration of asenapine with CYP1A2 inhibitors such as fluvoxamine should be approached with caution as asenapine plasma concentrations will increase resulting in more side effects. Cigarette smoking, which induces CYP1A2 activity, has a limited effect on asenapine plasma concentrations. Asenapine is a weak inhibitor of CYP2D6 and its coadministration with paroxetine (both a substrate and an inhibitor of CYP2D6) should be approached with caution. Long-term therapy with strong enzyme inducers (e.g. carbamazepine, phenytoin, rifampin) may decrease asenapine exposure and dosage adjustment may be needed.



Amiodarone

Normal Exposure to Amiodarone

INFORMATIVE

PATIENT INFORMATION

NAME: BRL SAMPLE
SAMPLE ID:
DOB: 1/20/1930
SEX: Male

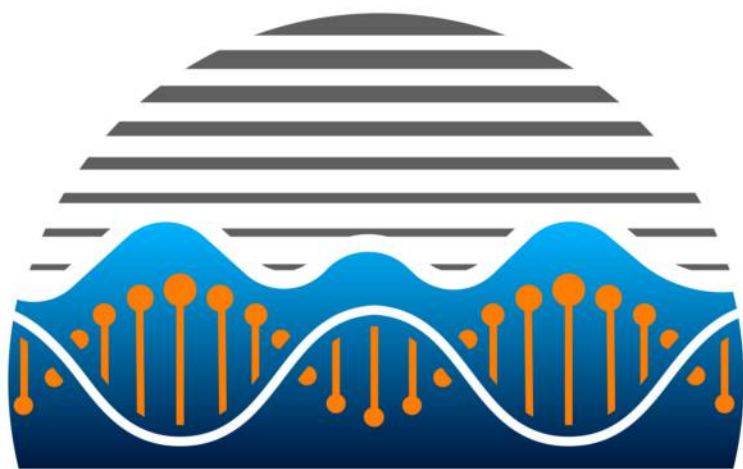
Patient Information Card

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: BRL SAMPLE		
DOB: 1/20/1930		
ACC #:		
Pharmacogenetic Test Summary		
CYP2C19	*1/*17	Rapid Metabolizer
CYP2C9	*1/*1	Normal Metabolizer
CYP2D6	*1/*2	Normal Metabolizer
CYP3A4	*1/*1	Normal Metabolizer
CYP3A5	*1/*3	Intermediate Metabolizer

MTHFR	c.665C>T GG	Normal MTHFR Activity
MTHFR	c.1286A>C TT c.665C>T GG	No Increased Risk of Hyperhomocysteinemia
VKORC1	-1639G>A G/A	Intermediate Warfarin Sensitivity



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STRATUS DIAGNOSTICS