GenoScribe™
BY EMGENEX & GENETRAIT LABORATORIES

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Comprehensive Pharmacogenetic Report Created for: Test Patient

Patient:	Test Patient	DOB:	1/1/1980
Accession #:	P00000000	Gender:	F
Collection Date:	1/20/2016	Received Date:	1/20/2016
Ordered By:	Emgenex Test	Report Generated:	1/27/2016

Current Patient Medications

Current Medication List: Abilify, Adderall, Crestor

Medications Affected by Patient Genetic Results

Adderall (Amphetamine)
Informative

Poor Response to Amphetamine salts (COMT Val158Met AA Low COMT Activity)

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

Abilify (Aripiprazole)
Actionable

Normal Sensitivity to Aripiprazole (CYP2D6 *2/*41 Normal Metabolizer)

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.

Crestor (Rosuvastatin)
Informative

Normal Myopathy Risk (SLCO1B1 521T>C TT)

Rosuvastatin plasma concentrations are not expected to increase, and unless other genetic or circumstantial risk factors are present, rosuvastatin can be prescribed at standard FDA-recommended starting doses and adjusted based on disease-specific guidelines. The myopathy risk increases with use of the 40 mg dose. (Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, high statin dose, comedications, and female gender.)

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Guidance Levels

Based upon the patient's genotype, a medication has potentially reduced efficacy or increased toxicity or the patient has an increased risk for the indicated condition.

Based upon the patient's genotype, guidelines exist for adjusting dosage or increased vigilance or the patient has a moderate risk for the indicated condition.

Based on this patient's genotype, the medication can be prescribed according to standard regimens or the patient's risk for the indicated condition is not increased.

Evidence Levels

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 new knowledge arises.
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.

Potentially Impacted Medications

The pharmacogenetic report is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. This report does not address drug-drug interactions, patient drug allergies, or non-genetic factors.

Category	Drug Class	Standard Precautions	Use With Caution	Consider Alternatives
Anticancer Agents	Antifolates		Methotrexate (Trexall)	
Cardiovascular	Angiotensin II Receptor Antagonists	Irbesartan (Avapro)		
	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)		
	Statins	Atorvastatin (Lipitor) Fluvastatin (Lescol) Lovastatin (Mevacor) Pitavastatin (Livalo) Pravastatin (Pravachol) Rosuvastatin (Crestor) Simvastatin (Zocor)		

Category	Drug Class	Standard Precautions	Use With Caution	Consider Alternatives
Diabetes	Sulfonylureas	Glimepiride (Amaryl) Glipizide (Glucotrol) Glyburide (Micronase) Tolbutamide (Orinase)		
Gastrointestinal	Antiemetics	Dolasetron (Anzemet) Metoclopramide (Reglan) Ondansetron (Zofran) Palonosetron (Aloxi)		
	Proton Pump Inhibitors	Dexlansoprazole (Dexilant, Kapidex) Esomeprazole (Nexium) Lansoprazole (Prevacid) Omeprazole (Prilosec) Pantoprazole (Protonix) Rabeprazole (Aciphex)		
Infections	Antifungals		Voriconazole (Vfend)	
Pain	Fibromyalgia Agents	Milnacipran (Savella)		
	Muscle Relaxants	Cyclobenzaprine (Flexeril, Amrix) Metaxalone (Skelaxin) Methocarbamol (Robaxin)	Carisoprodol (Soma) Tizanidine (Zanaflex)	
	NSAIDs	Celecoxib (Celebrex) Diclofenac (Voltaren) Flurbiprofen (Ansaid) Ibuprofen (Advil, Motrin) Indomethacin (Indocin) Ketoprofen (Orudis) Ketorolac (Toradol) Meloxicam (Mobic) Nabumetone (Relafen) Naproxen (Aleve) Piroxicam (Feldene) Sulindac (Clinoril)		
	Opioids	Alfentanil (Alfenta) Buprenorphine (Butrans, Buprenex) Codeine (Codeine; Fioricet with Codeine) Dihydrocodeine (Synalgos-DC) Hydromorphone (Dilaudid, Exalgo) Levorphanol (Levo Dromoran) Meperidine (Demerol) Oxycodone (Percocet, Oxycontin) Oxymorphone (Opana, Numorphan) Sufentanil (Sufenta) Tapentadol (Nucynta) Tramadol (Ultram)	Fentanyl (Actiq) Hydrocodone (Vicodin) Methadone (Dolophine) Morphine (MS Contin)	
	Antiaddictives	Naltrexone (Vivitrol)	Bupropion (Wellbutrin, Zyban, Aplenzin, Contrave)	

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

Category	Drug Class	Standard Precautions	Use With Caution	Consider Alternatives
	Antipsychotics	Aripiprazole (Abilify) Asenapine (Saphris) Brexpiprazole (Rexulti) Chlorpromazine (Thorazine) Fluphenazine (Prolixin) Haloperidol (Haldol) Iloperidone (Fanapt) Lurasidone (Latuda) Paliperidone (Invega) Perphenazine (Trilafon) Pimozide (Orap) Quetiapine (Seroquel) Risperidone (Risperdal) Thioridazine (Mellaril) Thiothixene (Navane) Trazodone (Oleptro) Trifluoperazine (Stelazine) Ziprasidone (Geodon)	Clozapine (Clozaril) Olanzapine (Zyprexa) Tetrabenazine (Xenazine)	
	Benzodiazepines	Alprazolam (Xanax) Clonazepam (Klonopin)	Clobazam (Onfi) Diazepam (Valium)	
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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Risk Management

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.

Hyperhomocysteinemia - Thrombosis

No Increased Risk of Hyperhomocysteinemia

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

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

The patient's MTHFR activity is slightly reduced.

Dosing Guidance

Clopidogrel (Plavix)
Actionable

Significantly Reduced Response to Clopidogrel (CYP2C19 *2/*2 Poor Metabolizer)
Consider alternative therapy. Examples of alternative drugs: prasugrel (contraindicated in TIA/Stroke patients), ticagrelor, aspirin, aspirin plus dipyridamole.

Amitriptyline (Elavil)
Actionable

Increased Sensitivity to Amitriptyline (CYP2C19 *2/*2 Poor Metabolizer)
Consider a 50% reduction of recommended amitriptyline starting dose, and monitor the plasma concentrations of amitriptyline and nortriptyline to adjust the dose.

Amphetamine (Adderall)
Informative

Poor Response to Amphetamine salts (COMT Val158Met AA Low COMT Activity)
The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, amphetamines should be administered at the lowest effective dose, and dosage should be individually adjusted.

Bupropion (Wellbutrin, Zyban, Aplenzin, Contrave)
Informative

Possible Altered Response to Bupropion (CYP2B6 *1/*5 Unknown Phenotype)
Bupropion is metabolized to its active metabolite hydroxybupropion by CYP2B6. This metabolite contributes to the therapeutic effects of bupropion when used as a smoking cessation agent or as an antidepressant. Until additional information is available for this genotype, bupropion can be prescribed at standard label-recommended dosage with careful monitoring of the patient's response. Therapeutic monitoring of hydroxybupropion levels may be considered to guide dosing adjustment if needed.

Carisoprodol (Soma)
Actionable

Altered Sensitivity to Carisoprodol (CYP2C19 *2/*2 Poor Metabolizer)
CYP2C19 poor metabolizers have a lower capacity to metabolize carisoprodol to meprobamate, and may therefore have an increased risk of developing concentration-dependent side effects such as drowsiness and hypotension when receiving standard doses of carisoprodol. Carisoprodol should be used with caution in patients with reduced CYP2C19 activity. Because there is insufficient data to allow calculation of dose adjustment, consider reducing the dose or using an alternative medication.

Citalopram (Celexa)
Actionable

Increased Sensitivity to Citalopram (CYP2C19 *2/*2 Poor Metabolizer)
At standard label-recommended dosage, citalopram plasma concentrations levels are expected to be high and adverse events may occur. Consider a 50% reduction of the recommended starting dose to help prevent concentration-dependent adverse events. Dose escalations over 20 mg/day for CYP2C19 poor metabolizers are not recommended. An alternative medication may also be considered.

Clobazam (Onfi)
Actionable

Increased Sensitivity to Clobazam (CYP2C19 *2/*2 Poor Metabolizer)
In CYP2C19 poor metabolizers, plasma levels of the active metabolite N-desmethylclobazam were 5-fold higher than those found in CYP2C19 normal metabolizers. Therefore, the starting dose should be 5 mg/day and dose titration should proceed slowly according to weight. Patients should be titrated initially to 10 mg /day (≤30 kg body weight) or 20 mg/day (>30 kg body weight). If necessary and based upon clinical response, an additional titration to the maximum doses 20 mg/day (≤30 kg body weight) or 40 mg/day (>30 kg body weight) may be started on day 21.

Clomipramine (Anafranil)
Actionable

Increased Sensitivity to Clomipramine (CYP2C19 *2/*2 Poor Metabolizer)
Consider a 50% reduction of recommended clomipramine starting dose, and monitor the plasma concentrations of clomipramine and desmethyl-clomipramine to adjust the dose.

Clozapine (Clozaril)
Informative

Unfavorable Response to Clozapine (HTR2A -1438G>A C/C Homozygous for the C allele (rs6311))
The patient does not carry the HTR2A variant rs6311. Preliminary studies suggest that this genotype may be associated with an unfavorable response to clozapine in patients with European ancestry.

Clozapine (Clozaril)
Informative

Non-Response to Clozapine (CYP1A2 *1F/*1F Normal Metabolizer - Higher Inducibility)
Smokers have a high risk for non-response at standard doses and may require higher doses. There is an association between high clozapine doses and the risk of seizures, and therefore careful monitoring is recommended during dosing adjustment. Smoking cessation will increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction is recommended in patients who have quit smoking.

Dexmethylphenidate (Focalin)
Informative

Poor Response to Dexmethylphenidate (COMT Val158Met AA Low COMT Activity)
The patient's genotype result predicts a reduced therapeutic response to dexmethylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

Dextroamphetamine (Dexedrine)
Informative

Poor Response to Dextroamphetamine (COMT Val158Met AA Low COMT Activity)
The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, dextroamphetamine should be administered at the lowest effective dose, and dosage should be individually adjusted.

Diazepam (Valium)
Actionable

Increased Sensitivity to Diazepam (CYP2C19 *2/*2 Poor Metabolizer)
CYP2C19 poor metabolizers have a lower capacity to metabolize diazepam and its active metabolite nordiazepam. Therefore, they may experience more concentration-dependent side effects, such as increased or prolonged sedation, if treated with standard doses of diazepam. Diazepam should be used with caution in these patients, and a reduced dose or longer dosing interval may be needed.

Doxepin (Silenor)
Actionable

Increased Sensitivity to Doxepin (CYP2C19 *2/*2 Poor Metabolizer)
Consider a 50% reduction of recommended doxepin starting dose, and monitor plasma concentrations of doxepin and desmethyl-doxepin to adjust the dose.

Escitalopram (Lexapro)
Actionable

Increased Sensitivity to Escitalopram (CYP2C19 *2/*2 Poor Metabolizer)
At standard label-recommended dosage, escitalopram plasma concentrations levels are expected to be high and adverse events may occur. Consider a 50% reduction of the recommended starting dose to help prevent concentration-dependent adverse events. An alternative medication may also be considered.

Fentanyl (Actiq)
Informative

Altered Response to Fentanyl (OPRM1 A118G AG Altered OPRM1 Function)
The patient carries one copy of the OPRM1 118A>G mutation. Acute postoperative and cancer pain: the patient's genotype has been shown to be associated with reduced analgesia at standard fentanyl doses. Therefore, the patient may require higher doses of this drug. 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.

Hydrocodone (Vicodin)
Informative

Altered Response to Hydrocodone (OPRM1 A118G AG Altered OPRM1 Function)
Acute postoperative and cancer pain: the patient's genotype has been shown to be associated with reduced analgesia and increased opioid side effects at standard or high hydrocodone doses. If the patient fails to respond to increased hydrocodone doses, an alternative opioid may be considered.

Imipramine (Tofranil)
Actionable

Increased Sensitivity to Imipramine (CYP2C19 *2/*2 Poor Metabolizer)
Consider a 50% reduction of the recommended imipramine starting dose, and monitor the plasma concentrations of imipramine and desipramine to adjust the dose.

Leflunomide (Arava)
Informative

Increased Sensitivity to Leflunomide (CYP2C19 *2/*2 Poor Metabolizer)
Leflunomide is metabolized by CYP2C19 and CYP1A2 to its active metabolite teriflunomide. Preliminary studies indicate that patients with decreased CYP2C19 activity have a higher risk of developing gastrointestinal side effects and hepatotoxicity. There is insufficient data to calculate dose adjustment. If leflunomide is prescribed at standard dosing, monitor closely the patient's response and be alert to increased side effects. Full blood cell count (CBC) and liver function parameters should be checked no more than 6 months before beginning treatment, and every month for the initial 6 months of therapy. Blood pressure should be checked before beginning treatment and periodically thereafter.

Lisdexamfetamine (Vyvanse)
Informative

Poor Response to Lisdexamfetamine (COMT Val158Met AA Low COMT Activity)
The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, lisdexamfetamine should be administered at the lowest effective dose, and dosage should be individually adjusted.

Methadone (Dolophine)
Informative

Unknown Sensitivity to Methadone (CYP2B6 *1/*5 Unknown Phenotype)
Until additional information is available, prescribe methadone with careful monitoring. If a genotype effect is suspected based on patient response, adjust dosage accordingly, or prescribe an alternative medication.

Methotrexate (Trexall)
Informative

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

Methylphenidate (Ritalin)
Informative

Poor Response to Methylphenidate (COMT Val158Met AA Low COMT Activity)
The patient's genotype result predicts a reduced therapeutic response to methylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

Morphine (MS Contin)
Informative

Altered Response to Morphine (COMT Val158Met AA Low COMT Activity)
The patient carries two COMT Val158Met mutations, which translates to a reduced COMT function. The patient may require lower doses of morphine for adequate pain control. The dosing regimen needs to be individualized for each patient, taking into account the patient's prior analgesic treatment experience.

Olanzapine (Zyprexa)
Informative

Increased Risk of Weight Gain with Olanzapine (HTR2C -759C>T C/C Homozygous for the C allele (rs3813929))
Genetic variations in the Serotonin 2C Receptor (HTR2C) gene in known to be partially involved in the adverse effects associated with atypical antipsychotic medications. The patient is homozygous for C allele of HTR2C variant rs3813929. Patients with this genotype may have an increased risk of weight gain when treated with olanzapine.

Olanzapine (Zyprexa)
Informative

Non-Response to Olanzapine (CYP1A2 *1F/*1F Normal Metabolizer - Higher Inducibility)
There is little evidence regarding the impact of CYP1A2 genetic variants on olanzapine response. Smokers may be at risk for non-response at standard doses. Careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

Phenobarbital (Luminal)
Informative

Possible Sensitivity to Phenobarbital (CYP2C19 *2/*2 Poor Metabolizer)
CYP2C19 is partly involved in the metabolism of phenobarbital, and although CYP2C19 poor metabolizers have a 20% lower clearance of phenobarbital than normal metabolizers, no significant changes in clinical outcome has been reported with this antiepileptic drug. Therefore, phenobarbital can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

Primidone (Mysoline)
Informative

Possible Sensitivity to Primidone (CYP2C19 *2/*2 Poor Metabolizer)
CYP2C19 is partly involved in the metabolism of primidone and although CYP2C19 poor metabolizers have a 20% lower clearance of phenobarbital (active metabolite) than normal metabolizers, no significant changes in clinical outcome has been reported with this antiepileptic drug. Therefore, primidone can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

Sertraline (Zoloft)
Actionable

Increased Sensitivity to Sertraline (CYP2C19 *2/*2 Poor Metabolizer)

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

Tetrabenazine (Xenazine)
Actionable

Normal Sensitivity to Tetrabenazine (CYP2D6 *2/*41 Normal Metabolizer)

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.

Tizanidine (Zanaflex)
Informative

Possible Non-Response to Tizanidine (CYP1A2 *1F/*1F Normal Metabolizer - Higher Inducibility)

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

Tofacitinib (Xeljanz)
Informative

Increased Sensitivity to Tofacitinib when coadministered with CYP3A4 Inhibitors (CYP2C19 *2/*2 Poor Metabolizer)

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

Trimipramine (Surmontil)
Actionable

Increased Sensitivity to Trimipramine (CYP2C19 *2/*2 Poor Metabolizer)

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

Voriconazole (Vfend)
Actionable

Increased Sensitivity to Voriconazole (CYP2C19 *2/*2 Poor Metabolizer)

Voriconazole plasma concentrations are expected to be high, which may increase the risk of dose-dependent adverse events. Voriconazole should be used with caution in patients with a reduced CYP2C19 activity, such as poor metabolizers. Monitor closely voriconazole plasma concentrations, and adjust the dose accordingly.

Warfarin (Coumadin)
Actionable

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

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.

Zonisamide (Zonegran)
Informative

Possible Sensitivity to Zonisamide (CYP2C19 *2/*2 Poor Metabolizer)

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

Alfentanil (Alfenta)
Informative

Normal Response to Alfentanil

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)
Informative

Normal Response to Alfuzosin

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**. Caution when this drug is prescribed with CYP3A4 moderate inhibitors, as drug levels may increase.

Alprazolam (Xanax)
Informative

Normal Response to Alprazolam

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)
Informative

Normal Sensitivity to Amoxapine (CYP2D6 *2/*41 Normal Metabolizer)

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

✓ **Apixaban (Eliquis)**
Informative

Normal Response to Apixaban

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)**
Actionable

Normal Response to Apremilast

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)**
Actionable

Normal Sensitivity to Aripiprazole (CYP2D6 *2/*41 Normal Metabolizer)

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)**
Informative

Normal Response to Asenapine

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)**
Actionable

Normal Sensitivity to Atomoxetine (CYP2D6 *2/*41 Normal Metabolizer)

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.

✓ **Atorvastatin (Lipitor)**
Informative

Normal Myopathy Risk (SLCO1B1 521T>C TT Normal Transporter Function)

Atorvastatin plasma concentrations are not expected to increase, and unless other genetic or circumstantial risk factors are present, atorvastatin 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.)

✓ **Atorvastatin (Lipitor)**
Informative

Normal Response to Atorvastatin (CYP3A4 *1/*1 Normal Metabolizer)

The genotype result indicates that the patient does not carry the CYP3A4*22 allele (this allele is associated with a decreased CYP3A4 enzyme activity). The patient is expected to achieve an optimal lipid control goal with standard atorvastatin dose requirements.

✓ **Avanafil (Stendra)**
Informative

Normal Response to Avanafil

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.

Brexpiprazole (Rexulti)
Actionable

Normal Sensitivity to Brexpiprazole (CYP2D6 *2/*41 Normal Metabolizer)
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.

Buprenorphine (Butrans, Buprenex)
Informative

Normal Response to Buprenorphine
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.

Carbamazepine (Tegretol, Carbatrol)
Informative

Normal Response to Carbamazepine
Pharmacogenetic guidance: 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)
Actionable

Normal Sensitivity to Carvedilol (CYP2D6 *2/*41 Normal Metabolizer)
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)
Actionable

Normal Sensitivity to Celecoxib (CYP2C9 *1/*1 Normal Metabolizer)
Celecoxib can be prescribed at standard label-recommended dosage and administration.

Chlorpromazine (Thorazine)
Informative

Normal Sensitivity to Chlorpromazine (CYP2D6 *2/*41 Normal Metabolizer)
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.

Clonazepam (Klonopin)
Informative

Normal Response to Clonazepam

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)
Informative

Normal Sensitivity to Clonidine (CYP2D6 *2/*41 Normal Metabolizer)

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.

Codeine (Codeine; Fioricet with Codeine)
Actionable

Normal Response to Codeine (CYP2D6 *2/*41 Normal Metabolizer)

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

Cyclobenzaprine (Flexeril, Amrix)
Informative

Normal Response to Cyclobenzaprine

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)
Informative

Normal Response to Dabigatran

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)
Actionable

Normal Response to Darifenacin (CYP2D6 *2/*41 Normal Metabolizer)

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

Desipramine (Norpramin)
Actionable

Normal Sensitivity to Desipramine (CYP2D6 *2/*41 Normal Metabolizer)

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

Desvenlafaxine (Pristiq)
Actionable

Normal Sensitivity to Desvenlafaxine (CYP2D6 *2/*41 Normal Metabolizer)

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

✓ **Dexlansoprazole (Dexilant, Kapidex)** Actionable	**Increased Response to Dexlansoprazole (CYP2C19 *2/*2 Poor Metabolizer)** Dexlansoprazole can be prescribed at standard label-recommended dosage and administration. A positive clinical effect is expected in poor metabolizers.
✓ **Diclofenac (Voltaren)** Informative	**Normal Sensitivity to Diclofenac (CYP2C9 *1/*1 Normal Metabolizer)** 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)** Actionable	**Normal Response to Dihydrocodeine (CYP2D6 *2/*41 Normal Metabolizer)** Dihydrocodeine can be prescribed at standard label-recommended dosage and administration.
✓ **Dolasetron (Anzemet)** Informative	**Normal Response to Dolasetron (CYP2D6 *2/*41 Normal Metabolizer)** Dolasetron can be prescribed at standard label-recommended dosage and administration.
✓ **Donepezil (Aricept)** Informative	**Normal Response to Donepezil (CYP2D6 *2/*41 Normal Metabolizer)** Donepezil can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended until a favorable response is achieved.
✓ **Doxazosin (Cardura)** Informative	**Normal Response to Doxazosin** **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)** Informative	**Normal Sensitivity to Duloxetine (CYP2D6 *2/*41 Normal Metabolizer)** Duloxetine can be prescribed at standard label-recommended dosage and administration.
✓ **Dutasteride (Avodart)** Informative	**Normal Response to Dutasteride** **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)** Informative	**Normal Response to Edoxaban** **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. Genetic polymorphisms of these genes are not expected to affect the efficacy or safety profiles of edoxaban. **Polypharmacy guidance:** Avoid the concomitant use of edoxaban with rifampin. No dose reduction is recommended for concomitant P-gp inhibitor use.

Eslicarbazepine (Aptiom)
Informative

Normal Response to Eslicarbazepine Acetate

Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** 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. In the presence of enzyme-inducing drugs, eslicarbazepine plasma levels are significantly decreased, and higher doses of the drug may be needed.

Esomeprazole (Nexium)
Actionable

Increased Reponse to Esomeprazole (CYP2C19 *2/*2 Poor Metabolizer)

Esomeprazole can be prescribed at standard label-recommended dosage and administration. A positive clinical effect is expected in poor metabolizers.

Ethosuximide (Zarontin)
Informative

Normal Response to Ethosuximide

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)
Informative

Normal Response to Ezogabine

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)
Informative

Normal Response to Felbamate

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.

Fesoterodine (Toviaz)
Actionable

Normal Sensitivity to Fesoterodine (CYP2D6 *2/*41 Normal Metabolizer)

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

Finasteride (Proscar)
Informative

Normal Response to Finasteride

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

✓ **Flecainide (Tambocor)**
Actionable

Normal Sensitivity to Flecainide (CYP2D6 *2/*41 Normal Metabolizer)
Flecainide can be prescribed at standard label-recommended dosage and administration. No action is needed besides the standard precautions.

✓ **Fluoxetine (Prozac, Sarafem)**
Informative

Normal Sensitivity to Fluoxetine (CYP2D6 *2/*41 Normal Metabolizer)
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)**
Informative

Normal Sensitivity to Fluphenazine (CYP2D6 *2/*41 Normal Metabolizer)
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)**
Actionable

Normal Sensitivity to Flurbiprofen (CYP2C9 *1/*1 Normal Metabolizer)
Flurbiprofen can be prescribed at standard label-recommended dosage and administration.

✓ **Fluvastatin (Lescol)**
Informative

Normal Myopathy Risk (SLCO1B1 521T>C TT Normal Transporter Function)
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)**
Actionable

Normal Sensitivity to Fluvastatin (CYP2C9 *1/*1 Normal Metabolizer)
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.

✓ **Fluvoxamine (Luvox)**
Actionable

Normal Sensitivity to Fluvoxamine (CYP2D6 *2/*41 Normal Metabolizer)
Fluvoxamine can be prescribed at standard label recommended-dosage and administration. Careful titration is recommended until a favorable response is achieved.

✓ **Fondaparinux (Arixtra)**
Informative

Normal Response to Fondaparinux
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)**
Actionable

Normal Sensitivity to Fosphenytoin (CYP2C9 *1/*1 Normal Metabolizer)
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)
Informative

Normal Response to Gabapentin

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

Galantamine (Razadyne)
Actionable

Normal Sensitivity to Galantamine (CYP2D6 *2/*41 Normal Metabolizer)

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

Glimepiride (Amaryl)
Actionable

Normal Sensitivity to Glimepiride (CYP2C9 *1/*1 Normal Metabolizer)

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)
Informative

Normal Sensitivity to Glipizide (CYP2C9 *1/*1 Normal Metabolizer)

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)
Actionable

Normal Sensitivity to Glyburide (CYP2C9 *1/*1 Normal Metabolizer)

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)
Informative

Normal Response to Guanfacine

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

Haloperidol (Haldol)
Actionable

Normal Sensitivity to Haloperidol (CYP2D6 *2/*41 Normal Metabolizer)

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

Hydromorphone (Dilaudid, Exalgo)
Informative

Normal Response to Hydromorphone

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

Ibuprofen (Advil, Motrin)
Informative

Normal Sensitivity to Ibuprofen (CYP2C9 *1/*1 Normal Metabolizer)

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

Iloperidone (Fanapt)
Actionable

Normal Sensitivity to Iloperidone (CYP2D6 *2/*41 Normal Metabolizer)
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)
Informative

Normal Sensitivity to Indomethacin (CYP2C9 *1/*1 Normal Metabolizer)
Indomethacin can be prescribed at standard label recommended-dosage and administration.

Irbesartan (Avapro)
Informative

Normal Sensitivity to Irbesartan (CYP2C9 *1/*1 Normal Metabolizer)
Irbesartan can be prescribed at standard label-recommended dosage and administration.

Ketoprofen (Orudis)
Informative

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

Ketorolac (Toradol)
Informative

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

Labetalol (Normodyne, Trandate)
Informative

Normal Response to Labetalol
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)
Informative

Normal Sensitivity to Lacosamide (CYP2C19 *2/*2 Poor Metabolizer)
CYP2C19 is partly involved in the metabolism of lacosamide, along with CYP2C9 and CYP3A. CYP2C19 reduced activity, seen in poor metabolizers, does not affect the pharmacokinetics of lacosamide, but results in lower plasma levels of its O-desmethylmetabolite (pharmacologically inactive). This change is not expected to affect the clinical outcome of this drug. Therefore, lacosamide can be prescribed at standard label-recommended dosage and administration.

Lamotrigine (Lamictal)
Informative

Normal Response to Lamotrigine
Pharmacogenetic guidance: 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.

Lansoprazole (Prevacid)
Actionable

Increased Response to Lansoprazole (CYP2C19 *2/*2 Poor Metabolizer)
Lansoprazole can be prescribed at standard label-recommended dosage and administration. A positive clinical effect is expected in poor metabolizers.

Levetiracetam (Keppra)
Informative

Normal Response to Levetiracetam
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)
Informative

Normal Response to Levomilnacipran
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)
Informative

Normal Response to Levorphanol
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.

Lovastatin (Mevacor)
Informative

Normal Response to Lovastatin (CYP3A4 *1/*1 Normal Metabolizer)
The genotype result indicates that the patient does not carry the CYP3A4*22 allele (this allele is associated with a decreased CYP3A4 enzyme activity). The patient is expected to achieve an optimal lipid control goal with standard lovastatin dose requirements.

Lurasidone (Latuda)
Actionable

Normal Response to Lurasidone
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)
Informative

Normal Sensitivity to Maprotiline (CYP2D6 *2/*41 Normal Metabolizer)
Maprotiline can be prescribed at standard label recommended-dosage and administration.

Meloxicam (Mobic)
Informative

Normal Sensitivity to Meloxicam (CYP2C9 *1/*1 Normal Metabolizer)
Meloxicam plasma concentrations are not expected to be altered. Meloxicam can be prescribed at standard label-recommended dosage and administration.

Memantine (Namenda)
Informative

Normal Response to Memantine

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)
Informative

Normal Response to Meperidine

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)
Informative

Normal Response to Metaxalone

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.

Methocarbamol (Robaxin)
Informative

Normal Response to Methocarbamol

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

Metoclopramide (Reglan)
Informative

Normal Response to Metoclopramide (CYP2D6 *2/*41 Normal Metabolizer)

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

Metoprolol (Lopressor)
Actionable

Normal Sensitivity to Metoprolol (CYP2D6 *2/*41 Normal Metabolizer)

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

Mexiletine (Mexitil)
Actionable

Normal Sensitivity to Mexiletine (CYP2D6 *2/*41 Normal Metabolizer)

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)
Informative

Normal Response to Milnacipran

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

Mirabegron (Myrbetriq)
Actionable

Normal Sensitivity to Mirabegron (CYP2D6 *2/*41 Normal Metabolizer)

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

Mirtazapine (Remeron)
Actionable

Normal Sensitivity to Mirtazapine (CYP2D6 *2/*41 Normal Metabolizer)

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

Nabumetone (Relafen)
Informative

Normal Response to Nabumetone

Pharmacogenetic guidance: Nabumetone is a prodrug, which is converted by CYP1A2 to an active metabolite (6-MNA) that is further metabolized by CYP2C9 to an inactive metabolite. Theoretically, individuals with reduced CYP2C9 activity (i.e CYP2C9 poor metabolizers) may have higher levels of the active metabolite, but it is unknown whether this results in 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.

Naltrexone (Vivitrol)
Informative

Good Response to Naltrexone (OPRM1 A118G AG Altered OPRM1 Function)

Treatment of alcohol dependence: the patient has the OPRM1 118AG heterozygous genotype that is associated with a good clinical outcome with naltrexone therapy. Naltrexone-treated patients carrying the 118A> G mutation are more likely to respond to this drug. They have a higher percentage of days abstinent and a lower percentage of heavy drinking days than those who are not carriers of this mutation.

Naproxen (Aleve)
Informative

Normal Sensitivity to Naproxen

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.

Nebivolol (Bystolic)
Actionable

Normal Sensitivity to Nebivolol (CYP2D6 *2/*41 Normal Metabolizer)

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)
Informative

Normal Sensitivity to Nefazodone (CYP2D6 *2/*41 Normal Metabolizer)

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)
Actionable

Normal Sensitivity to Nortriptyline (CYP2D6 *2/*41 Normal Metabolizer)

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

✓ **Omeprazole (Prilosec)** Actionable	**Increased Response to Omeprazole (CYP2C19 *2/*2 Poor Metabolizer)** Omeprazole can be prescribed at standard label-recommended dosage and administration. A positive clinical effect is expected in poor metabolizers.
✓ **Ondansetron (Zofran)** Actionable	**Normal Response to Ondansetron (CYP2D6 *2/*41 Normal Metabolizer)** Ondansetron can be prescribed at standard label-recommended dosage and administration.
✓ **Oxcarbazepine (Trileptal)** Informative	**Normal Response to Oxcarbazepine** **Pharmacogenetic guidance:** No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** 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). In the presence of enzyme-inducing drugs, the plasma levels of the active metabolite (MHD) are decreased by 30%.
✓ **Oxybutynin (Ditropan)** Informative	**Normal Response to Oxybutynin** **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)** Actionable	**Normal Response to Oxycodone (CYP2D6 *2/*41 Normal Metabolizer)** Oxycodone can be prescribed at standard label-recommended dosage and administration.
✓ **Oxymorphone (Opana, Numorphan)** Informative	**Normal Response to Oxymorphone** 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)** Actionable	**Normal Sensitivity to Paliperidone (CYP2D6 *2/*41 Normal Metabolizer)** Paliperidone can be prescribed at standard label-recommended dosage and administration.
✓ **Palonosetron (Aloxi)** Informative	**Normal response to Palonosetron (CYP2D6 *2/*41 Normal Metabolizer)** Palonosetron can be prescribed at standard label-recommended dosage and administration.
✓ **Pantoprazole (Protonix)** Actionable	**Increased Response to Pantoprazole (CYP2C19 *2/*2 Poor Metabolizer)** Lansoprazole can be prescribed at standard label-recommended dosage and administration. A positive clinical effect is expected in poor metabolizers.
✓ **Paroxetine (Paxil, Brisdelle)** Actionable	**Normal Sensitivity to Paroxetine (CYP2D6 *2/*41 Normal Metabolizer)** Paroxetine can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended until a favorable response is achieved.

Perampanel (Fycompa)
Informative

Normal Response to Perampanel

Pharmacogenetic guidance: No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Perampanel is eliminated either unchanged or following oxidative metabolism by CYP3A4 and CYP3A5. 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)
Actionable

Normal Sensitivity to Perphenazine (CYP2D6 *2/*41 Normal Metabolizer)

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

Phenytoin (Dilantin)
Actionable

Normal Sensitivity to Phenytoin (CYP2C9 *1/*1 Normal Metabolizer)

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.

Pimozide (Orap)
Actionable

Normal Sensitivity to Pimozide (CYP2D6 *2/*41 Normal Metabolizer)

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)
Actionable

Normal Sensitivity to Piroxicam (CYP2C9 *1/*1 Normal Metabolizer)

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

Pitavastatin (Livalo)
Informative

Normal Myopathy Risk (SLCO1B1 521T>C TT Normal Transporter Function)

Pitavastatin plasma concentrations are not expected to increase, and unless other genetic or circumstantial risk factors are present, pitavastatin can be prescribed at standard FDA-recommended starting doses and adjusted based on disease-specific guidelines. The myopathy risk increases with use of the 4 mg daily dose. (Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, high statin dose, comedications, and female gender.)

Prasugrel (Effient)
Actionable

Normal Response to Prasugrel (CYP2C19 *2/*2 Poor Metabolizer)

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.

Pravastatin (Pravachol)
Informative

Normal Myopathy Risk (SLCO1B1 521T>C TT Normal Transporter Function)

Pravastatin plasma concentrations are not expected to increase, and unless other genetic or circumstantial risk factors are present, pravastatin 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.)

✓ **Pregabalin (Lyrica)**
Informative

Normal Response to Pregabalin

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.

✓ **Propafenone (Rythmol)**
Actionable

Normal Sensitivity to Propafenone (CYP2D6 *2/*41 Normal Metabolizer)

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)**
Actionable

Normal Sensitivity to Propranolol (CYP2D6 *2/*41 Normal Metabolizer)

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)**
Actionable

Normal Sensitivity to Protriptyline (CYP2D6 *2/*41 Normal Metabolizer)

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

✓ **Quetiapine (Seroquel)**
Informative

Normal Response to Quetiapine

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)**
Actionable

Increased Response to Rabeprazole (CYP2C19 *2/*2 Poor Metabolizer)

Rabeprazole can be prescribed at standard label-recommended dosage and administration. A positive clinical effect is expected in poor metabolizers.

✓ **Ranolazine (Ranexa)**
Actionable

Normal Sensitivity to Ranolazine (CYP2D6 *2/*41 Normal Metabolizer)

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.

✓ **Risperidone (Risperdal)**
Actionable

Normal Sensitivity to Risperidone (CYP2D6 *2/*41 Normal Metabolizer)

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

✓ **Rivaroxaban (Xarelto)**
Informative

Normal Response to Rivaroxaban

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

✓ **Rosuvastatin (Crestor)**
Informative

Normal Myopathy Risk (SLCO1B1 521T>C TT)

Rosuvastatin plasma concentrations are not expected to increase, and unless other genetic or circumstantial risk factors are present, rosuvastatin can be prescribed at standard FDA-recommended starting doses and adjusted based on disease-specific guidelines. The myopathy risk increases with use of the 40 mg dose. (Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, high statin dose, comedications, and female gender.)

✓ **Rufinamide (Banzel)**
Informative

Normal Response to Rufinamide

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

✓ **Sildenafil (Viagra)**
Informative

Normal Response to Sildenafil

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)**
Informative

Normal Response to Silodosin

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

✓ **Simvastatin (Zocor)**
Actionable

Normal Myopathy Risk (SLCO1B1 521T>C TT Normal Transporter Function)

Simvastatin plasma concentrations are not expected to be elevated, and unless other genetic or circumstantial risk factors are present, simvastatin can be prescribed at standard FDA-recommended starting doses and adjusted based on disease-specific guidelines. **The FDA recommends against the use of the 80 mg daily dose unless the patient had already tolerated this dose for 12 months without evidence of myopathy.** Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, high statin dose, comedications, and female gender.

✓ **Simvastatin (Zocor)**
Informative

Normal Response to Simvastatin (CYP3A4 *1/*1 Normal Metabolizer)

The genotype result indicates that the patient does not carry the CYP3A4*22 allele (this allele is associated with a decreased CYP3A4 enzyme activity). The patient is expected to achieve an optimal lipid control goal with standard simvastatin dose requirements.

✓ **Solifenacin (Vesicare)**
Informative

Normal Response to Solifenacin

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)
Informative

Normal Response to Sufentanil

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

Sulindac (Clinoril)
Informative

Normal Response to Sulindac

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

Tacrolimus (Prograf)
Actionable

Typical response to Tacrolimus (CYP3A5 *3/*3 Poor Metabolizer)

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)
Informative

Normal Response to Tadalafil

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)
Actionable

Normal Response to Tamsulosin (CYP2D6 *2/*41 Normal Metabolizer)

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

Tapentadol (Nucynta)
Informative

Normal Response to Tapentadol

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

Terazosin (Hytrin)
Informative

Normal Response to Terazosin

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)
Actionable

Normal Sensitivity to Thioridazine (CYP2D6 *2/*41 Normal Metabolizer)

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

Thiothixene (Navane)
Informative

Normal Response to Thiothixene

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

Tiagabine (Gabitril)
Informative

Normal Response to Tiagabine

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)
Informative

Normal Response to Ticagrelor (CYP3A5 *3/*3 Poor Metabolizer)

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

Timolol (Timoptic)
Actionable

Normal Sensitivity to Timolol (CYP2D6 *2/*41 Normal Metabolizer)

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

Tolbutamide (Orinase)
Actionable

Normal Sensitivity to Tolbutamide (CYP2C9 *1/*1 Normal Metabolizer)

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)
Informative

Normal Sensitivity to Tolterodine (CYP2D6 *2/*41 Normal Metabolizer)

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

Topiramate (Topamax)
Informative

Normal Response to Topiramate

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

Tramadol (Ultram)
Actionable

Normal Response to Tramadol (CYP2D6 *2/*41 Normal Metabolizer)

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

✓ **Trazodone (Oleptro)**
Informative

Normal Response to Trazodone

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)**
Informative

Normal Response to Trifluoperazine

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)**
Informative

Normal Response to Trospium

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)**
Informative

Normal Response to Valproic acid

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.

✓ **Vardenafil (Levitra)**
Actionable

Normal Response to Vardenafil

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)**
Actionable

Normal Sensitivity to Venlafaxine (CYP2D6 *2/*41 Normal Metabolizer)

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

✓ **Vigabatrin (Sabril)**
Informative

Normal Response to Vigabatrin

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)**
Informative

Normal Response to Vilazodone

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)**
Actionable

Normal Response to Vorapaxar

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 (Brintellix)**
Actionable

Normal Sensitivity to Vortioxetine (CYP2D6 *2/*41 Normal Metabolizer)

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.

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BY EMGENEX & GENETRAIT LABORATORIES

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✓ **Ziprasidone (Geodon)**
Informative

Normal Response to Ziprasidone

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.).

Test Details

Gene	Genotype	Phenotype	Alleles Tested
COMT	Val158Met AA	Low COMT Activity	Val158Met
CYP1A2	*1F/*1F	Normal Metabolizer - Higher Inducibility	*1C, *1F, *1K, *1L
CYP2B6	*1/*5	Unknown Phenotype	*4, *5, *6, *9, *18
CYP2C19	*2/*2	Poor Metabolizer	*2, *3, *4, *4B, *5, *6, *7, *8, *17
CYP2C9	*1/*1	Normal Metabolizer	*2, *3, *5, *6, *11, *14, *27, *8
CYP2D6	*2/*41	Normal Metabolizer	*2, *3, *4, *4M, *6, *7, *8, *9, *10, *17, *19, *20, *29, *41, *5 (gene deletion), XN (gene duplication), *14A, *14B
CYP3A4	*1/*1	Normal Metabolizer	*2, *3, *17, *22
CYP3A5	*3/*3	Poor Metabolizer	*1D, *3, *3C, *6, *7
Factor II	20210G>A GG	Normal Thrombosis Risk	20210G>A
Factor V Leiden	1691G>A GG	Normal Thrombosis Risk	1691G>A
HTR2A	-1438G>A C/C	Homozygous for the C allele (rs6311)	-1438G>A
HTR2C	-759C>T C/C	Homozygous for the C allele (rs3813929)	-759C>T
MTHFR	1298A>C AA	Normal MTHFR Activity	1298A>C
MTHFR	677C>T CT	Reduced MTHFR Activity	677C>T
OPRM1	A118G AG	Altered OPRM1 Function	A118G
SLCO1B1	521T>C TT	Normal Transporter Function	521T>C
VKORC1	-1639G>A G/A	Intermediate Warfarin Sensitivity	-1639G>A

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Please refer to Proteus_Translational Pharmacogenomics Report for further interpretation. Based on the parameters outlined in the Proteus report, the genotype determined by Proteus Labs is used to predict the individual's phenotype. The capacity of the tests to predict clinical outcomes may be altered by the patient's ability to absorb the drug, the ability to metabolize the drug in non-CYP450 pathways, and the ability to eliminate the drug through renal or hepatic excretion. The healthcare professional responsible for this patient’s care should make all clinical decisions on an individual basis and assumes ultimate responsibility for all treatment decisions based on the genotype analysis provided by Proteus Labs, LLC.

The genotyping assays were performed using the Agena MassARRAY iPLEX Platform in order to determine the identity of single nucleotide polymorphism (SNP) within the genes listed in the above table. The assay consists of an initial locus-specific PCR reaction, followed by single base extension using mass-modified dideoxynucleotide terminators of an oligonucleotide primer which anneals immediately upstream of the polymorphic site of interest.

These SNPs were chosen because they affect drug metabolism and/or the risk of drug-induced toxicity or have been associated with risk of disease.

Each test has been validated, and the performance characteristics of the assays have been determined by Proteus Laboratories. The tests have not been cleared or approved by the U.S. Food and Drug Administration because the FDA has determined that such clearance or approval is not necessary.

Laboratory Certification: CLIA # 01D2098265

This test was performed by Proteus Labs, LLC. on behalf of Emgenex.

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Patient Information Card

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

Proteus

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Patient Name	DOB	Requisition ID
Test Patient	**1/1/1980**	**P00000000**

Pharmacogenetic Test Summary

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

VKORC1	-1639G>A G/A	Intermediate Warfarin Sensitivity
MTHFR	1298A>C AA 677C>T CT	No Increased Risk of Hyperhomocysteinemia
Factor II Factor V Leiden	20210G>A GG 1691G>A GG	No Increased Risk of Thrombosis

For a complete report contact Proteus Molecular and Clinical Lab

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