COMPREHENSIVE PHARMACOGENETIC REPORT

PATIENT NAME

DATE OF BIRTH

ORDERING PHYSICIAN

REFFERRING FACILITY

DATE REPORTED

ACCESSION NUMBER

Test Details

Gene	Genotype	Phenotype	Alleles Tested
COMT	Val158Met A/G	Intermediate COMT Activity	Val158Met
CYP1A2	*1A/*1F	Normal Metabolizer - Higher Inducibility	*1C, *1D, *1E, *1F, *1J, *1K, *1L, *1V, *1W
CYP2C19	*1/*1	Normal Metabolizer	*2, *3, *4, *4B, *5, *6, *7, *8, *9, *10, *17
CYP2C9	*1/*2	Intermediate Metabolizer	*2, *3, *4, *5, *6, *11
CYP2D6	*1/*2	Normal Metabolizer	*2, *3, *4, *4M, *6, *7, *8, *9, *10, *12, *14A, *14B, *17, *29, *41, *5 (gene deletion), XN (gene duplication)
CYP3A4	*1/*1	Normal Metabolizer	*1B, *2, *3, *12, *17, *22
CYP3A5	*3/*3	Poor Metabolizer	*2, *3, *3B, *3C, *6, *7, *8, *9
SLCO1B1	521T>C T/T	Normal Function	521T>C
VKORC1 and CYP2C9	-1639G>A G/A, *1/*2	Moderate Sensitivity to Warfarin	-1639G>A

Potentially Impacted Medications

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

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Gastrointestinal	Antiemetics	Aprepitant (Emend-oral) Dolasetron (Anzemet) Dronabinol (Marinol) Fosaprepitant (Emend-i.v) Granisetron (Sancuso, Sustol) Metoclopramide (Reglan) Netupitant-Palonosetron (Akynzeo) Ondansetron (Zofran, Zuplenz) Palonosetron (Aloxi) Rolapitant (Varubi)		
	Proton Pump Inhibitors	Dexlansoprazole (Dexilant, Kapidex) Esomeprazole (Nexium) Lansoprazole (Prevacid) Omeprazole (Prilosec) Pantoprazole (Protonix) Rabeprazole (Aciphex)		
Gaucher Disease	Endocrine-Metabolic Agents	Eliglustat (Cerdelga) Imiglucerase (Cerezyme) Miglustat (Zavesca) Taliglucerase alfa (Elelyso) Velaglucerase alfa (Vpriv)		
Infections	Antifungals	Amphotericin B (AmBisome, Abelcet) Anidulafungin (Eraxis) Caspofungin (Cancidas) Fluconazole (Diflucan) Isavuconazonium (Cresemba) Itraconazole (Sporanox) Micafungin (Mycamine) Posaconazole (Noxafil) Voriconazole (Vfend)		
	Anti-HIV Agents	Dolutegravir (Tivicay, Triumeq) Raltegravir (Isentress, Dutrebis)		
	Antimalarials	Proguanil (Malarone)		

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Pain	Fibromyalgia Agents	Milnacipran (Savella)		
	Muscle Relaxants	Carisoprodol (Soma) Cyclobenzaprine (Flexeril, Amrix) Metaxalone (Skelaxin) Methocarbamol (Robaxin)	Tizanidine (Zanaflex)	
	NSAIDs	Ibuprofen (Advil, Motrin) Ketoprofen (Orudis) Ketorolac (Toradol) Nabumetone (Relafen) Naproxen (Aleve) Sulindac (Clinoril)	Celecoxib (Celebrex) Diclofenac (Voltaren) Flurbiprofen (Ansaid) Indomethacin (Indocin) Meloxicam (Mobic) Piroxicam (Feldene)	
	Opioids	Alfentanil (Alfenta) Buprenorphine (Butrans, Buprenex) Codeine (Codeine; Fioricet with Codeine) Dihydrocodeine (Synalgos-DC) Fentanyl (Actiq) Hydrocodone (Vicodin) Hydromorphone (Dilaudid, Exalgo) Levorphanol (Levo Dromoran) Meperidine (Demerol) Morphine (MS Contin) Oxycodone (Percocet, Oxycontin) Oxymorphone (Opana, Numorphan) Sufentanil (Sufenta) Tapentadol (Nucynta) Tramadol (Ultram)		
	Anti-ADHD Agents	Amphetamine (Adderall, Evekeo) Atomoxetine (Strattera) Clonidine (Kapvay) Dextroamphetamine (Dexedrine) Guanfacine (Intuniv) Lisdexamfetamine (Vyvanse)	Dexmethylphenidate (Focalin) Methylphenidate (Ritalin, Aptensio XR, Concerta, Metadate ER, Quillivant ER)	

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Psychiatry and Neurology	Anticonvulsants	Brivaracetam (Briviact) Cannabidiol (Epidiolex) Carbamazepine (Tegretol, Carbatrol, Epitol) Eslicarbazepine (Aptiom) Ethosuximide (Zarontin) Ezogabine (Potiga) Felbamate (Felbatol) Gabapentin (Neurontin) Lacosamide (Vimpat) Lamotrigine (Lamictal) Levetiracetam (Keppra) Oxcarbazepine (Trileptal, Oxtellar XR) Perampanel (Fycompa) Phenobarbital (Luminal) Pregabalin (Lyrica) Primidone (Mysoline) Rufinamide (Banzel) Stiripentol (Diacomit) Tiagabine (Gabitril) Topiramate (Topamax) Valproic Acid (Depakote, Depakene) Vigabatrin (Sabril) Zonisamide (Zonegran)	Fosphenytoin (Cerebyx) Phenytoin (Dilantin)	
	Antidementia Agents	Donepezil (Aricept) Galantamine (Razadyne) Memantine (Namenda)		
	Antidepressants	Amitriptyline (Elavil) Amoxapine (Amoxapine) Citalopram (Celexa) Clomipramine (Anafranil) Desipramine (Norpramin) Desvenlafaxine (Pristiq) Doxepin (Silenor) Duloxetine (Cymbalta) Escitalopram (Lexapro) Fluoxetine (Prozac, Sarafem) Fluvoxamine (Luvox) Imipramine (Tofranil) Levomilnacipran (Fetzima) Maprotiline (Ludiomil) Mirtazapine (Remeron) Nefazodone (Serzone) Nortriptyline (Pamelor) Paroxetine (Paxil, Brisdelle) Protriptyline (Vivactil) Sertraline (Zoloft) Trazodone (Oleptro) Trimipramine (Surmontil) Venlafaxine (Effexor) Vilazodone (Viibryd) Vortioxetine (Trintellix)		

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
	Antipsychotics	Aripiprazole (Abilify, Aristada) Asenapine (Saphris) Brexpiprazole (Rexulti) Cariprazine (Vraylar) Chlorpromazine (Thorazine) Flupenthixol (Depixol, Fluanxol) Fluphenazine (Prolixin) Haloperidol (Haldol) Iloperidone (Fanapt) Loxapine (Loxitane, Adasuve) Lurasidone (Latuda) Paliperidone (Invega) Perphenazine (Trilafon) Pimavanserin (Nuplazid) Pimozide (Orap) Quetiapine (Seroquel) Risperidone (Risperdal) Thioridazine (Mellaril) Thiothixene (Navane) Trifluoperazine (Stelazine) Ziprasidone (Geodon) Zuclopenthixol (Clopixol)	Clozapine (Clozaril) Olanzapine (Zyprexa)	
	Benzodiazepines	Alprazolam (Xanax) Clobazam (Onfi) Clonazepam (Klonopin) Diazepam (Valium)		
	Other Neurological Agents	Deutetrabenazine (Austedo) Dextromethorphan / Quinidine (Nuedexta) Flibanserin (Addyi) Valbenazine (Ingrezza)	Tetrabenazine (Xenazine)	
Rheumatology	Anti-Hyperuricemics and Anti-Gout Agents	Colchicine (Mitigare) Febuxostat (Uloric) Lesinurad (Zurampic)		
	Immunomodulators	Apremilast (Otezla) Leflunomide (Arava) Tofacitinib (Xeljanz)		
Sjogren's Syndrome	Cholinergic Agonists	Cevimeline (Evoxac)		
Transplantation	Immunosuppressants	Tacrolimus (Prograf)		

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
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)		

Dosing Guidance

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

Celecoxib Celebrex	Possible Sensitivity to Celecoxib (CYP2C9: Intermediate Metabolizer) Celecoxib can be prescribed at standard label-recommended dosage and administration. Evaluate response the first week and be alert to gastrointestinal adverse events.	INFORMATIVE
Clozapine Clozaril	Non-Response to Clozapine (CYP1A2: Normal Metabolizer - Higher Inducibility) Smokers have a high risk for non-response at standard doses and may require higher doses. There is an association between high clozapine doses and the risk of seizures, and therefore careful monitoring is recommended during dosing adjustment. Smoking cessation will increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction is recommended in patients who have quit smoking.	INFORMATIVE
Dexmethylphenidate Focalin	Decreased Response to Dexmethylphenidate (COMT: Intermediate COMT Activity) The patient's genotype result predicts a less optimal response to dexmethylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.	INFORMATIVE
Diclofenac Voltaren	Possible Sensitivity to Diclofenac (CYP2C9: Intermediate Metabolizer) Diclofenac is extensively metabolized by hydroxylation and direct glucuronidation. About 50% of diclofenac is eliminated as a 4-hydroxymetabolite, a reaction mediated by CYP2C9. Other CYP enzymes including CYP2C8, CYP2C19 and CYP3A4 are also involved in the formation of a 5-hydroxymetabolite. A substantial portion of the drug is also directly glucuronidated by UGT2B7 and UGT2B4. Individuals with decreased CYP2C9 activity (i.e intermediate metabolizers) should be closely monitored for increased gastrointestinal adverse events when prescribed diclofenac and lower doses may be more appropriate for these patients.	INFORMATIVE
Flurbiprofen Ansaid	Possible Sensitivity to Flurbiprofen (CYP2C9: Intermediate Metabolizer) The patient may have high plasma levels of the drug. Flurbiprofen can be prescribed at standard label-recommended dosage and administration with closer monitoring for gastrointestinal side effects.	INFORMATIVE
Fluvastatin Lescol	Possible Sensitivity to Fluvastatin (CYP2C9: Intermediate Metabolizer) Increased fluvastatin plasma concentrations due to reduced CYP2C9 activity may occur, resulting in myotoxicity/hepatotoxicity. Consider monitoring the patient for treatment-related adverse effects, and adjust dose as needed. 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.	ACTIONABLE
Fosphenytoin Cerebyx	Moderate Sensitivity to Fosphenytoin (CYP2C9: Intermediate Metabolizer) The genotype results indicate that the patient is a CYP2C9 substrate intermediate metabolizer. Plasma concentrations of phenytoin are likely to increase, resulting in an increased risk of mild to moderate neurological toxicity. Consider a standard loading dose, and reduce the maintenance dose by 25%. Evaluate response and serum concentrations after 7-10 days. Be alert to neurological concentration-related adverse events.	ACTIONABLE
Indomethacin Indocin	Possible Sensitivity to Indomethacin (CYP2C9: Intermediate Metabolizer) Indomethacin is metabolized mainly by O-demethylation to its inactive metabolite O-desmethylindomethacin, a reaction catalyzed by CYP2C9. At standard doses, indomethacin plasma concentrations may be higher in individuals with decreased CYP2C9 function. Although indomethacin can be prescribed at standard label recommended-dosage and administration, a closer monitoring for signs of gastrointestinal toxicity during long-term administration is recommended.	INFORMATIVE
Meloxicam Mobic	Possible Sensitivity to Meloxicam (CYP2C9: Intermediate Metabolizer) Meloxicam plasma concentrations may be higher in individual with decreased CYP2C9 function. A reduction in meloxicam dosage may be needed with a closer monitoring for signs of gastrointestinal toxicity during long-term administration.	INFORMATIVE

⚠ Methylphenidate Ritalin, Aptensio XR, Concerta, Metadate ER, Quillivant ER	Decreased Response to Methylphenidate (COMT: Intermediate COMT Activity) The patient's genotype result predicts a less optimal response to methylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.	INFORMATIVE
⚠ Olanzapine Zyprexa	Non-Response to Olanzapine (CYP1A2: 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.	INFORMATIVE
⚠ Phenytoin Dilantin	Moderate Sensitivity to Phenytoin (CYP2C9: Intermediate Metabolizer) The genotype results indicate that the patient is a CYP2C9 substrate intermediate metabolizer. Plasma concentrations of phenytoin are likely to increase, resulting in an increased risk of mild to moderate neurological toxicity. Consider a standard loading dose, and reduce the maintenance dose by 25%. Evaluate response and serum concentrations after 7-10 days. Be alert to neurological concentration-related adverse events.	ACTIONABLE
⚠ Piroxicam Feldene	Possible Sensitivity to Piroxicam (CYP2C9: Intermediate Metabolizer) Piroxicam plasma concentrations may be higher in individual with decreased CYP2C9 function. Although piroxicam can be prescribed at standard label-recommended dosage and administration, a closer monitoring for signs of gastrointestinal toxicity during long-term administration is recommended.	INFORMATIVE
⚠ Tetrabenazine Xenazine	Normal Sensitivity to Tetrabenazine (CYP2D6: Normal Metabolizer) For treating chorea associated with Huntington's disease: Individualization of dose with careful weekly titration is required. The first week's starting dose is 12.5 mg daily; second week, 25 mg (12.5 mg twice daily); then slowly titrate at weekly intervals by 12.5 mg to a tolerated dose. The maximum daily dose in CYP2D6 normal metabolizers is 100 mg, with a maximum single dose of 37.5 mg . If serious adverse events occur, titration should be stopped and the dose of tetrabenazine should be reduced. If the adverse event(s) do not resolve, consider withdrawal of tetrabenazine.	ACTIONABLE
⚠ Tizanidine Zanaflex	Possible Non-Response to Tizanidine (CYP1A2: 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.	INFORMATIVE
⚠ Warfarin Coumadin	Moderate Sensitivity to Warfarin (CYP2C9 *1/*2 VKORC1 -1639G>A G/A) Initiation Therapy: a dose decrease may be required. Consider using the following warfarin dose range provided in the FDA-approved label: 3-4 mg/day. OR consider using a personalized dose as calculated by a pharmacogenetic algorithm. The estimated time to reach steady state is 8-10 days.	ACTIONABLE
✓ Alfentanil Alfenta	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.	INFORMATIVE

✓	**Alfuzosin** UroXatral	**Normal Response to Alfuzosin** — INFORMATIVE Pharmacogenetic guidance: No genetically-guided drug selection or dosing recommendations are available. Polypharmacy guidance: Alfuzosin is extensively metabolized by CYP3A4 into pharmacologically inactive metabolites. Alfuzosin is contraindicated with strong CYP3A4 inhibitors, as the risk for QTc prolongation induced by this drug is increased at higher concentrations . Take caution when this drug is prescribed with CYP3A4 moderate inhibitors, as drug levels may increase.
✓	**Alprazolam** Xanax	**Normal Response to Alprazolam** — INFORMATIVE Pharmacogenetic guidance: Alprazolam is primarily eliminated by metabolism via CYP3A4 and CYP3A5. Genetic polymorphisms of these genes are not expected to affect the efficacy or safety profiles of this drug. Polypharmacy guidance: The concomitant use of alprazolam with CYP3A4 inhibitors may result in increased alprazolam levels and prolonged sedation. Impairment of motor skills are also observed with some combinations. Monitor patients for exaggerated sedative effects. If possible, alprazolam should be avoided in patients receiving strong inhibitors of CYP3A4 such as ketoconazole, itraconazole and ritonavir. Drugs that induce CYP3A enzymes may decrease alprazolam levels, which results in a loss of efficacy.
✓	**Amitriptyline** Elavil	**Normal Sensitivity to Amitriptyline (CYP2D6: Normal Metabolizer)** — ACTIONABLE Amitriptyline can be prescribed at standard label-recommended dosage and administration.
✓	**Amitriptyline** Elavil	**Normal Sensitivity to Amitriptyline (CYP2C19: Normal Metabolizer)** — ACTIONABLE Amitriptyline can be prescribed at standard label-recommended dosage and administration.
✓	**Amoxapine** Amoxapine	**Normal Sensitivity to Amoxapine (CYP2D6: Normal Metabolizer)** — INFORMATIVE Amoxapine can be prescribed at standard label recommended-dosage and administration.
✓	**Amphetamine** Adderall, Evekeo	**Normal Exposure to Amphetamine (CYP2D6: Normal Metabolizer)** — INFORMATIVE Amphetamine can be prescribed at standard label-recommended dosage and administration. Individualize the dosage according to the therapeutic needs and response of the patient.
✓	**Amphetamine** Adderall, Evekeo	**Good Response to Amphetamine salts (COMT: Intermediate COMT Activity)** — INFORMATIVE The patient's genotype result predicts a favorable response to amphetamine stimulants. Amphetamines should be administered at the lowest effective dose, and dosage should be individually adjusted.
✓	**Amphotericin B** AmBisome, Abelcet	**Normal Response to Amphotericin B** — ACTIONABLE Pharmacogenetic guidance: Amphotericin B is excreted very slowly (over weeks to months) by the kidneys with 2 to 5% of a given dose being excreted in the biologically active form. Details of possible metabolic pathways are unknown. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Nephrotoxic medications such as aminoglycosides, cyclosporine, and pentamidine may enhance the potential for amphotericin B-induced renal toxicity, and should be used concomitantly only with great caution. Intensive monitoring of renal function is recommended in patients requiring any combination of nephrotoxic medications.
✓	**Anidulafungin** Eraxis	**Normal Response to Anidulafungin** — ACTIONABLE Pharmacogenetic guidance: Anidulafungin undergoes slow chemical degradation to a peptide that lacks antifungal activity and which is subsequently converted to peptidic degradants and eliminated. Hepatic metabolism of anidulafungin has not been observed. Anidulafungin is not a substrate, inducer, or inhibitor of cytochrome P450 enzymes. No genetically guided drug selection or dosing recommendations are available.

Apixaban
Eliquis

Normal Response to Apixaban
INFORMATIVE

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

Apremilast
Otezla

Normal Response to Apremilast
ACTIONABLE

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

Aprepitant
Emend-oral

Normal Response to Aprepitant
ACTIONABLE

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

Aripiprazole
Abilify, Aristada

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

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

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

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

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

Asenapine
Saphris

Normal Response to Asenapine — INFORMATIVE

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

Atenolol
Tenormin

Normal Response to Atenolol — INFORMATIVE

Pharmacogenetic guidance: The bioavailability of atenolol is approximately 40–50% and renal excretion eliminates approximately 90% of the absorbed drug in its unchanged form. A negligible amount of the drug is metabolized. Atenolol is a substrate of several organic anion and cation transporters including SLC22A1, SLC22A2, SLC47A1, and SLC47A2. No genetically-guided drug selection or dosing recommendations are available.

Atomoxetine
Strattera

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

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

Atorvastatin
Lipitor

Normal Myopathy Risk (SLCO1B1: Normal Function) — INFORMATIVE

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

Normal Response to Atorvastatin (CYP3A4: Normal Metabolizer) — INFORMATIVE

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

Normal Response to Avanafil — INFORMATIVE

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

Azilsartan
Edarbi, Edarbyclor

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

Azilsartan medoxomil is hydrolyzed to azilsartan, its active metabolite, in the gastrointestinal tract during absorption. Azilsartan is further metabolized to inactive metabolites by CYP2C9. Consider standard label-recommended dosage and administration.

Betrixaban
Bevyxxa

Normal Response to Betrixaban — ACTIONABLE

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

Bisoprolol
Zebeta

Normal Response to Bisoprolol — INFORMATIVE

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

Brexpiprazole
Rexulti

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

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

Adjunctive Treatment of Major Depression Disorder : the recommended starting doses are 0.5 mg or 1 mg once daily. The daily maintenance doses and maximum recommended dose are 1-2 mg and 3 mg, respectively. Schizophrenia : the recommended starting dose is 1 mg once daily. The daily maintenance doses and maximum recommended dose are 2-4 mg and 4 mg, respectively.

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

Brivaracetam
Briviact

Normal Sensitivity to Brivaracetam (CYP2C19: Normal Metabolizer) — ACTIONABLE

Brivaracetam is primarily metabolized by hydrolysis and to a minor extent by hydroxylation, which is mediated by CYP2C19. Brivaracetam can be prescribed at the standard label recommended dosage.

Buprenorphine
Butrans, Buprenex

Normal Response to Buprenorphine — INFORMATIVE

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

Candesartan
Atacand

Normal Sensitivity to Candesartan Cilexetil — ACTIONABLE

Pharmacogenetic guidance: Candesartan cilexetil is hydrolyzed to candesartan its active metabolite in the gastrointestinal tract during absorption. Candesartan undergoes minor hepatic metabolism by O-deethylation to an inactive metabolite. Genetic variability of the cytochrome P450 genes is not expected to affect the patient's response to candesartan cilexetil. No genotype-based dosing adjustments are available.

Cannabidiol
Epidiolex

Normal Response to Cannabidiol — INFORMATIVE

Pharmacogenetic guidance: Cannabidiol is metabolized to oxidative metabolites by CYP3A4 and CYP2C19 and by direct glucuronidation. There are insufficient studies documenting the impact of genetic polymorphisms of these metabolizing enzymes on cannabidiol response. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Enzyme-inducing drugs increase cannabidiol clearance significantly, and careful titration is recommended when the drug is prescribed with enzyme-inducing-antiepileptic drugs. Coadministration of CYP3A4 inhibitors increase cannabidiol exposure by 2-fold, and a dose reduction should be considered in presence of CYP3A inhibitors.

Carbamazepine
Tegretol, Carbatrol, Epitol

Normal Response to Carbamazepine — INFORMATIVE

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

Cariprazine
Vraylar

Normal Response to Cariprazine — ACTIONABLE

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

Carisoprodol
Soma

Normal Sensitivity to Carisoprodol (CYP2C19: Normal Metabolizer) — INFORMATIVE

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

Carvedilol
Coreg

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

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

Caspofungin
Cancidas

Normal Response to Caspofungin — ACTIONABLE

Pharmacogenetic guidance: Caspofungin is cleared slowly and is metabolized by hydrolysis and N-acetylation. The drug undergoes also spontaneous chemical degradation. Distribution, rather than excretion or biotransformation, is the dominant mechanism influencing plasma clearance. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Co-administration of caspofungin with metabolizing enzyme inducers (e.g., rifampin, efavirenz, nevirapine, phenytoin, or carbamazepine) may result in clinically meaningful reductions in caspofungin concentrations which may require dosing adjustment.

Cevimeline
Evoxac

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

Cevimeline can be prescribed according to standard label-recommended dosage and administration.

Chlorpromazine
Thorazine

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

Chlorpromazine is metabolized by CYP2D6, CYP3A4 and flavin-containing monooxygenases. This drug can be prescribed at standard label recommended-dosage and administration. Careful titration is recommended until a favorable response is achieved.

Chlorpropamide
Diabenese

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

Chlorpropamide is metabolized by CYP2C9, and while this clearance pathway is diminished in subjects with reduced CYP2C9 activity, such change has not been shown to be of clinical significance. Therefore, this drug can be prescribed according to standard label-recommended dosage and administration (dose titration in response to plasma levels of glucose/glycosylated hemoglobin).

Citalopram
Celexa

Normal sensitivity to Citalopram (CYP2C19: Normal Metabolizer) — ACTIONABLE

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

Clobazam
Onfi

Normal Sensitivity to Clobazam (CYP2C19: Normal Metabolizer) — ACTIONABLE

Clobazam can be prescribed at standard label-recommended dosage and administration. Individualize dosing within each body weight group, based on clinical efficacy and tolerability. Do not proceed with dose escalation more rapidly than weekly, because serum concentrations of clobazam and its active metabolite require 5 and 9 days, respectively, to reach steady state. Recommended daily dosing: ≤30 kg body weight: starting dose 5 mg; day 7: 10 mg and day 14: 20 mg; >30 kg body weight: starting dose 10 mg, day 7: 20 mg and day 14: 40 mg.

✓ Clomipramine Anafranil	Normal Sensitivity to Clomipramine (CYP2D6: Normal Metabolizer) Clomipramine can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended with monitoring until a favorable response is achieved.	ACTIONABLE
✓ Clomipramine Anafranil	Normal Sensitivity to Clomipramine (CYP2C19: Normal Metabolizer) Clomipramine can be prescribed at standard label-recommended dosage and administration.	ACTIONABLE
✓ Clonazepam Klonopin	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.	INFORMATIVE
✓ Clonidine Kapvay	Normal Sensitivity to Clonidine (CYP2D6: 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.	INFORMATIVE
✓ Clopidogrel Plavix	Normal Response to Clopidogrel (CYP2C19: Normal Metabolizer) Clopidogrel can be prescribed at standard label-recommended dosage.	ACTIONABLE
✓ Codeine Codeine; Fioricet with Codeine	Normal Response to Codeine (CYP2D6: Normal Metabolizer) Codeine can be prescribed at standard label-recommended dosage and administration.	ACTIONABLE
✓ Colchicine Mitigare	Normal Response to Colchicine Pharmacogenetic guidance: Colchicine in eliminated both by renal excretion and metabolism. While 50% of the absorbed dose in eliminated unchanged in urine, less than 20% is metabolized by CYP3A4. Glucuronidation is also a metabolic pathway for colchicine. Colchicine is a substrate of P-glycoprotein (encoded by ABCB1 gene) and its efflux by this transporter is important in its disposition. Colchicine has a narrow therapeutic index. Preliminary and limited studies indicate a lack of an effect of CYP3A4 or ABCB1 genetic polymorphisms on clinical response to colchicine in individuals with familial Mediterranean fever (FMF). There are no available genetically-guided drug selection or dosing recommendations. Polypharmacy guidance: Because colchicine is a substrate for both the CYP3A4 metabolizing enzyme and the P-glycoprotein efflux transporter, inhibition of either of these pathways may lead to colchicine-related toxicity. Inhibition of both CYP3A4 and P-gp by dual inhibitors such as clarithromycin has been reported to produce life-threatening or fatal colchicine toxicity due to significant increases in systemic colchicine levels. Therefore, concomitant use of colchicine and inhibitors of CYP3A4 or P-glycoprotein should be avoided.	INFORMATIVE
✓ Cyclobenzaprine Flexeril, Amrix	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.	INFORMATIVE

Dabigatran Etexilate
Pradaxa

Normal Response to Dabigatran — INFORMATIVE

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

Darifenacin
Enablex

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

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

Desipramine
Norpramin

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

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

Desvenlafaxine
Pristiq

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

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

Deutetrabenazine
Austedo

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

For treating chorea associated with Huntington's disease: Individualization of dose with careful weekly titration is required. The first week's starting dose is 6 mg once daily then slowly titrate at weekly intervals by 6 mg per day to a tolerated dose up to a maximum recommended daily dosage of 48 mg (24 mg twice daily).

Dexlansoprazole
Dexilant, Kapidex

Normal Response to Dexlansoprazole (CYP2C19: Normal Metabolizer) — INFORMATIVE

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

Dextroamphetamine
Dexedrine

Normal Exposure to Dextroamphetamine (CYP2D6: Normal Metabolizer) — INFORMATIVE

Dextroamphetamine can be prescribed at standard label-recommended dosage and administration. Individualize the dosage according to the therapeutic needs and response of the patient.

Dextroamphetamine
Dexedrine

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

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

Dextromethorphan / Quinidine
Nuedexta

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

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

✓ Diazepam Valium	Normal Sensitivity to Diazepam (CYP2C19: Normal Metabolizer) Diazepam can be prescribed at standard label-recommended dosage and administration.	INFORMATIVE
✓ Dihydrocodeine Synalgos-DC	Normal Response to Dihydrocodeine (CYP2D6: Normal Metabolizer) Dihydrocodeine can be prescribed at standard label-recommended dosage and administration.	INFORMATIVE
✓ Dolasetron Anzemet	Normal Response to Dolasetron (CYP2D6: Normal Metabolizer) Dolasetron can be prescribed at standard label-recommended dosage and administration.	INFORMATIVE
✓ Dolutegravir Tivicay, Triumeq	Normal Response to Dolutegravir Pharmacogenetic guidance: Dolutegravir is eliminated mainly through metabolism by UGT1A1 and a minor contribution from CYP3A. Although UGT1A1 poor metabolizers or patients taking inhibitors of UGT1A1 activity have increased plasma levels of dolutegravir, these changes are not clinically significant. No dosing adjustments are required for dolutegravir due to genetic variations in UGT1A1. Polypharmacy guidance : Coadministration of dolutegravir with drugs that are strong enzyme inducers, such as rifampin, may result in reduced plasma concentrations of this drug.	ACTIONABLE
✓ Donepezil Aricept	Normal Response to Donepezil (CYP2D6: Normal Metabolizer) Donepezil can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended until a favorable response is achieved.	INFORMATIVE
✓ Doxazosin Cardura	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.	INFORMATIVE
✓ Doxepin Silenor	Normal Sensitivity to Doxepin (CYP2D6: Normal Metabolizer) Doxepin can be prescribed at standard label-recommended dosage and administration.	ACTIONABLE
✓ Doxepin Silenor	Normal Sensitivity to Doxepin (CYP2C19: Normal Metabolizer) Doxepin can be prescribed at standard label-recommended dosage and administration.	ACTIONABLE
✓ Dronabinol Marinol	Normal Sensitivity to Dronabinol (CYP2C9: Intermediate Metabolizer) The patient's genotype predicts a reduced CYP2C9 metabolic activity. Dronabinol can be prescribed at standard label-recommended dosage and administration.	INFORMATIVE
✓ Duloxetine Cymbalta	Normal Sensitivity to Duloxetine (CYP2D6: Normal Metabolizer) Duloxetine can be prescribed at standard label-recommended dosage and administration.	INFORMATIVE
✓ Dutasteride Avodart	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.	INFORMATIVE

Edoxaban
Savaysa

Normal Response to Edoxaban — INFORMATIVE

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

Eliglustat
Cerdelga

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

Eliglustat can be prescribed according to standard label-recommended dosage and administration (84 mg orally twice daily).
Dose adjustments with comedications: Co-administration of eliglustat with drugs that inhibit CYP2D6 and CYP3A may significantly increase the exposure to eliglustat and result in prolongation of the PR, QTc, and/or QRS cardiac interval, which could result in cardiac arrhythmias. Eliglustat is contraindicated if a strong/moderate CYP2D6 inhibitor AND a strong/moderate CYP3A inhibitor are co-administered. Reduce the dosage of eliglustat to 84 mg once daily if the patient is also taking strong/moderate CYP2D6 inhibitors or strong/moderate CYP3A inhibitors.

Eprosartan
Teveten

Normal Sensitivity to Eprosartan — ACTIONABLE

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

Escitalopram
Lexapro

Normal Sensitivity to Escitalopram (CYP2C19: Normal Metabolizer) — ACTIONABLE

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

Eslicarbazepine
Aptiom

Normal Response to Eslicarbazepine — INFORMATIVE

Pharmacogenetic guidance: Genotype results obtained from the pharmacogenetic test performed in this patient cannot be used to identify patients at risk for severe cutaneous adverse reactions such as anticonvulsant hypersensitivity syndrome, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Eslicarbazepine acetate (prodrug) is converted by a reductase to its active metabolite, eslicarbazepine. Eslicarbazepine is eliminated primarily by renal excretion unchanged and as a glucuronide conjugate. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: In the presence of enzyme-inducing drugs, eslicarbazepine plasma levels are significantly decreased, and higher doses of the drug may be needed.

Esomeprazole
Nexium

Normal Response to Esomeprazole (CYP2C19: Normal Metabolizer) — ACTIONABLE

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

Ethosuximide
Zarontin

Normal Response to Ethosuximide — INFORMATIVE

Pharmacogenetic guidance: No genetically guided drug selection or dosing recommendations are available.
Polypharmacy guidance: ethosuximide is extensively metabolized by CYP3A4, and therefore this drug should be used with caution when prescribed with CYP3A4 inhibitors. Inducers of CYP3A4 increase ethosuximide clearance, and higher doses may be needed when the drug is coadministered with enzyme-inducing drugs.

Ezogabine
Potiga

Normal Response to Ezogabine — INFORMATIVE

Pharmacogenetic guidance: although NAT2 rapid acetylators have a 30% increase in the exposure of ezogabine active metabolite, no dose adjustment is necessary in these individuals. Polypharmacy guidance: Ezogabine is extensively metabolized primarily via glucuronidation (by UGT1A4 and UGT1A1) and acetylation (by NAT2). There is no evidence of oxidative metabolism of ezogabine by cytochrome P450 enzymes, and genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Enzyme-inducing drugs such as carbamazepine and phenytoin increase ezogabine clearance by 30%, and dose increase should be considered when this drug is coadministered with enzyme-inducing antiepileptic drugs.

Febuxostat
Uloric

Normal Response to Febuxostat — INFORMATIVE

Pharmacogenetic guidance: Febuxostat is eliminated by both hepatic metabolism and renal excretion. The drug is metabolized both by glucuronidation and oxidative pathways. The oxidative metabolism of this drug involves several cytochrome P450 enzymes (CYPs): CYP1A2, CYP2C8 and CYP2C9 as well as other non-CYP enzymes. Febuxostat is also metabolized to an acyl glucuronide, primarily by UGT1A1 with contributions from UGT1A3, UGT1A9 and UGT2B7. There are no available genetically-guided drug selection or dosing recommendations. Polypharmacy guidance: Concomitant administration of probenecid a xanthine oxidase inhibitor, with substrate drugs such as theophylline, azathioprine or mercaptopurine could increase plasma concentrations of these drugs resulting in severe toxicity.

Felbamate
Felbatol

Normal Response to Felbamate — INFORMATIVE

Pharmacogenetic guidance: No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: About 40-50% of absorbed felbamate dose appears unchanged in urine, and an additional 50% is present as metabolites and conjugates. Felbamate is a substrate of CYP3A4 and CYP2E1, but these pathways are minor for drug elimination when the drug is given as a monotherapy. This pathway is enhanced by concomitant use of enzyme-inducing antiepileptic drugs, which results in a 30-50% decrease in felbamate plasma concentrations. Felbamate should be titrated slowly, and dose adjustment must be considered in presence of inducers.

Fentanyl
Actiq

Normal Response to Fentanyl — INFORMATIVE

Pharmacogenetic guidance: Preliminary findings indicate that fentanyl exposure is 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: Fentanyl, a narrow therapeutic window drug, is extensively metabolized by CYP3A4 and CYP3A5. The concomitant use of fentanyl with all CYP3A4 inhibitors may result in an increase in fentanyl plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression . Monitor patients receiving fentanyl and any CYP3A4 inhibitor. Inducers of CYP3A4/5 may decrease the concentration and the response of this drug.

Fesoterodine
Toviaz

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

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

Finasteride
Proscar

Normal Response to Finasteride — INFORMATIVE

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

Flecainide
Tambocor

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

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

Flibanserin
Addyi

Normal Exposure to Flibanserin (CYP2C19: Normal Metabolizer) — ACTIONABLE

For treating premenopausal women with acquired, generalized hypoactive sexual desire disorder (HSDD): Flibanserin is primarily metabolized by CYP3A4 and, to a lesser extent, by CYP2C19. The genotype results predict that the patient is expected to have a normal clearance and a typical exposure to flibanserin. Use label-recommended dosage and follow standard precautions.

Fluconazole
Diflucan

Normal Response to Fluconazole — ACTIONABLE

Pharmacogenetic guidance: Fluconazole not extensively metabolized and is eliminated primarily by renal excretion, with approximately 80% of the administered dose appearing in the urine as unchanged drug and 11% as metabolites. The pharmacokinetics of fluconazole is markedly affected by reduction in renal function. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Fluconazole is a moderate inhibitor of CYP3A4, CYP2C9 and CYP2C19 enzymes. Fluconazole treated patients who are concomitantly treated with drugs with a narrow therapeutic window metabolized by CYP2C9, CYP2C19 or CYP3A4 should be monitored. The enzyme inhibiting effect of fluconazole persists 4-5 days after discontinuation of the drug due to its long half-life.

Fluoxetine
Prozac, Sarafem

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

Fluoxetine is metabolized to its active metabolite norfluoxetine and to other metabolites by multiple enzymes including CYP2D6, CYP2C19, CYP2C9, and CYP3A4. Fluoxetine can be prescribed at standard label-recommended dosage and administration.

Flupenthixol
Depixol, Fluanxol

Normal Response to Flupenthixol — ACTIONABLE

Pharmacogenetic guidance: Flupenthixol is metabolized via sulphoxidation, N-dealkylation and glucuronic acid conjugation. No genetically guided drug selection or dosing recommendations are available. Polypharmacy Guidance: Flupenthixol may increase QT interval and therefore co-administration of other drugs known to significantly increase the QT interval should be avoided.

Fluphenazine
Prolixin

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

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

Fluvoxamine
Luvox

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

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

Fondaparinux
Arixtra

Normal Response to Fondaparinux — INFORMATIVE

Pharmacogenetic guidance: Fondaparinux is eliminated unchanged through renal excretion and is not metabolized by CYPs, and therefore genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. no genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: The concomitant use of fondaparinux with aspirin or NSAIDS may enhance the risk of hemorrhage. Discontinue agents that may enhance the risk of hemorrhage prior to initiation of therapy with fondaparinux unless essential. If co-administration is necessary, monitor patients closely for hemorrhage.

Fosaprepitant
Emend-i.v

Normal Response to Fosaprepitant — ACTIONABLE

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

Gabapentin
Neurontin

Normal Response to Gabapentin — INFORMATIVE

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

Galantamine
Razadyne

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

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

Gefitinib
Iressa

Normal Exposure to Gefitinib (CYP2D6: Normal Metabolizer) — ACTIONABLE

Gefitinib undergoes extensive hepatic metabolism in humans by CYP3A4 and CYP2D6. CYP2D6 metabolizes gefitinib to its major active metabolite, O-desmethyl gefitinib. The patient's genotype predicts a normal exposure to gefitinib. Gefitinib can be prescribed at label-recommended dosage and administration.

Glimepiride
Amaryl

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

Glimepiride is metabolized by CYP2C9, and while this clearance pathway is diminished in subjects with reduced CYP2C9 activity, such change has not been shown to be of clinical significance. Therefore, this drug can be prescribed according to standard label-recommended dosage and administration (dose titration in response to plasma levels of glucose/glycosylated hemoglobin).

Glipizide
Glucotrol

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

Glipizide is metabolized partially by CYP2C9, and while this clearance pathway is diminished in subjects with reduced CYP2C9 activity, such change has not been shown to be of clinical significance. Therefore, this drug can be prescribed according to standard label-recommended dosage and administration (dose titration in response to plasma levels of glucose/glycosylated hemoglobin).

Glyburide
Micronase

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

Glyburide is metabolized partially by CYP2C9, and while this clearance pathway is diminished in subjects with reduced CYP2C9 activity, such change has not been shown to be of clinical significance. Therefore, this drug can be prescribed according to standard label-recommended dosage and administration (dose titration in response to plasma levels of glucose/glycosylated hemoglobin).

Granisetron
Sancuso, Sustol

Normal Response to Granisetron — ACTIONABLE

Pharmacogenetic guidance: Granisetron is extensively metabolized to 7-hydroxygranisetron and 9-desmethylgranisetron by CYP3A4, CYP3A5 and CYP1A1. A preliminary pharmacokinetic study conducted in pregnant women reported an increased granisetron clearance in carriers of the CYP1A1*2A increased function allele and a lower clearance of the drug in subjects with the CYP3A5*3/*3 genotype. The same study showed that genetic polymorphisms within the CYP3A4 or ABCB1 genes, had no effect on granisetron clearance while other reports in cancer patients found an association with granisetron efficacy and ABCB1 genetic polymorphisms. The significance of these preliminary findings is unclear and no genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Inducers or inhibitors of CYP1A1 and CYP3A4 enzymes may affect the clearance of granisetron. However, the potential for an in vivo pharmacokinetic interaction with strong CYP3A4 inhibitors such as ketoconazole is not known. Administration of granisetron with metabolizing enzyme inducers, results in a 25% increase in granisetron clearance and the clinical significance of this change is not known.

✓	Guanfacine Intuniv	Normal Response to Guanfacine Pharmacogenetic guidance: Guanfacine is predominantly metabolized by CYP3A4. No genetically guided drug selection or dosing recommendations are available and guanfacine extended-release should be titrated based on the clinical response and tolerability of the individual patient. Polypharmacy guidance : The dose of guanfacine extended-release should be reduced to one half of the standard dose when co-medicated with a strong CYP3A4 inhibitor (e.g., ketoconazole, itraconazole, indinavir, ritonavir, nefazodone). When the strong CYP3A4 inhibitor is discontinued, the dose should be increased to the standard recommended dose. Guanfacine dose should be increased up to double the recommended dose when used in combination with a strong CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, St. John's wort etc.). When the CYP3A4 inducer is discontinued, the dose should be reduced to the standard recommended dose within 7-14 days.	INFORMATIVE
✓	Haloperidol Haldol	Normal Sensitivity to Haloperidol (CYP2D6: Normal Metabolizer) Haloperidol can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended until a favorable response is achieved.	ACTIONABLE
✓	Hydrocodone Vicodin	Normal Response to Hydrocodone (CYP2D6: Normal Metabolizer) Hydrocodone can be prescribed at standard label-recommended dosage and administration.	INFORMATIVE
✓	Hydromorphone Dilaudid, Exalgo	Normal Response to Hydromorphone No genetically guided drug selection or dosing recommendations are available. Hydromorphone is not metabolized by CYPs, and genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Hydromorphone can be prescribed at standard label-recommended dosage and administration.	INFORMATIVE
✓	Ibuprofen Advil, Motrin	Normal Sensitivity to Ibuprofen (CYP2C9: Intermediate Metabolizer) Ibuprofen is extensively metabolized into hydroxylate or carboxylate metabolites by CYP2C8 and CYP2C9. Individuals with a moderately decreased CYP2C9 activity (i.e intermediate metabolizers) can be prescribed ibuprofen according to standard label recommended-dosage and administration.	INFORMATIVE
✓	Iloperidone Fanapt	Normal Sensitivity to Iloperidone (CYP2D6: 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.	ACTIONABLE
✓	Imiglucerase Cerezyme	Normal Response to Imiglucerase Pharmacogenetic guidance: Imiglucerase is a monomeric glycoprotein enzyme produced by recombinant DNA technology. Imiglucerase dosage should be individualized to each patient. Individual patient dosage may require increase or decrease based on therapeutic goals. Imiglucerase is not metabolized by the CYP450 enzymes. No genetically-guided drug selection or dosing recommendations are available.	ACTIONABLE
✓	Imipramine Tofranil	Normal Sensitivity to Imipramine (CYP2D6: Normal Metabolizer) Imipramine can be prescribed at standard label-recommended dosage and administration.	ACTIONABLE
✓	Imipramine Tofranil	Normal Sensitivity to Imipramine (CYP2C19: Normal Metabolizer) Imipramine can be prescribed at standard label-recommended dosage and administration.	ACTIONABLE

Irbesartan
Avapro

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

The plasma concentrations of irbesartan may be higher than expected, but its efficacy and safety profiles are not affected. Consider standard label-recommended dosage and administration.

Isavuconazonium
Cresemba

Normal Response to Isavuconazonium — ACTIONABLE

Pharmacogenetic guidance: Isavuconazonium sulfate is a prodrug that is rapidly hydrolyzed in plasma by butylcholinesterase into its active moiety isavuconazole. Isavuconazole is extensively metabolized CYP3A4 and CYP3A5 and Common genetic polymorphism of these metabolizing enzymes gene are not expected to affect isavuconazole exposure. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Isavuconazole is a sensitive CYP3A4 substrate and its use with strong CYP3A4 inhibitors or inducers contraindicated.

Itraconazole
Sporanox

Normal Response to Itraconazole — ACTIONABLE

Pharmacogenetic guidance: Itraconazole is extensively metabolized to several metabolites by CYP3A4. The main metabolite is hydroxy-itraconazole, which has in vitro antifungal activity comparable to itraconazole; trough plasma concentrations of this metabolite are about twice those of itraconazole. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Coadministration of itraconazole with potent CYP3A4 inducers may decrease the bioavailability of itraconazole and hydroxy-itraconazole to such an extent that efficacy may be reduced. Therefore, administration of potent CYP3A4 inducers with itraconazole is not recommended and the use of these drugs should be avoided 2 weeks before and during treatment with itraconazole. Potent CYP3A4 inhibitors may increase the bioavailability of itraconazole and these drugs should be used with caution when coadministered with this antifungal. Itraconazole inhibit the metabolism of drugs metabolized by CYP3A4 or transported by P-glycoprotein, which may result in increased plasma concentrations of these drugs and/or their active metabolite(s) when they are coadministered. These elevated plasma concentrations may increase or prolong both therapeutic and adverse effects of these drugs. When using concomitant medication, it is recommended that the corresponding label be consulted for information on possible contraindications or need for dose adjustments.

Ketoprofen
Orudis

Normal Response to Ketoprofen — INFORMATIVE

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

Ketorolac
Toradol

Normal Response to Ketorolac — INFORMATIVE

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

Labetalol
Normodyne, Trandate

Normal Response to Labetalol — INFORMATIVE

Pharmacogenetic guidance: Labetalol is extensively metabolized by UGT2B7, UGT1A1, and CYP2C19 to inactive metabolites. Preliminary studies indicate that following a single 200-mg oral dose, labetalol plasma concentrations are 2.9-fold higher in Chinese individuals with the CYP2C19 *2/*2 genotype than those with the CYP2C19 *1/*1 genotype. The clinical impact of this change is unknown. Polypharmacy guidance: Cimetidine increases the bioavailability of labetalol, and clinical monitoring is advised when both drugs are coadministered.

Lacosamide
Vimpat

Normal Sensitivity to Lacosamide (CYP2C19: Normal Metabolizer) — INFORMATIVE

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

Lamotrigine
Lamictal

Normal Response to Lamotrigine — INFORMATIVE

Pharmacogenetic guidance: Genotype results obtained from the pharmacogenetic test performed in this patient cannot be used to identify patients at risk for severe cutaneous adverse reactions such as anticonvulsant hypersensitivity syndrome, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Lamotrigine is metabolized by glucuronidation, which is mediated primarily by UGT1A4 with some contribution from UGT1A1 and UGBT2B7. There are insufficient studies documenting the impact of genetic polymorphisms of these metabolizing enzymes on lamotrigine response. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Enzyme-inducing drugs increase lamotrigine clearance significantly, and higher doses of this drug are required to maintain therapeutic concentrations. Coadministration of valproic acid, an inhibitor of UGT enzymes, increases lamotrigine levels and may result in serious lamotrigine adverse effects (neurological and cutaneous). A low starting dose with a slow titration schedule is recommended when lamotrigine is added to existing valproic acid treatment.

Lansoprazole
Prevacid

Normal Response to Lansoprazole (CYP2C19: Normal Metabolizer) — ACTIONABLE

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

Leflunomide
Arava

Normal Sensitivity to Leflunomide (CYP2C19: Normal Metabolizer) — INFORMATIVE

Leflunomide can be prescribed according to standard label-recommended dosage and administration. Full blood cell count (CBC) and liver function parameters should be checked no more than 6 months before beginning treatment, and every month for the initial 6 months of therapy. Blood pressure should be checked before beginning treatment and periodically thereafter.

Lesinurad
Zurampic

Normal Sensitivity to Lesinurad (CYP2C9: Intermediate Metabolizer) — ACTIONABLE

The patient's genotype result predicts a moderately reduced CYP2C9 metabolic activity. Lesinurad can be prescribed at standard label-recommended dosage and administration.

Levetiracetam
Keppra

Normal Response to Levetiracetam — INFORMATIVE

Pharmacogenetic guidance: No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Levetiracetam is minimally metabolized by non-CYP enzymes (esterases) and is primarily excreted unchanged in urine. Coadministration of enzyme-inducing antiepileptic drugs produce modest decreases in levetiracetam plasma levels.

Levomilnacipran
Fetzima

Normal Response to Levomilnacipran — INFORMATIVE

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

Levorphanol
Levo Dromoran

Normal Response to Levorphanol — INFORMATIVE

Pharmacogenetic guidance: Levorphanol is metabolized by glucuronidation which is mediated by UGT2B7. There are no studies documenting the impact of genetic polymorphisms of this metabolizing enzyme on levorphanol response. And no genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Enzyme inducing drugs are expected to increase levorphanol clearance significantly.

Lisdexamfetamine
Vyvanse

Normal Exposure to Lisdexamfetamine (CYP2D6: Normal Metabolizer) — INFORMATIVE

Lisdexamfetamine can be prescribed at standard label-recommended dosage and administration. Individualize the dosage according to the therapeutic needs and response of the patient.

✓	Lisdexamfetamine Vyvanse	Good Response to Lisdexamfetamine (COMT: Intermediate COMT Activity) The patient's genotype result predicts a favorable response to amphetamine stimulants. Lisdexamfetamine should be administered at the lowest effective dose, and dosage should be individually adjusted.	INFORMATIVE
✓	Losartan Cozaar, Hyzaar	Normal Response to Losartan (CYP2C9: Intermediate Metabolizer) Losartan is metabolized to its active metabolite by CYP2C9 and CYP3A4. The patient's genotype predicts a normal exposure to losartan and its active metabolite. Losartan can be prescribed at label-recommended dosage and administration.	INFORMATIVE
✓	Lovastatin Mevacor, Altoprev, Advicor	Normal Myopathy Risk (SLCO1B1: Normal Function) Lovastatin acid plasma concentration is not expected to be elevated. Unless other genetic or circumstantial risk factors are present, lovastatin 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.	INFORMATIVE
✓	Lovastatin Mevacor, Altoprev, Advicor	Normal Response to Lovastatin (CYP3A4: 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.	INFORMATIVE
✓	Loxapine Loxitane, Adasuve	Normal Response to Loxapine Pharmacogenetic guidance: Loxapine is metabolized extensively in the liver following oral administration, with multiple metabolites formed. Loxapine metabolism occurs via hydroxylation and oxidation catalyzed by CYP1A2 along with contributions from CYP3A4, CYP2D6 and FMO. There are no studies documenting the effect of genetic polymorphisms of these metabolizing enzymes on Loxapine disposition and there are no available genetically-guided drug selection or dosing recommendations. Polypharmacy guidance: Loxapine is a central nervous system (CNS) depressant. The concurrent use of Loxapine with other CNS depressants (e.g., alcohol, opioid analgesics, benzodiazepines, tricyclic antidepressants, general anesthetics, phenothiazines, sedative/hypnotics, muscle relaxants, and/or illicit CNS depressants) can increase the risk of respiratory depression, hypotension, profound sedation, and syncope. Therefore, consider dose reduction/modification of CNS depressants if used concomitantly with Loxapine. Loxapine has anticholinergic activity and concomitant use with other anticholinergic drugs can increase the risk of adverse reactions, including exacerbation of glaucoma and urinary retention.	INFORMATIVE
✓	Lurasidone Latuda	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.	ACTIONABLE
✓	Maprotiline Ludiomil	Normal Sensitivity to Maprotiline (CYP2D6: Normal Metabolizer) Maprotiline can be prescribed at standard label recommended-dosage and administration.	INFORMATIVE

Memantine
Namenda

Normal Response to Memantine — INFORMATIVE

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

Meperidine
Demerol

Normal Response to Meperidine — INFORMATIVE

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

Metaxalone
Skelaxin

Normal Response to Metaxalone — INFORMATIVE

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

Methocarbamol
Robaxin

Normal Response to Methocarbamol — INFORMATIVE

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

Metoclopramide
Reglan

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

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

Metoprolol
Lopressor

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

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

Mexiletine
Mexitil

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

Mexiletine can be prescribed at standard label-recommended dosage. A careful titration with ECG recording and monitoring of mexiletine plasma concentrations are recommended until a favorable clinical response is achieved.

Micafungin
Mycamine

Normal Response to Micafungin — ACTIONABLE

Pharmacogenetic guidance: Micafungin is metabolized by arylsulfatase, catechol-O-methyltransferase and cytochrome P450 enzymes. Even though micafungin is a substrate for and a weak inhibitor of CYP3A in vitro, hydroxylation by CYP3A is not a major pathway for micafungin metabolism in vivo. No genetically guided drug selection or dosing recommendations are available.

✓ Miglustat Zavesca	Normal Response to Miglustat Pharmacogenetic guidance: Miglustat is not metabolized by human CYP450 enzymes and the drug is mainly eliminated by renal excretion. No genetically-guided drug selection or dosing recommendations are available.	ACTIONABLE
✓ Milnacipran Savella	Normal Response to Milnacipran Pharmacogenetic guidance: milnacipran is minimally metabolized by UGT enzymes and primarily excreted unchanged in urine. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: coadministration of drugs that inhibit or induce CYP or UGT enzymes are unlikely to affect the exposure of milnacipran.	INFORMATIVE
✓ Mirabegron Myrbetriq	Normal Sensitivity to Mirabegron (CYP2D6: Normal Metabolizer) Mirabegron can be prescribed at standard label-recommended dosage and administration.	ACTIONABLE
✓ Mirtazapine Remeron	Normal Sensitivity to Mirtazapine (CYP2D6: Normal Metabolizer) Mirtazapine can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended until a favorable response is achieved.	ACTIONABLE
✓ Morphine MS Contin	Average Response to Morphine (COMT: Intermediate COMT Activity) The patient carries one COMT Val158Met mutation, which translates to a reduced COMT function. The patient may require average to low doses of morphine for adequate pain control. The dosing regimen needs to be individualized for each patient, taking into account the patient's prior analgesic treatment experience.	INFORMATIVE
✓ Nabumetone Relafen	Normal Response to Nabumetone Pharmacogenetic guidance: Nabumetone is a prodrug, which is converted by CYP1A2 to an active metabolite (6-MNA) that is further metabolized by CYP2C9 to an inactive metabolite. Theoretically, individuals with reduced CYP2C9 activity (i.e CYP2C9 poor metabolizers) may have higher levels of the active metabolite, but it is unknown whether this results in 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.	INFORMATIVE
✓ Naproxen Aleve	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.	INFORMATIVE
✓ Nateglinide Starlix	Normal Sensitivity to Nateglinide (SLCO1B1: Normal Function) The patient carries two copies of SLCO1B1 rs4149056 T allele, which is associated with normal transporter function. Nateglinide can be prescribed at label-recommended standard dosage and administration.	INFORMATIVE
✓ Nateglinide Starlix	Normal Sensitivity to Nateglinide (CYP2C9: Intermediate Metabolizer) The patient's genotype predicts a normal exposure to nateglinide, and this drug can be prescribed at label-recommended dosage and administration.	INFORMATIVE
✓ Nebivolol Bystolic	Normal Sensitivity to Nebivolol (CYP2D6: 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.	ACTIONABLE

Nefazodone
Serzone

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

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

Netupitant-Palonosetron
Akynzeo

Normal Response to Netupitant-Palonosetron (CYP2D6: Normal Metabolizer) — INFORMATIVE

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

Nortriptyline
Pamelor

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

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

Olmesartan
Benicar

Normal Sensitivity to Olmesartan Medoxomil — ACTIONABLE

Pharmacogenetic guidance: Olmesartan medoxomil is hydrolyzed to olmesartan its active metabolite in the gastrointestinal tract during absorption. There is virtually no further metabolism of olmesartan. Genetic variability of the cytochrome P450 genes is not expected to affect the patient's response to olmesartan medoxomil. No genotype-based dosing adjustments are available.

Omeprazole
Prilosec

Normal Response to Omeprazole (CYP2C19: Normal Metabolizer) — ACTIONABLE

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

Ondansetron
Zofran, Zuplenz

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

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

Oxcarbazepine
Trileptal, Oxtellar XR

Normal Response to Oxcarbazepine — INFORMATIVE

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

Oxybutynin
Ditropan

Normal Response to Oxybutynin — INFORMATIVE

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

Oxycodone
Percocet, Oxycontin

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

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

✓ Oxymorphone Opana, Numorphan	Normal Response to Oxymorphone 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.	INFORMATIVE
✓ Paliperidone Invega	Normal Sensitivity to Paliperidone (CYP2D6: Normal Metabolizer) Paliperidone can be prescribed at standard label-recommended dosage and administration.	ACTIONABLE
✓ Palonosetron Aloxi	Normal response to Palonosetron (CYP2D6: Normal Metabolizer) Palonosetron can be prescribed at standard label-recommended dosage and administration.	INFORMATIVE
✓ Pantoprazole Protonix	Normal Response to Pantoprazole (CYP2C19: Normal Metabolizer) Pantoprazole can be prescribed at standard label-recommended dosage and administration.	ACTIONABLE
✓ Paroxetine Paxil, Brisdelle	Normal Sensitivity to Paroxetine (CYP2D6: Normal Metabolizer) Paroxetine can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended until a favorable response is achieved.	ACTIONABLE
✓ Perampanel Fycompa	Normal Response to Perampanel Pharmacogenetic guidance: Perampanel is eliminated either unchanged or following oxidative metabolism by CYP3A4 and CYP3A5. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Enzyme-inducing drugs decrease perampanel plasma concentrations by 50-60%, and the initial dosage of the drug should be increased when it is added to a stable therapy regimen containing enzyme-inducing antiepileptic drugs. Coadministration with strong enzyme-inducers others than antiepileptic drugs (e.g., rifampin) should be avoided. Coadministration with perampanel with strong CYP3A4 inhibitors such as ketoconazole increases perampanel exposure by 20%.	INFORMATIVE
✓ Perphenazine Trilafon	Normal Sensitivity to Perphenazine (CYP2D6: Normal Metabolizer) Perphenazine can be prescribed at standard label-recommended dosage and administration.	ACTIONABLE
✓ Phenobarbital Luminal	Normal Sensitivity to Phenobarbital (CYP2C19: Normal Metabolizer) CYP2C19 is partly involved in the metabolism of phenobarbital, and this drug can be prescribed at standard label-recommended dosage and administration.	INFORMATIVE
✓ Pimavanserin Nuplazid	Normal Response to Pimavanserin Pharmacogenetic guidance: Pimavanserin is predominantly metabolized by CYP3A4 and CYP3A5 and to a lesser extent by CYP2J2, CYP2D6, and other CYP and FMO enzymes. CYP3A4 is the major enzyme responsible for the formation of its major active metabolite (AC-279). There are no available genetically-guided drug selection or dosing recommendations. Polypharmacy guidance: Pimavanserin prolongs the QT interval and its use should be avoided in patients with known QT prolongation or in combination with other drugs known to prolong QT interval including Class 1A antiarrhythmics (e.g., quinidine, procainamide) or Class 3 antiarrhythmics (e.g., amiodarone, sotalol), certain antipsychotic medications (e.g., ziprasidone, chlorpromazine, thioridazine), and certain antibiotics (e.g., gatifloxacin, moxifloxacin). Concomitant use of pimavanserin with CYP3A4 inhibitor increases pimavanserin exposure and a dose reduction of 50% is needed when this drug is coadministered with strong CYP3A inhibitors. Coadministration of pimavanserin with strong CYP3A inducers may result in reduced efficacy and a dose increase may be needed.	INFORMATIVE

Pimozide
Orap

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

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

Pitavastatin
Livalo

Normal Myopathy Risk (SLCO1B1: Normal Function) — INFORMATIVE

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.)

Posaconazole
Noxafil

Normal Response to Posaconazole — ACTIONABLE

Pharmacogenetic guidance: Posaconazole is cleared primarily as unchanged drug. The excreted metabolites in urine and feces account for approximately 17% of the administered dose. The metabolic pathways for posaconazole include direct glucuronidation, minor oxidation and dealkylation. CYP3A4 (and possibly CYP1A1 and CYP3A5), UGT1A4, and P-glycoprotein are enzymes and transporters that play a role in the elimination of this antifungal. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: UGT and P-glycoprotein inhibitors or inducers may affect posaconazole plasma concentrations. Concomitant use of posaconazole and these agents should be avoided unless the benefit to the patient outweighs the risk.

Prasugrel
Effient

Normal Response to Prasugrel — ACTIONABLE

Pharmacogenetic guidance : Prasugrel is a prodrug that is hydrolyzed in the intestine to a thiolactone, which is then converted to the active metabolite primarily by CYP3A4 and CYP2B6, and to a lesser extent by CYP2C9 and CYP2C19. Prasugrel active metabolite exposure and platelet reactivity are not affected by CYP2C19 genetic variants. Prasugrel efficacy or safety profile are also unaffected by CYP2B6, CYP3A5, and CYP2C9 genetic variants. No genetically-guided drug selection or dosing recommendations are available. Polypharmacy guidance : Prasugrel can be administered with drugs that are inducers or inhibitors of cytochrome P450 enzymes.

Pravastatin
Pravachol

Normal Myopathy Risk (SLCO1B1: Normal Function) — INFORMATIVE

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

Normal Response to Pregabalin — INFORMATIVE

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

Primidone
Mysoline

Normal Sensitivity to Primidone (CYP2C19: Normal Metabolizer) — INFORMATIVE

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

Proguanil
Malarone

Normal Response to Proguanil (CYP2C19: Normal Metabolizer) — INFORMATIVE

Proguanil is metabolized to an active metabolite cycloguanil by CYP2C19. The patient's genotype is associated with a normal metabolism of proguanil to cycloguanil. Proguanil can be prescribed at standard label-recommended dosage and administration.

Propafenone
Rythmol

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

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

Dose adjustments with co-medications: concurrent use of propafenone along with CYP3A4 inhibitors and CYP2D6 inhibitors may significantly increase the plasma concentration of propafenone and thereby increase the risk of proarrhythmia and other adverse events. Therefore, avoid simultaneous use of propafenone with both a CYP2D6 inhibitor and a CYP3A4 inhibitor.

Propranolol
Inderal

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

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

Protriptyline
Vivactil

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

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

Quetiapine
Seroquel

Normal Response to Quetiapine — INFORMATIVE

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

Rabeprazole
Aciphex

Normal Response to Rabeprazole (CYP2C19: Normal Metabolizer) — ACTIONABLE

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

Raltegravir
Isentress, Dutrebis

Normal Response to Raltegravir — ACTIONABLE

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

Ranolazine
Ranexa

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

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

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

Ranolazine is a QTc prolonging drug. Caution should be observed when treating: 1- patients with a history of congenital or a family history of long QT syndrome, 2- patients with known acquired QT interval prolongation, and 3- patients treated with drugs affecting the QTc interval. Administration of CYP3A4 inhibitors increases the exposure of ranolazine significantly. As a consequence, the QTc prolongation by ranolazine in the presence of potent CYP3A inhibitors is significantly elevated relative to when the drug is administered alone.

Repaglinide
Prandin, Prandimet

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

The patient carries two copies of SLCO1B1 rs4149056 T allele, which is associated with normal transporter function. Repaglinide can be prescribed at label-recommended standard dosage and administration.

Risperidone
Risperdal

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

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

Rivaroxaban
Xarelto

Normal Response to Rivaroxaban — INFORMATIVE

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

Rolapitant
Varubi

Normal Response to Rolapitant — ACTIONABLE

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

Rosuvastatin
Crestor

Normal Myopathy Risk (SLCO1B1 521T>C T/T) — INFORMATIVE

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

Normal Response to Rufinamide — INFORMATIVE

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

Sertraline
Zoloft

Normal Sensitivity to Sertraline (CYP2C19: Normal Metabolizer) — ACTIONABLE

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

Sildenafil
Viagra

Normal Response to Sildenafil — INFORMATIVE

Pharmacogenetic guidance: Preliminary findings indicate that sildenafil exposure is 1.5 times higher in individuals with CYP3A5*3/*3 genotype compared to those with CYP3A5*1/*1 genotype. The clinical significance of this change is unknown. Polypharmacy guidance: Sildenafil is metabolized by CYP3A4 (major route) and CYP2C9 (minor route). In patients taking strong CYP3A inhibitors, sildenafil exposure is significantly increased, and it is recommended not to exceed a maximum single dose of 25 mg in a 48-hour period. Inducers of CYP3A may decrease the concentration of the drug.

Silodosin
Rapaflo

Normal Response to Silodosin — INFORMATIVE

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

Simvastatin
Zocor

Normal Myopathy Risk (SLCO1B1: Normal Function) — ACTIONABLE

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

Normal Response to Simvastatin (CYP3A4: Normal Metabolizer) — INFORMATIVE

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

Normal Response to Solifenacin — INFORMATIVE

Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Coadministration of a CYP3A4 strong inhibitor increases solifenacin serum concentrations significantly. Therefore, it is recommended not to exceed a 5 mg daily dose of solifenacin when coadministered with strong CYP3A4 inhibitors, as the risk for QTc prolongation induced by this drug is increased at higher concentrations. Although the effects of moderate CYP3A4 inhibitors were not examined, use caution when this drug is administered with moderate CYP3A4 inhibitors.

Stiripentol
Diacomit

Normal Sensitivity to Stiripentol — INFORMATIVE

Pharmacogenetic guidance: CYP2C19 is partly involved in the metabolism of stiripentol along with CYP3A4 and CYP1A2. This drug can be prescribed at standard recommended dosage and administration regardless of the CYP2C19 phenotype status. Polypharmacy guidance: Inducers of cytochrome P450 enzymes increase stiripentol clearance by 3-fold, and the initial dosage of the drug should be considered carefully when added to a stable therapy regimen containing enzyme-inducing antiepileptic drugs.

Sufentanil
Sufenta

Normal Response to Sufentanil — INFORMATIVE

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

Sulindac
Clinoril

Normal Response to Sulindac — INFORMATIVE

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

Tacrolimus
Prograf

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

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

Tadalafil
Cialis

Normal Response to Tadalafil — INFORMATIVE

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

Taliglucerase alfa
Elelyso

Normal Response to Taliglucerase alfa — ACTIONABLE

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

Tamsulosin
Flomax

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

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

Tapentadol
Nucynta

Normal Response to Tapentadol — INFORMATIVE

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

Telmisartan
Micardis

Normal Sensitivity to Telmisartan — ACTIONABLE

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

Terazosin
Hytrin

Normal Response to Terazosin — INFORMATIVE

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

Thioridazine
Mellaril

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

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

Thiothixene
Navane

Normal Response to Thiothixene — INFORMATIVE

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

Tiagabine
Gabitril

Normal Response to Tiagabine — INFORMATIVE

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

Ticagrelor
Brilinta

Normal Response to Ticagrelor — INFORMATIVE

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

Timolol
Timoptic

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

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

Tofacitinib
Xeljanz

Normal Sensitivity to Tofacitinib (CYP2C19: Normal Metabolizer) — INFORMATIVE

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

Tolbutamide
Orinase

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

Tolbutamide is extensively metabolized by CYP2C9, and while this clearance pathway is diminished in subjects with reduced CYP2C9 activity, such change has not been shown to be of clinical significance. Therefore, this drug can be prescribed according to standard label-recommended dosage and administration (dose titration in response to plasma levels of glucose/glycosylated hemoglobin).

Tolterodine
Detrol

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

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

Topiramate
Topamax

Normal Response to Topiramate — INFORMATIVE

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

Torsemide
Demadex

Normal Response to Torsemide (CYP2C9: Intermediate Metabolizer) — INFORMATIVE

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

Tramadol
Ultram

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

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

Trazodone
Oleptro

Normal Response to Trazodone — INFORMATIVE

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

Trifluoperazine
Stelazine

Normal Response to Trifluoperazine — INFORMATIVE

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

Trimipramine
Surmontil

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

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

Trimipramine
Surmontil

Normal Sensitivity to Trimipramine (CYP2C19: Normal Metabolizer) — ACTIONABLE

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

Trospium
Sanctura

Normal Response to Trospium — INFORMATIVE

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

Valbenazine
Ingrezza

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

Valbenazine can be prescribed at standard label-recommended dosage and administration. The initial dose is 40 mg once daily which can be increased after a week of therapy to the recommended dose of 80 mg once daily.

Dose adjustments with comedications: reduce the daily recommended dose to 40 mg if a strong CYP3A4 inhibitor is coadministered. In presence of a CYP2D6 inhibitor, the daily recommended dose may be reduced based on tolerability. Concomitant use with CYP3A4 inducers should be avoided.

Valproic Acid
Depakote, Depakene

Normal Response to Valproic acid — INFORMATIVE

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

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

Valsartan
Diovan, Entresto

Normal Sensitivity to Valsartan — ACTIONABLE

Pharmacogenetic guidance: Valsartan is excreted largely as unchanged compound. CYP2C9 is responsible for the formation of a minor metabolite, valeryl 4-hydroxy valsartan, which accounts for about 9% of a dose. Given the limited contribution of CYP2C9 in the overall disposition of valsartan, genetic variability of the CYP2C9 gene is not expected to affect the patient's response to valsartan. No genotype-based dosing adjustments are available.

Vardenafil
Levitra

Normal Response to Vardenafil — ACTIONABLE

Pharmacogenetic guidance: Preliminary findings indicate that vardenafil exposure is 3 times higher in individuals with CYP3A5*3/*3 genotype compared to those with CYP3A5*1/*1 genotype. The clinical impact of this change is unknown.
Polypharmacy guidance: The dosage of vardenafil may require adjustment in patients receiving strong CYP3A4 inhibitors such as ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, atazanavir, or clarithromycin, as well as in patients receiving moderate CYP3A4 inhibitors such as erythromycin. For ritonavir, a single dose of 2.5 mg vardenafil should not be exceeded in a 72-hour period. For indinavir, saquinavir, atazanavir, or ketoconazole: 400 mg daily . For itraconazole: 400 mg daily. For clarithromycin: a single dose of 2.5 mg vardenafil should not be exceeded in a 24-hour period. For ketoconazole: 200 mg daily. For itraconazole: 200 mg daily. For erythromycin: a single dose of 5 mg vardenafil should not be exceeded in a 24-hour period. Inducers of CYP3A4 may decrease the concentrations of vardenafil.

Velaglucerase alfa
Vpriv

Normal Response to Velaglucerase alfa — ACTIONABLE

Pharmacogenetic guidance: Velaglucerase alfa is a hydrolytic lysosomal glucocerebroside-specific enzyme produced in human fibroblasts. Velaglucerase alfa dosage should be individualized to each patient. Individual patient dosage may require increase or decrease based on therapeutic goals. Velaglucerase alfa is not metabolized by the CYP450 enzymes. No genetically-guided drug selection or dosing recommendations are available.

Venlafaxine
Effexor

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

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

Vigabatrin
Sabril

Normal Response to Vigabatrin — INFORMATIVE

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

Vilazodone
Viibryd

Normal Response to Vilazodone — INFORMATIVE

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

Vorapaxar
Zontivity

Normal Response to Vorapaxar — ACTIONABLE

Pharmacogenetic guidance: vorapaxar is metabolized primarily by CYP3A4, with contribution from CYP2J2. Genetic polymorphisms of these genes are not expected to affect the efficacy or safety profiles of this drug. Vorapaxar is contraindicated in people who have had a stroke, transient ischemic attack (TIA), or intracranial hemorrhage, (ICH) because of the increased bleeding risk. Polypharmacy guidance: Avoid concomitant use of vorapaxar with strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, lopinavir/ritonavir, ritonavir, indinavir, and conivaptan). Significant increases in vorapaxar exposure may increase bleeding risk. Avoid concomitant use with drugs that are strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, rifampin, and St. John's wort).

Voriconazole
Vfend

Normal Sensitivity to Voriconazole (CYP2C19: Normal Metabolizer) — ACTIONABLE

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

Vortioxetine
Trintellix

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

Vortioxetine can be prescribed at standard label-recommended dosage and administration. The recommended starting dose is 10 mg/day, which can then be increased to 20 mg/day, as tolerated.

Ziprasidone
Geodon

Normal Response to Ziprasidone — INFORMATIVE

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

Zonisamide
Zonegran

Normal Sensitivity to Zonisamide (CYP2C19: Normal Metabolizer) — INFORMATIVE

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

Zuclopenthixol
Clopixol

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

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

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

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

Lab Disclaimer: The performance characteristics of this test were validated by Dept. Clinical Chemistry at Erasmus MC, Rotterdam, The Netherlands. The test has not been cleared or approved by the U.S. Food and Drug Administration.

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

Additional note:The software uses the interpretation and translation as valid and used at this moment in the USA. Genotype to phenotype relationships are defined within CPIC guidelines; they may differ in some cases from those defined by the current Dutch interpretation as presented by the DPWG. In particular: a) CYP2C19*1/*17 is translated by CPIC as "rapid metabolizer" against "normal metabolizer" by the DPWG; b) CYP2D6 1 active and 1 inactive allele is defined as "normal metabolizer" by CPIC against "intermediate metabolizer" by DPWG, and c) CYP2D6*10/*10 is defined as "normal metabolizer" by CPIC against "intermediate metabolizer" by the DPWG.

Approved by: Prof. Dr. RHN van Schaik – Laboratory Director Director Erasmus MC International Expertcenter Pharmacogenetics: Prof. Dr. RHN van Schaik

Patient Information Card

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

REPORT DETAILS

Patient:
DOB:
ACC #:

Pharmacogenetic Test Summary

CYP1A2	*1A/*1F	Normal Metabolizer - Higher Inducibility
CYP2C19	*1/*1	Normal Metabolizer
CYP2C9	*1/*2	Intermediate Metabolizer
CYP2D6	*1/*2	Normal Metabolizer
CYP3A4	*1/*1	Normal Metabolizer
CYP3A5	*3/*3	Poor Metabolizer
VKORC1 and CYP2C9	-1639G>A G/A, *1/*2	Moderate Sensitivity to Warfarin

For a complete report contact Erasmus MC
www.erasmusmc.nl/farmacogenetica