PrimaHealth

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	JILLIAN DOE	**COLLECTION DATE:**	7/19/2016	DOCTOR JONES
ACC #:	1607190464	**RECEIVED DATE:**	7/19/2016	
DOB:	1/1/1753	**REPORT DATE:**	8/11/2016	1^ABC CLINICAL LAB
SEX:	Female			

Comprehensive PGX and DDI Profile

Current Patient Medications

Naltrexone, Lexapro, Cymbalta, Clomipramine, Warfarin

Clomipramine
Anafranil

Increased Sensitivity to Clomipramine (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

Consider an alternative drug, or consider prescribing clomipramine at standard dose and monitor the plasma concentrations of clomipramine and desmethyl-clomipramine to guide dose adjustments.

Lexapro
Escitalopram

Insufficient Reponse to Escitalopram (CYP2C19: Ultra-Rapid Metabolizer) — ACTIONABLE

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.

Naltrexone
Vivitrol, Contrave

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

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

Warfarin
Coumadin

Normal Sensitivity to Warfarin (CYP2C9 *1/*1 VKORC1 -1639G>A G/A) — ACTIONABLE

Initiation Therapy: consider using the following standard warfarin dose range as provided in the FDA-approved label: **5-7 mg/day**. OR consider using a personalized dose calculated by a pharmacogenetic algorithm. The estimated time to reach steady state is 4-5 days.

Cymbalta
Duloxetine

Normal Sensitivity to Duloxetine (CYP2D6: Normal Metabolizer) — INFORMATIVE

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

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

Risk Management

Antipsychotic-Induced Tardive Dyskinesia

Moderate Risk of Antipsychotic-Induced Tardive Dyskinesia

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

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

Monitor the patient for any signs of tardive dyskinesia.

Antipsychotic-Induced Hyperprolactinemia

Moderate Risk of Antipsychotic-induced Hyperprolactinemia

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

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

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

Antipsychotic-Induced Weight Gain

Moderate Risk of Antipsychotic-Induced Weight Gain

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

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

Monitor patient closely for signs of weight gain.

Hyperlipidemia/Atherosclerotic Cardiovascular Disease

Increased risk of hyperlipidemia/atherosclerotic vascular disease

The patient is positive for the APOE 388 T>C (Arg112Cys) mutation and negative for the 526 C>T (Cys158Arg) mutation. The patient's genotype is ε3/ε4 (frequency: 15-28%). The APOE E3 is the normal APOE. The APOE E4 confers a limitation of HDL binding to its receptor, and is associated with increased plasma cholesterol, LDL, and triglycerides.

The ε4 allele is associated with an increased risk of hyperlipidemia/atherosclerotic vascular disease, and individuals that are heterozygous for this allele may have higher total cholesterol levels and elevated LDL cholesterol levels.

Consider dietary adjustment (very low fat diet) and statins (or HMG-CoA reductase inhibitors).

Hyperhomocysteinemia - Depression

No Increased Risk of Hyperhomocysteinemia

The patient does not carry the MTHFR C677T 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.

Thrombophilia

No Increased Risk of Thrombosis

The patient does not carry the Factor V Leiden G1691A mutation or Factor II G20210A mutation (wild-type).

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.

Unless other genetic and/or circumstantial risk factors are present (e.g., smoking or obesity...), estrogen-containing contraceptive and hormone replacement therapy can be used by the patient.

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Hyperhomocysteinemia - Thrombosis

No Increased Risk of Hyperhomocysteinemia

The patient does not carry the MTHFR C677T or MTHFR A1298C mutation (wild-type). MTHFR enzyme activity is normal.

With a normal MTHFR activity, this patient is unlikely to have elevated plasma levels of homocysteine, which is a known risk factor for cardiovascular diseases and thrombosis. Unless other risk factors are present, the patient is not expected to have an increased risk for venous thromboembolism (VTE).

MTHFR enzyme activity is normal.

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Potentially Impacted Medications

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Cardiovascular	Angiotensin II Receptor Antagonists	Azilsartan (Edarbi, Edarbyclor) Candesartan (Atacand) Eprosartan (Teveten) Irbesartan (Avapro) Losartan (Cozaar, Hyzaar) Olmesartan (Benicar) Telmisartan (Micardis) Valsartan (Diovan, Entresto)		
	Antianginal Agents	Ranolazine (Ranexa)		
	Antiarrhythmics	Flecainide (Tambocor) Mexiletine (Mexitil) Propafenone (Rythmol)		
	Anticoagulants	Apixaban (Eliquis) Dabigatran Etexilate (Pradaxa) Edoxaban (Savaysa) Fondaparinux (Arixtra) Rivaroxaban (Xarelto)	Warfarin (Coumadin)	
	Antiplatelets	Prasugrel (Effient) Ticagrelor (Brilinta) Vorapaxar (Zontivity)	Clopidogrel (Plavix)	
	Beta Blockers	Carvedilol (Coreg) Labetalol (Normodyne, Trandate) Metoprolol (Lopressor) Nebivolol (Bystolic) Propranolol (Inderal) Timolol (Timoptic)		
	Diuretics	Torsemide (Demadex)		
	Statins	Fluvastatin (Lescol)	Atorvastatin (Lipitor) Lovastatin (Mevacor, Altoprev, Advicor) Pitavastatin (Livalo) Pravastatin (Pravachol) Rosuvastatin (Crestor)	Simvastatin (Zocor)
Diabetes	Meglitinides	Nateglinide (Starlix) Repaglinide (Prandin, Prandimet)		
	Sulfonylureas	Chlorpropamide (Diabenese) Glimepiride (Amaryl) Glipizide (Glucotrol) Glyburide (Micronase) Tolbutamide (Orinase)		

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Gastrointestinal	Antiemetics	Dolasetron (Anzemet) Metoclopramide (Reglan) Ondansetron (Zofran, Zuplenz) Palonosetron (Aloxi)		
	Proton Pump Inhibitors	Rabeprazole (Aciphex)	Dexlansoprazole (Dexilant, Kapidex) Esomeprazole (Nexium) Lansoprazole (Prevacid) Omeprazole (Prilosec) Pantoprazole (Protonix)	
Infections	Antifungals		Voriconazole (Vfend)	
	Antimalarials	Proguanil (Malarone)		
Pain	Fibromyalgia Agents	Milnacipran (Savella)		
	Muscle Relaxants	Cyclobenzaprine (Flexeril, Amrix) Metaxalone (Skelaxin) Methocarbamol (Robaxin) Tizanidine (Zanaflex)	Carisoprodol (Soma)	
	NSAIDs	Celecoxib (Celebrex) Diclofenac (Voltaren) Flurbiprofen (Ansaid) Ibuprofen (Advil, Motrin) Indomethacin (Indocin) Ketoprofen (Orudis) Ketorolac (Toradol) Meloxicam (Mobic) Nabumetone (Relafen) Naproxen (Aleve) Piroxicam (Feldene) Sulindac (Clinoril)		
	Opioids	Alfentanil (Alfenta) Buprenorphine (Butrans, Buprenex) Codeine (Codeine; Fioricet with Codeine) Dihydrocodeine (Synalgos-DC) Fentanyl (Actiq) Hydrocodone (Vicodin) Hydromorphone (Dilaudid, Exalgo) Levorphanol (Levo Dromoran) Meperidine (Demerol) Methadone (Dolophine) Morphine (MS Contin) Oxycodone (Percocet, Oxycontin) Oxymorphone (Opana, Numorphan) Sufentanil (Sufenta) Tapentadol (Nucynta) Tramadol (Ultram)		
	Antiaddictives		Bupropion (Wellbutrin, Zyban, Aplenzin, Contrave) Naltrexone (Vivitrol, Contrave)	

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

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
	Antipsychotics	Aripiprazole (Abilify) Asenapine (Saphris) Brexpiprazole (Rexulti) Chlorpromazine (Thorazine) Clozapine (Clozaril) Fluphenazine (Prolixin) Haloperidol (Haldol) Iloperidone (Fanapt) Loxapine (Loxitane, Adasuve) Lurasidone (Latuda) Olanzapine (Zyprexa) Paliperidone (Invega) Perphenazine (Trilafon) Pimavanserin (Nuplazid) Pimozide (Orap) Quetiapine (Seroquel) Risperidone (Risperdal) Thioridazine (Mellaril) Thiothixene (Navane) Trazodone (Oleptro) Trifluoperazine (Stelazine) Ziprasidone (Geodon)	Tetrabenazine (Xenazine)	
	Benzodiazepines	Alprazolam (Xanax) Clobazam (Onfi) Clonazepam (Klonopin)	Diazepam (Valium)	
	Other Neurological Agents	Dextromethorphan / Quinidine (Nuedexta) Flibanserin (Addyi)		
Rheumatology	Immunomodulators	Apremilast (Otezla) Leflunomide (Arava) Tofacitinib (Xeljanz)		
Transplantation	Immunosupressants	Tacrolimus (Prograf)		
Urologicals	5-Alpha Reductase Inhibitors for Benign Prostatic Hyperplasia	Dutasteride (Avodart) Finasteride (Proscar)		
	Alpha-Blockers for Benign Prostatic Hyperplasia	Alfuzosin (UroXatral) Doxazosin (Cardura) Silodosin (Rapaflo) Tamsulosin (Flomax) Terazosin (Hytrin)		
	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

Amitriptyline
Elavil

Increased Sensitivity to Amitriptyline (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

Consider an alternative drug, or consider prescribing amitriptyline at standard dose and monitor the plasma concentrations of amitriptyline and nortriptyline to guide dose adjustments.

Citalopram
Celexa

Insufficient Response to Citalopram (CYP2C19: Ultra-Rapid Metabolizer) — ACTIONABLE

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.

Clomipramine
Anafranil

Increased Sensitivity to Clomipramine (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

Consider an alternative drug, or consider prescribing clomipramine at standard dose and monitor the plasma concentrations of clomipramine and desmethyl-clomipramine to guide dose adjustments.

Doxepin
Silenor

Increased Sensitivity to Doxepin (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

Consider an alternative drug, or consider prescribing doxepin at standard dose and monitor the plasma concentrations of doxepin and desmethyl-doxepin to guide dose adjustments.

Escitalopram
Lexapro

Insufficient Reponse to Escitalopram (CYP2C19: Ultra-Rapid Metabolizer) — ACTIONABLE

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.

Imipramine
Tofranil

Increased Sensitivity to Imipramine (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

Consider an alternative drug, or consider prescribing imipramine at the standard dose and monitor the plasma concentrations of imipramine and desipramine to guide dose adjustments.

Simvastatin
Zocor

Intermediate Myopathy Risk (SLCO1B1: Decreased Function) — ACTIONABLE

Simvastatin plasma concentrations are expected to be elevated. **Consider avoiding simvastatin,** and prescribe an alternative statin or another hypolipidemic drug, or consider prescribing simvastatin at a lower starting dose (20 mg/day). Routine creatine kinase (CK) monitoring is also advised. **The FDA recommends against the 80 mg daily dose.** Although the association between the SLCO1B1 521C>T variant and myopathy risk is not clearly established for other statins such as atorvastatin, pitavastatin, rosuvastatin, and pravastatin, caution is advised if high doses of these statins are used in this patient. Fluvastatin plasma levels are not affected by the SLCO1B1 521C>T variant.

Trimipramine
Surmontil

Increased Sensitivity to Trimipramine (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

Consider an alternative drug, or consider prescribing trimipramine at standard dose and monitor the plasma concentrations of trimipramine and desmethyl-trimipramine to guide dose adjustments.

Atorvastatin
Lipitor

Increased Myopathy Risk (SLCO1B1: Decreased Function) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated atorvastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high atorvastatin doses in this patient should be avoided. If atorvastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

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Bupropion
Wellbutrin, Zyban, Aplenzin, Contrave

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

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

Carisoprodol
Soma

Altered Sensitivity to Carisoprodol (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

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.

Clopidogrel
Plavix

Increased Response to Clopidogrel (CYP2C19: Ultra-Rapid Metabolizer) — ACTIONABLE

Clopidogrel can be prescribed at standard label-recommended dosage. Individuals with the *17 allele may have an increased risk of bleeding while taking clopidogrel.

Dexlansoprazole
Dexilant, Kapidex

Insufficient Response to Dexlansoprazole (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

- Helicobacter pylori eradication: increase dose by 200% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 200%.

Dexmethylphenidate
Focalin

Decreased Response to Dexmethylphenidate (COMT: Intermediate COMT Activity) — INFORMATIVE

The patient's genotype result predicts a less optimal 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.

Diazepam
Valium

Possible Altered Sensitivity to Diazepam (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

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.

Esomeprazole
Nexium

Insufficient Response to Esomeprazole (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

- Helicobacter pylori eradication: increase dose by 50-100% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 50-100%.

Lansoprazole
Prevacid

Insufficient Response to Lansoprazole (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

- Helicobacter pylori eradication: increase dose by 200% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 200%.

Lovastatin
Mevacor, Altoprev, Advicor

Increased Myopathy Risk (SLCO1B1: Decreased Function) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated lovastatin acid plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high lovastatin doses in this patient should be avoided. If lovastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

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Methylphenidate
Ritalin

Decreased Response to Methylphenidate (COMT: Intermediate COMT Activity) — INFORMATIVE

The patient's genotype result predicts a less optimal 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.

Naltrexone
Vivitrol, Contrave

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

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

Omeprazole
Prilosec

Insufficient Response to Omeprazole (CYP2C19: Ultra-Rapid Metabolizer) — ACTIONABLE

- Helicobacter pylori eradication: increase dose by 100-200% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 100-200%.

Pantoprazole
Protonix

Insufficient Response to Pantoprazole (CYP2C19: Ultra-Rapid Metabolizer) — ACTIONABLE

- Helicobacter pylori eradication: increase dose by 400% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 400%.

Pitavastatin
Livalo

Increased Myopathy Risk (SLCO1B1: Decreased Function) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated pitavastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high pitavastatin doses in this patient should be avoided. If pitavastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

Pravastatin
Pravachol

Increased Myopathy Risk (SLCO1B1: Decreased Function) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated pravastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high pravastatin doses in this patient should be avoided. If pravastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

Rosuvastatin
Crestor

Increased Myopathy Risk (SLCO1B1 521T>C TC) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated rosuvastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high rosuvastatin doses in this patient should be avoided. If rosuvastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

Sertraline
Zoloft

Possible Reduced Response to Sertraline (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

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

Tetrabenazine
Xenazine

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

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.

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Voriconazole
Vfend

Non-response to Voriconazole (CYP2C19: Ultra-Rapid Metabolizer) — ACTIONABLE

Voriconazole plasma concentrations may be low when standard dosage is used, increasing the risk of loss of response and effectiveness. Closely monitor voriconazole plasma concentrations, and adjust the dose accordingly.

Warfarin
Coumadin

Normal Sensitivity to Warfarin (CYP2C9 *1/*1 VKORC1 -1639G>A G/A) — ACTIONABLE

Initiation Therapy: consider using the following standard warfarin dose range as provided in the FDA-approved label: **5-7 mg/day**. OR consider using a personalized dose calculated by a pharmacogenetic algorithm. The estimated time to reach steady state is 4-5 days.

Alfentanil
Alfenta

Normal Response to Alfentanil — INFORMATIVE

Pharmacogenetic guidance: alfentanil is primarily metabolized by CYP3A4 and CYP3A5. Studies in healthy subjects showed that CYP3A5 genotype had no effect on the systemic or apparent oral clearances, or pharmacodynamics of alfentanil. **Polypharmacy guidance:** Alfentanil should be used with caution when prescribed to patients taking CYP3A4 inhibitors or inducers.

Alfuzosin
UroXatral

Normal Response to Alfuzosin — INFORMATIVE

Pharmacogenetic guidance: No genetically-guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Alfuzosin is extensively metabolized by CYP3A4 into pharmacologically inactive metabolites. Alfuzosin is **contraindicated with strong CYP3A4 inhibitors, as the risk for QTc prolongation induced by this drug is increased at higher concentrations**. Take caution when this drug is prescribed with CYP3A4 moderate inhibitors, as drug levels may increase.

Alprazolam
Xanax

Normal Response to Alprazolam — INFORMATIVE

Pharmacogenetic guidance: Alprazolam is primarily eliminated by metabolism via CYP3A4 and CYP3A5. Genetic polymorphisms of these genes are not expected to affect the efficacy or safety profiles of this drug. **Polypharmacy guidance:** The concomitant use of alprazolam with CYP3A4 inhibitors may result in increased alprazolam levels and prolonged sedation. Impairment of motor skills are also observed with some combinations. Monitor patients for exaggerated sedative effects. If possible, alprazolam should be avoided in patients receiving strong inhibitors of CYP3A4 such as ketoconazole, itraconazole and ritonavir. Drugs that induce CYP3A enzymes may decrease alprazolam levels, which results in a loss of efficacy.

Amoxapine
Amoxapine

Normal Sensitivity to Amoxapine (CYP2D6: Normal Metabolizer) — INFORMATIVE

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

Amphetamine
Adderall

Good Response to Amphetamine salts (COMT: Intermediate COMT Activity) — INFORMATIVE

The patient's genotype result predicts a favorable response to amphetamine stimulants. Amphetamines should be administered at the lowest effective dose, and dosage should be individually adjusted.

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.

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.

Aripiprazole
Abilify

Normal Sensitivity to Aripiprazole (CYP2D6: Normal Metabolizer)
ACTIONABLE

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

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

Monthly dosing (intramuscular): the starting and maintenance monthly recommended dose is 400 mg. Reduce the monthly dose to 300 mg if a CYP2D6 inhibitor or a CYP3A4 inhibitor is coadministered to patients receiving aripiprazole at 400 mg, and reduce dose to 200 mg in patients receiving aripiprazole at 300 mg. Reduce the dose to 200 mg if both a CYP2D6 inhibitor and a CYP3A4 inhibitor are coadministered to patients receiving aripiprazole at 400 mg, and reduce the dose to 160 mg in patients receiving aripiprazole at 300 mg.

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.

Atomoxetine
Strattera

Normal Sensitivity to Atomoxetine (CYP2D6: Normal Metabolizer)
ACTIONABLE

Atomoxetine can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended until a favorable response is achieved. The maximum recommended daily dose is 1.4 mg/kg for patients with a body weight up to 70 kg, and 100 mg for patients with a body weight above 70 kg.

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.

Azilsartan
Edarbi, Edarbyclor

Normal Sensitivity to Azilsartan Medoxomil (CYP2C9: Normal Metabolizer)
INFORMATIVE

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.

Brexpiprazole
Rexulti

Normal Sensitivity to Brexpiprazole (CYP2D6: Normal Metabolizer)
ACTIONABLE

Brexpiprazole can be prescribed 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 comedications: reduce dose by 50% if a strong CYP2D6 inhibitor or a strong CYP3A4 inhibitor is coadministered. Administer a quarter of the usual dose if both a strong/moderate CYP2D6 inhibitor and a strong/moderate CYP3A4 inhibitor are coadministered. Double usual dose over 1 to 2 weeks if a strong CYP3A4 inducer is coadministered.

Brivaracetam
Briviact

Normal Sensitivity to Brivaracetam (CYP2C19: Ultra-Rapid Metabolizer)
ACTIONABLE

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.

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.

Candesartan
Atacand

Normal Sensitivity to Candesartan Cilexetil
ACTIONABLE

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.

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.

Carvedilol
Coreg

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

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

Celecoxib
Celebrex

Normal Sensitivity to Celecoxib (CYP2C9: Normal Metabolizer) — ACTIONABLE

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

Chlorpromazine
Thorazine

Normal Sensitivity to Chlorpromazine (CYP2D6: Normal Metabolizer) — INFORMATIVE

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.

Chlorpropamide
Diabenese

Normal Sensitivity to Chlorpropamide (CYP2C9: Normal Metabolizer) — INFORMATIVE

The patient's genotype predicts a normal exposure to chlorpropamide, and this drug can be prescribed at label-recommended dosage and administration (dose titration in response to plasma levels of glucose/glycosylated hemoglobin).

Clobazam
Onfi

Normal Sensitivity to Clobazam (CYP2C19: Ultra-Rapid Metabolizer) — ACTIONABLE

The genotype result predicts a rapid or an ultra-rapid metabolizer phenotype, which translates to an increased CYP2C19 function. Rapid and ultra-rapid metabolizers have a higher capacity to metabolize N-desmethylclobazam, 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.

Clonazepam
Klonopin

Normal Response to Clonazepam — INFORMATIVE

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.

Clonidine
Kapvay

Normal Sensitivity to Clonidine (CYP2D6: Normal Metabolizer) — INFORMATIVE

Approximately 40-60% of an orally administered dose of clonidine is eliminated unchanged by the kidneys, with the remainder undergoing hepatic metabolism. CYP2D6 plays a major role in clonidine oxidative metabolism, followed by CYP3A and CYP1A2. Clonidine can be prescribed at standard label recommended-dosage and administration. The dose should be individualized according to the therapeutic needs and response of the patient.

Clozapine
Clozaril

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

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

Clozapine
Clozaril

Normal Response to Clozapine (CYP1A2: Normal Metabolizer- Possible Inducibility) — INFORMATIVE

Clozapine can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended with monitoring until a favorable response is achieved. Extrinsic factors such as diet (cruciferous vegetables, heavy coffee consumption, char-grilled meats) smoking, and certain medications (omeprazole, modafinil, carbamazepine) are known to increase CYP1A2 activity.

Codeine
Codeine; Fioricet with Codeine

Normal Response to Codeine (CYP2D6: Normal Metabolizer) — ACTIONABLE

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

Cyclobenzaprine
Flexeril, Amrix

Normal Response to Cyclobenzaprine — INFORMATIVE

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
Pradaxa

Normal Response to Dabigatran — INFORMATIVE

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.

Darifenacin
Enablex

Normal Response to Darifenacin (CYP2D6: Normal Metabolizer) — ACTIONABLE

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

Desipramine
Norpramin

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

Desipramine can be prescribed at 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.

Dextroamphetamine
Dexedrine

Good Response to Dextroamphetamine (COMT: Intermediate COMT Activity) — INFORMATIVE

The patient's genotype result predicts a favorable response to amphetamine stimulants. Dextroamphetamine should be administered at the lowest effective dose, and dosage should be individually adjusted.

Dextromethorphan / Quinidine
Nuedexta

Normal Sensitivity to Dextromethorphan-Quinidine (CYP2D6: Normal Metabolizer) — ACTIONABLE

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.

Diclofenac
Voltaren

Normal Sensitivity to Diclofenac (CYP2C9: Normal Metabolizer) — INFORMATIVE

Individuals with a normal CYP2C9 activity (i.e normal metabolizers) can be prescribed diclofenac according to standard label recommended-dosage and administration.

Dihydrocodeine
Synalgos-DC

Normal Response to Dihydrocodeine (CYP2D6: Normal Metabolizer) — ACTIONABLE

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

Dolasetron
Anzemet

Normal Response to Dolasetron (CYP2D6: Normal Metabolizer) — INFORMATIVE

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

Donepezil
Aricept

Normal Response to Donepezil (CYP2D6: Normal Metabolizer) — INFORMATIVE

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

Doxazosin
Cardura

Normal Response to Doxazosin — INFORMATIVE

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.

Duloxetine
Cymbalta

Normal Sensitivity to Duloxetine (CYP2D6: Normal Metabolizer) — INFORMATIVE

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

Dutasteride
Avodart

Normal Response to Dutasteride — INFORMATIVE

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.

Edoxaban
Savaysa

Normal Response to Edoxaban — INFORMATIVE

Pharmacogenetic guidance: Edoxaban is eliminated primarily as unchanged drug in urine. There is minimal metabolism via hydrolysis (mediated by carboxylesterase 1), conjugation, and oxidation by CYP3A4. Edoxaban is a substrate of the efflux transporter P-gp and its active metabolite (formed by carboxylesterase 1) is a substrate of the uptake transporter SLCO1B1. Preliminary studies indicate that the 521C single nucleotide polymorphism (rs4149056) of the SLCO1B1 gene does not affect edoxaban pharmacokinetics. **Polypharmacy guidance:** Avoid the concomitant use of edoxaban with rifampin. No dose reduction is recommended for concomitant P-gp inhibitor use.

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.

Eslicarbazepine
Aptiom

Normal Response to Eslicarbazepine — 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). 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.

Ethosuximide
Zarontin

Normal Response to Ethosuximide — INFORMATIVE

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.

Ezogabine
Potiga

Normal Response to Ezogabine — INFORMATIVE

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.

Felbamate
Felbatol

Normal Response to Felbamate — INFORMATIVE

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.

Fentanyl
Actiq

Good Response to Fentanyl (OPRM1: Normal OPRM1 Function) — INFORMATIVE

The patient does not carry the OPRM1 118A>G mutation. 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.

Fesoterodine
Toviaz

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

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

Finasteride
Proscar

Normal Response to Finasteride — INFORMATIVE

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.

Flecainide
Tambocor

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

Flecainide can be prescribed at standard label-recommended dosage and administration. No action is needed besides the standard precautions.

Flibanserin
Addyi

Normal Exposure to Flibanserin (CYP2C19: Ultra-Rapid Metabolizer) — ACTIONABLE

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.

Fluoxetine
Prozac, Sarafem

Normal Sensitivity to Fluoxetine (CYP2D6: Normal Metabolizer) — INFORMATIVE

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.

Fluphenazine
Prolixin

Normal Sensitivity to Fluphenazine (CYP2D6: Normal Metabolizer) — INFORMATIVE

Fluphenazine can be prescribed at standard label recommended-dosage and administration. Therapy must be initiated cautiously with oral or parenteral fluphenazine hydrochloride. When the pharmacological effects and an appropriate dosage are apparent, an equivalent dose of fluphenazine decanoate (IM or SC) may be administered and subsequent dosage adjustments may be necessary.

Flurbiprofen
Ansaid

Normal Sensitivity to Flurbiprofen (CYP2C9: Normal Metabolizer) — ACTIONABLE

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

Fluvastatin
Lescol

Normal Myopathy Risk (SLCO1B1: Decreased Function) — INFORMATIVE

Fluvastatin plasma concentrations are not expected to increase, and unless other genetic or circumstantial risk factors are present, fluvastatin can be prescribed at standard FDA-recommended starting doses and adjusted based on disease-specific guidelines. (Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, high statin dose, comedications, and female gender.)

Fluvastatin
Lescol

Normal Sensitivity to Fluvastatin (CYP2C9: Normal Metabolizer) — ACTIONABLE

Fluvastatin plasma concentrations are not expected to increase, and unless other genetic or circumstantial risk factors are present, fluvastatin can be prescribed at standard FDA-recommended starting doses and adjusted based on disease-specific guidelines. Other adverse events and predisposing factors include advanced age (≥65), diabetes, hypothyroidism, renal or hepatic impairments, high statin dose, CYP2C9 inhibitors, ABCG2 inhibitors, and female gender.

PrimaHealth

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	JILLIAN DOE	**COLLECTION DATE:**	7/19/2016	DOCTOR JONES
ACC #:	1607190464	**RECEIVED DATE:**	7/19/2016	
DOB:	1/1/1753	**REPORT DATE:**	8/11/2016	1^ABC CLINICAL LAB
SEX:	Female			

Fluvoxamine
Luvox

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

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

Fondaparinux
Arixtra

Normal Response to Fondaparinux — INFORMATIVE

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.

Fosphenytoin
Cerebyx

Normal Sensitivity to Fosphenytoin (CYP2C9: Normal Metabolizer) — ACTIONABLE

The genotype results indicate that the patient is a CYP2C9 substrate normal metabolizer. Fosphenytoin can be prescribed at a standard loading dose and a standard maintenance dose. Evaluate response and serum concentrations 7-10 days after starting therapy.

Gabapentin
Neurontin

Normal Response to Gabapentin — INFORMATIVE

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.

Galantamine
Razadyne

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

Galantamine can be prescribed at standard label-recommended dosage and administration. Individualization of dose with weekly titration is recommended.

Glimepiride
Amaryl

Normal Sensitivity to Glimepiride (CYP2C9: Normal Metabolizer) — ACTIONABLE

Glimepiride can be prescribed according to standard label-recommended dosage and administration (dose titration in response to plasma levels of glucose/glycosylated hemoglobin).

Glipizide
Glucotrol

Normal Sensitivity to Glipizide (CYP2C9: Normal Metabolizer) — INFORMATIVE

Glipizide can be prescribed according to standard label-recommended dosage and administration (dose titration in response to plasma levels of glucose/glycosylated hemoglobin).

Glyburide
Micronase

Normal Sensitivity to Glyburide (CYP2C9: Normal Metabolizer) — ACTIONABLE

Glyburide can be prescribed according to standard label-recommended dosage and administration (dose titration in response to plasma levels of glucose/glycosylated hemoglobin).

Guanfacine
Intuniv

Normal Response to Guanfacine — INFORMATIVE

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.

Haloperidol
Haldol

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

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

Hydrocodone
Vicodin

Good Response to Hydrocodone (OPRM1: Normal OPRM1 Function) — INFORMATIVE

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.

Hydrocodone
Vicodin

Normal Response to Hydrocodone (CYP2D6: Normal Metabolizer) — INFORMATIVE

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

Hydromorphone
Dilaudid, Exalgo

Normal Response to Hydromorphone — INFORMATIVE

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.

Ibuprofen
Advil, Motrin

Normal Sensitivity to Ibuprofen (CYP2C9: Normal Metabolizer) — INFORMATIVE

Individuals with a normal CYP2C9 activity (i.e normal metabolizers) can be prescribed ibuprofen according to standard label recommended-dosage and administration.

Iloperidone
Fanapt

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.

Indomethacin
Indocin

Normal Sensitivity to Indomethacin (CYP2C9: Normal Metabolizer) — INFORMATIVE

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

Irbesartan
Avapro

Normal Sensitivity to Irbesartan (CYP2C9: Normal Metabolizer) — INFORMATIVE

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

Ketoprofen
Orudis

Normal Response to Ketoprofen — INFORMATIVE

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
Toradol

Normal Response to Ketorolac — INFORMATIVE

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.

Labetalol
Normodyne, Trandate

Normal Response to Labetalol — INFORMATIVE

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.

Lacosamide
Vimpat

Normal Sensitivity to Lacosamide (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

CYP2C19 is partly involved in the metabolism of lacosamide, along with CYP2C9 and CYP3A, and this drug can be prescribed at standard label-recommended dosage and administration.

Lamotrigine
Lamictal

Normal Response to Lamotrigine — 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). Lamotrigine is metabolized by glucuronidation, which is mediated primarily by UGT1A4 with some contribution from UGT1A1 and UGBT2B7. 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. Coadministration 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
Arava

Normal Sensitivity to Leflunomide (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

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.

Levetiracetam
Keppra

Normal Response to Levetiracetam — INFORMATIVE

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.

Levomilnacipran
Fetzima

Normal Response to Levomilnacipran — INFORMATIVE

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, itrazonazole, and ritonavir.

Levorphanol
Levo Dromoran

Normal Response to Levorphanol — INFORMATIVE

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.

Lisdexamfetamine
Vyvanse

Good Response to Lisdexamfetamine (COMT: Intermediate COMT Activity) — INFORMATIVE

The patient's genotype result predicts a favorable response to amphetamine stimulants. Lisdexamfetamine should be administered at the lowest effective dose, and dosage should be individually adjusted.

Losartan
Cozaar, Hyzaar

Normal Response to Losartan (CYP2C9: Normal Metabolizer) — INFORMATIVE

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.

Loxapine
Loxitane, Adasuve

Normal Response to Loxapine — INFORMATIVE

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 (*e.g.*, 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.

Lurasidone
Latuda

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.

Maprotiline
Ludiomil

Normal Sensitivity to Maprotiline (CYP2D6: Normal Metabolizer) — INFORMATIVE

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

Meloxicam
Mobic

Normal Sensitivity to Meloxicam (CYP2C9: Normal Metabolizer) — INFORMATIVE

Meloxicam plasma concentrations are not expected to be altered. Meloxicam can be prescribed at standard label-recommended dosage and administration.

Memantine
Namenda

Normal Response to Memantine — INFORMATIVE

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.

Meperidine
Demerol

Normal Response to Meperidine — INFORMATIVE

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.

Metaxalone
Skelaxin

Normal Response to Metaxalone — INFORMATIVE

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.

Methadone
Dolophine

Normal Sensitivity to Methadone (CYP2B6: Normal Metabolizer) — INFORMATIVE

Methadone can be prescribed at standard label-recommended dosage. No action is needed besides the standard precautions.

Methocarbamol
Robaxin

Normal Response to Methocarbamol — INFORMATIVE

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.

Metoclopramide
Reglan

Normal Response to Metoclopramide (CYP2D6: Normal Metabolizer) — INFORMATIVE

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

Metoprolol
Lopressor

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

Metoprolol can be prescribed at standard label-recommended dosage and administration. Selection of proper dosage requires individual titration.

Mexiletine
Mexitil

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

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.

Milnacipran
Savella

Normal Response to Milnacipran — INFORMATIVE

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.

Mirabegron
Myrbetriq

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

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

Mirtazapine
Remeron

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

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

Morphine
MS Contin

Good Response to Morphine (OPRM1: Normal OPRM1 Function) — INFORMATIVE

The patient does not carry the OPRM1 118A>G mutation. Acute postoperative and cancer pain: the patient is expected to experience good analgesia at standard morphine doses. The dosing regimen needs to be individualized for each patient, taking into account the patient's prior analgesic treatment experience.

Morphine
MS Contin

Average Response to Morphine (COMT: Intermediate COMT Activity) — INFORMATIVE

The patient carries one COMT Val158Met mutation, which translates to a reduced COMT function. The patient may require average to low 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.

Nabumetone
Relafen

Normal Response to Nabumetone — INFORMATIVE

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 an 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.

Naproxen
Aleve

Normal Sensitivity to Naproxen — INFORMATIVE

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
Starlix

Normal Sensitivity to Nateglinide (SLCO1B1: Decreased Function) — INFORMATIVE

The patient carries one copy of SLCO1B1 rs4149056 C allele, which is associated with intermediate transporter function. Nateglinide can be prescribed at label-recommended standard dosage and administration.

Nateglinide
Starlix

Normal Sensitivity to Nateglinide (CYP2C9: Normal Metabolizer) — INFORMATIVE

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

Nebivolol
Bystolic

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

Nebivolol can be prescribed at standard label-recommended dosage and administration. Caution is recommended during up-titration until a favorable response is achieved.

Nefazodone
Serzone

Normal Sensitivity to Nefazodone (CYP2D6: Normal Metabolizer) — INFORMATIVE

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.

Nortriptyline
Pamelor

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

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

Olanzapine
Zyprexa

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

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

Olanzapine
Zyprexa

Normal Response to Olanzapine (CYP1A2: Normal Metabolizer- Possible Inducibility) — INFORMATIVE

Olanzapine can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended with monitoring until a favorable response is achieved. Extrinsic factors such as diet (cruciferous vegetables, heavy coffee consumption, char-grilled meats) smoking, and certain medications (omeprazole, modafinil, carbamazepine) are known to increase CYP1A2 activity.

Olmesartan
Benicar

Normal Sensitivity to Olmesartan Medoxomil — ACTIONABLE

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.

Ondansetron
Zofran, Zuplenz

Normal Response to Ondansetron (CYP2D6: Normal Metabolizer) — ACTIONABLE

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

Oxcarbazepine
Trileptal, Oxtellar XR

Normal Response to Oxcarbazepine — 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). Oxcarbazepine (prodrug) in 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%.

Oxybutynin
Ditropan

Normal Response to Oxybutynin — INFORMATIVE

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.

Oxycodone
Percocet, Oxycontin

Normal Response to Oxycodone (CYP2D6: Normal Metabolizer) — ACTIONABLE

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

Oxymorphone
Opana, Numorphan

Normal Response to Oxymorphone — INFORMATIVE

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.

Paliperidone
Invega

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

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

Palonosetron
Aloxi

Normal response to Palonosetron (CYP2D6: Normal Metabolizer) — INFORMATIVE

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

Paroxetine
Paxil, Brisdelle

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

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

Perampanel
Fycompa

Normal Response to Perampanel — INFORMATIVE

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%.

Perphenazine
Trilafon

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

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

Phenobarbital
Luminal

Normal Sensitivity to Phenobarbital (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

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

Phenytoin
Dilantin

Normal Sensitivity to Phenytoin (CYP2C9: Normal Metabolizer) — ACTIONABLE

The genotype results indicate that the patient is a CYP2C9 substrate normal metabolizer. Phenytoin can be prescribed at a standard loading dose and a standard maintenance dose. Evaluate response and serum concentrations 7-10 days after starting therapy.

Pimavanserin
Nuplazid

Normal Response to Pimavanserin — INFORMATIVE

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.

Pimozide
Orap

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

Pimozide can be prescribed at standard label-recommended dosage and administration. Starting dose: 1 to 2 mg/day (adult) or 0.05 mg/kg/day (children). Doses may be increased to a maximum of 10 mg/day or 0.2 mg/kg/day.

Piroxicam
Feldene

Normal Sensitivity to Piroxicam (CYP2C9: Normal Metabolizer) — ACTIONABLE

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

Prasugrel
Effient

Normal Response to Prasugrel (CYP2C19: Ultra-Rapid Metabolizer) — ACTIONABLE

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 metabolizer status.

Pregabalin
Lyrica

Normal Response to Pregabalin — INFORMATIVE

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.

Primidone
Mysoline

Normal Sensitivity to Primidone (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

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.

Proguanil
Malarone

Normal Response to Proguanil (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

Proguanil is metabolized to an active metabolite cycloguanil by CYP2C19. Although the patient's genotype predicts an increased metabolism of proguanil to cycloguanil, there is insufficient data to whether such change has a significant clinical impact. Proguanil can be prescribed at standard label-recommended dosage and administration with frequent monitoring of the patient's response.

Propafenone
Rythmol

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

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

Propranolol
Inderal

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

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

Protriptyline
Vivactil

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

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

Quetiapine
Seroquel

Normal Response to Quetiapine — INFORMATIVE

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.

Rabeprazole
Aciphex

Normal Response to Rabeprazole (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

Rabeprazole can be prescribed at standard dosage and administration.

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 CYP3A inhibitors is significantly elevated relative to when the drug is administered alone.

Repaglinide
Prandin, Prandimet

Normal Sensitivity to Repaglinide (SLCO1B1: Decreased Function) — INFORMATIVE

The patient carries one copy of SLCO1B1 rs4149056 C allele, which is associated with intermediate transporter function. Repaglinide can be prescribed at label-recommended standard dosage and administration.

Risperidone
Risperdal

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

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

Rivaroxaban
Xarelto

Normal Response to Rivaroxaban — INFORMATIVE

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.

Rufinamide
Banzel

Normal Response to Rufinamide — INFORMATIVE

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.

Sildenafil
Viagra

Normal Response to Sildenafil — INFORMATIVE

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.

Silodosin
Rapaflo

Normal Response to Silodosin — INFORMATIVE

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.

Solifenacin
Vesicare

Normal Response to Solifenacin — INFORMATIVE

Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Coadministration 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.

Sufentanil
Sufenta

Normal Response to Sufentanil — INFORMATIVE

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.

Sulindac
Clinoril

Normal Response to Sulindac — INFORMATIVE

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.

Tacrolimus
Prograf

Typical response to Tacrolimus (CYP3A5: Poor Metabolizer) — ACTIONABLE

The genotype result predicts that the patient does not express the CYP3A5 protein. Therefore, there is no risk that the patient may metabolize tacrolimus more rapidly. Careful titration of tacrolimus in response to therapeutic drug monitoring is recommended until a favorable response is achieved.

Tadalafil
Cialis

Normal Response to Tadalafil — INFORMATIVE

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.

Tamsulosin
Flomax

Normal Response to Tamsulosin (CYP2D6: Normal Metabolizer) — ACTIONABLE

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

Tapentadol
Nucynta

Normal Response to Tapentadol — INFORMATIVE

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.

Telmisartan
Micardis

Normal Sensitivity to Telmisartan — ACTIONABLE

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.

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.

Thioridazine
Mellaril

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

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

Thiothixene
Navane

Normal Response to Thiothixene — INFORMATIVE

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).

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.

Ticagrelor
Brilinta

Normal Response to Ticagrelor (CYP3A5: Poor Metabolizer) — INFORMATIVE

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

Timolol
Timoptic

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

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

Tizanidine
Zanaflex

Normal Response to Tizanidine (CYP1A2: Normal Metabolizer- Possible Inducibility) — INFORMATIVE

Tizanidine can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended with monitoring until a favorable response is achieved. Extrinsic factors such as diet (cruciferous vegetables, heavy coffee consumption, char-grilled meats) smoking, and certain medications (omeprazole, modafinil, carbamazepine) are known to increase CYP1A2 activity.

Tofacitinib
Xeljanz

Normal Sensitivity to Tofacitinib (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

Tofacitinib is metabolized primarily by CYP3A4 with some contribution from CYP2C19. Genetic variations in the CYP2C19 gene do not significantly influence tofacitinib exposure. Tofacitinib can be prescribed according to standard label-recommended dosage and administration (i.e 5 mg twice daily).

Tolbutamide
Orinase

Normal Sensitivity to Tolbutamide (CYP2C9: Normal Metabolizer) — ACTIONABLE

Tolbutamide can be prescribed according to standard label-recommended dosage and administration (dose titration in response to plasma levels of glucose/glycosylated hemoglobin).

Tolterodine
Detrol

Normal Sensitivity to Tolterodine (CYP2D6: Normal Metabolizer) — INFORMATIVE

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

Topiramate
Topamax

Normal Response to Topiramate — INFORMATIVE

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.

Torsemide
Demadex

Normal Response to Torsemide (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.

Tramadol
Ultram

Normal Response to Tramadol (CYP2D6: Normal Metabolizer) — ACTIONABLE

Tramadol can be prescribed at standard label-recommended dosage and administration. Individualization of dose with careful weekly titration is recommended.

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 are inhibit CYP3A4 should be approached with caution.

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.

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.

Valproic Acid
Depakote, Depakene

Normal Response to Valproic acid — INFORMATIVE

Pharmacogenetic guidance: 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.

Valsartan
Diovan, Entresto

Normal Sensitivity to Valsartan — ACTIONABLE

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.

Vardenafil
Levitra

Normal Response to Vardenafil — ACTIONABLE

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.
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.

Venlafaxine
Effexor

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

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

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.

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.

Vorapaxar
Zontivity

Normal Response to Vorapaxar — ACTIONABLE

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).

Vortioxetine
Trintellix

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

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.

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.).

PrimaHealth

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	JILLIAN DOE	**COLLECTION DATE:**	7/19/2016	**DOCTOR JONES**
ACC #:	1607190464	**RECEIVED DATE:**	7/19/2016	
DOB:	1/1/1753	**REPORT DATE:**	8/11/2016	**1^ABC CLINICAL LAB**
SEX:	Female			

Zonisamide

Zonegran

Normal Sensitivity to Zonisamide (CYP2C19: Ultra-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.

PrimaHealth

PATIENT INFORMATION

NAME: JILLIAN DOE
ACC #: 1607190464
DOB: 1/1/1753
SEX: Female

SPECIMEN DETAILS

COLLECTION DATE: 7/19/2016
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ORDERED BY

DOCTOR JONES

1^ABC CLINICAL LAB

Test Details

Gene	Genotype	Phenotype	Alleles Tested
ANKK1/DRD2	DRD2:Taq1A AG	**Altered DRD2 function**	DRD2:Taq1A
Apolipoprotein E	ε3/ε4	**Increased Risk of Hyperlipidemia/Atherosclerotic Vascular Disease**	ε2, ε4, (ε3 is reference)
COMT	Val158Met AG	**Intermediate COMT Activity**	Val158Met
CYP1A2	*1A/*1V	**Normal Metabolizer- Possible Inducibility**	*1C, *1D, *1F, *1K, *1L, *1V, *1W
CYP2B6	*1/*1	**Normal Metabolizer**	*6, *9
CYP2C19	*17/*17	**Ultra-Rapid Metabolizer**	*2, *3, *4, *4B, *6, *7, *8, *9, *10, *17
CYP2C9	*1/*1	**Normal Metabolizer**	*2, *3, *4, *5, *6, *11
CYP2D6	*1/*35	**Normal Metabolizer**	*2, *3, *4, *4M, *6, *7, *8, *9, *10, *12, *14A, *14B, *17, *29, *35, *41
CYP3A4	*1/*1	**Normal Metabolizer**	*1B, *2, *3, *12, *17, *22
CYP3A5	*3/*3	**Poor Metabolizer**	*1D, *2, *3, *3C, *6, *7, *8, *9
Factor II **Factor V Leiden**	20210G>A GG 1691G>A GG	**No Increased Risk of Thrombosis**	20210G>A, 1691G>A
MTHFR	677C>T CC	**Normal MTHFR Activity**	1298A>C, 677C>T
MTHFR	1298A>C AA 677C>T CC	**No Increased Risk of Hyperhomocysteinemia**	1298A>C, 677C>T
OPRM1	A118G AA	**Normal OPRM1 Function**	A118G
SLCO1B1	521T>C TC	**Decreased Function**	521T>C, 388A>G
VKORC1	-1639G>A G/A	**Intermediate Warfarin Sensitivity**	-1639G>A

Disclaimer: Only a physician, pharmacist or other healthcare professional should advise a patient on the use of information in this report.

Methodology: All single nucleotide polymorphisms tested in duplicate by PCR-reporter probe technology. Copy number variation tested in quadruplicate with PCR-reporter probe technology.

Limitations: This test will not detect all the known mutations that result in altered or inactive tested genes. Absence of a detectable gene mutation or polymorphism does not rule out the possibility that a patient has intermediate or high sensitivity phenotypes due to the presence of an undetected polymorphism or due to drug-drug interactions.