PHARMACOGENETIC TESTING

REPORT

Ayass bioscience LLC™
Bridging Science and Precision Patient Care

Patient Name: XXXXX XXXXXXX
Date of Birth: XX/XX/XXXX
Accession #: XXXXXXXXXXXX

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Medical Management Report

Patient:	**XXXX XXXXXX**	Accession #:	**XXXXXX**	Received Date:	**XX/XX/2017**
Gender:	**Male**	Report Date:	**XX/XX/2017**	Collection Date:	**XX/XX/2017**
DOB:	**XX/XX/1970**	Ordered By:	**XXXX X. XXXXXX, MD**	Specimen Type:	**Blood**

GUIDANCE LEVELS		EVIDENCE LEVELS	
⊗	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.

Current Patient Medications

Clonidine, Edarbi, Hydrochlorothiazide, Soma, Coreg, Tylenol with Codeine, Metformin

⊗ Tylenol with Codeine
Codeine

Increased Response to Codeine (CYP2D6: Ultra-Rapid Metabolizer) — **ACTIONABLE**

Codeine is converted into its active metabolite morphine by CYP2D6. Since this patient is a ultra-rapid metabolizer, greatly increased morphine levels are expected, and the patient is at high risk of toxicity when taking codeine. The ultra-rapid conversion of codeine to morphine in breast feeding mothers can result in high and unsafe levels of morphine in the breast milk potentially causing life threatening respiratory depression in the breastfed infant. Avoid prescribing codeine, and consider an alternative opioid or a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids not sensitive to CYP2D6 function include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

⚠ Clonidine
Kapvay

Possible Altered Response to Clonidine (CYP2D6: Ultra-Rapid Metabolizer) — **INFORMATIVE**

Treatment with clonidine can cause dose related decreases in blood pressure and heart rate Measure heart rate and blood pressure prior to initiation of therapy, following dose increases, and periodically while on therapy. Titrate Clonidine slowly in patients with a history of hypotension, and those with underlying conditions that may be worsened by hypotension and bradycardia.

⚠ Soma
Carisoprodol

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

There is insufficient data to allow calculation of dose adjustment. If carisoprodol is prescribed, it is recommended to use a lower dose, and to carefully monitor the patient for side effects.

✓ Coreg
Carvedilol

Normal Sensitivity to Carvedilol (CYP2D6: Ultra-Rapid Metabolizer) — **INFORMATIVE**

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

✓ Edarbi
Azilsartan

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

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

Medications outside the scope of the report: Hydrochlorothiazide, Metformin

Risk Management

✓ Antipsychotic-Induced Hyperprolactinemia

Normal Risk of Antipsychotic-Induced Hyperprolactinemia

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

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

Monitor the patients closely for any signs of hyperprolactinemia.

⚠ Antipsychotic-Induced Tardive Dyskinesia

Increased Risk of Antipsychotic-Induced Tardive Dyskinesia

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

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

Closely monitor the patient for signs of tardive dyskinesia.

✓ Antipsychotic-Induced Weight Gain

Low Risk of Antipsychotic-Induced Weight Gain

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

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

Monitor the patient closely for signs weight gain.

✓ Hyperhomocysteinemia - Depression

No Increased Risk of Hyperhomocysteinemia

The patient does not carry the MTHFR C677T variant. MTHFR enzyme activity is normal.

Patients diagnosed with depression often have low folate levels and homocysteine is a highly sensitive marker of folate status. Functional folate deficiency is indicated by elevated homocysteine. With a normal MTHFR activity, this patient can process folate normally and is unlikely to have elevated plasma levels of homocysteine.

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

✓ Hyperhomocysteinemia - Thrombosis

No Increased Risk of Hyperhomocysteinemia

The patient carries one MTHFR A1298C mutation (heterozygous). MTHFR enzyme activity is reduced (80% of normal activity).

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

The patient's MTHFR activity is slightly reduced.

✓ Thrombophilia

No Increased Risk of Thrombosis

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

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

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

Type III Hyperlipoproteinemia

Not Associated with Type III Hyperlipoproteinemia

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

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

No action is needed when a patient is normolipidemic.

Pharmacogenetic Test Results

Gene	Genotype	Phenotype	Clinical Consequences	Alleles Tested
ABCB1	3435C>T C/C	Variant Allele Not Present	Consistent with high transporter expression.	3435C>T
ANKK1/DRD2	DRD2:Taq1A G/G	Unaltered DRD2 function	Consistent with a normal dopamine receptor D2 function.	DRD2:Taq1A
Apolipoprotein E	ε3/ε3	Normal APOE function	Not associated with type III hyperlipoproteinemia - No increased risk of cardiovascular disease	ε2, ε4, (ε3 is reference)
COMT	Val158Met G/G	High/Normal COMT Activity	Consistent with a normal catechol O-methyltransferase (COMT) function.	Val158Met
CYP1A2	*1L/*1L	Unknown Phenotype	The patient's CYP1A2 metabolism status cannot be determined based on the genotype results. Caution if CYP1A2 drug substrates are prescribed.	*1C, *1F, *1K, *1L, *7, *11
CYP2B6	*1/*6	Intermediate Metabolizer	Consistent with a moderate deficiency in CYP2B6 activity. Potential risk for side effects or loss of efficacy with drug substrates.	*16, *6, *9, *18
CYP2C19	*1/*17	Rapid Metabolizer	Consistent with a significant increase in CYP2C19 activity. Potential risk for side effects or loss of efficacy with drug substrates.	*2, *3, *4, *4B, *5, *6, *7, *8, *17
CYP2C9	*1/*1	Normal Metabolizer	Consistent with a typical CYP2C9 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.	*2, *3, *4, *5, *6, *8, *11, *12, *13, *15, *25
CYP2D6	*1/*2 XN	Ultra-Rapid Metabolizer	Consistent with a significant increase in CYP2D6 activity. Potential risk for side effects or loss of efficacy with drug substrates.	*2, *3, *4, *4M, *6, *7, *9, *10, *11, *12, *14A, *14B, *15, *17, *19, *20, *29, *41, *5 (gene deletion), XN (gene duplication)
CYP3A4	*1/*1	Normal Metabolizer	Consistent with a typical CYP3A4 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.	*2, *17, *22
CYP3A5	*1/*6	Intermediate Metabolizer	Consistent with an intermediate CYP3A5 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.	*2, *3, *3C, *6, *7
Factor II Factor V Leiden	20210G>A GG 1691G>A GG	No Increased Risk of Thrombosis	The patient's risk of thrombosis is not increased (average risk of clotting is about 1 in 1000 for anyone in a year). However, because this test cannot find all of the inherited reasons for abnormal clotting, other factors may affect this risk assessment.	20210G>A, 1691G>A
MTHFR	677C>T CC	Normal MTHFR Activity	The patient does not carry the MTHFR C677T mutation (wild-type) and the patient's MTHFR activity is normal. This is not associated with an increased risk of hyperhomocysteinemia.	1298A>C, 677C>T
MTHFR	1298A>C AC 677C>T CC	No Increased Risk of Hyperhomocysteinemia	The patient's slightly reduced MTHFR activity is not a risk factor for hyperhomocysteinemia. Unless other risk factors are present, the patient is not expected to have an increased risk for venous thromboembolism (VTE).	1298A>C, 677C>T
OPRM1	A118G A/A	Normal OPRM1 Function	Consistent with a normal OPRM1 receptor signaling efficiency induced by exogenous opioids. This is associated with a good analgesia following standard opioid doses and a poor response to naltrexone.	A118G

SLCO1B1	521T>C T/T	**Normal Function**	Consistent with a typical SLCO1B1 transporter function. The patient's risk for statin-induced myopathy is not increased.	521T>C
VKORC1	-1639G>A G/G	**Low Warfarin Sensitivity**	VKORC1 is the site of action of warfarin. The patient may require an increase in warfarin dose.	-1639G>A

Approved By: Dr. Ihsan Housini, MD on GMT

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

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

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These assays do not detect polymorphisms other than those listed. Rare false positive or false negative results may occur. These assays have been developed and performance characteristics determined by Ayass Lung Clinic LLC.; and therefore are classified as Laboratory Developed Tests. These assays have not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance is not necessary. These tests are used for clinical purposes and should not be considered as investigational. Results of genotyping should be interpreted in the full context of the patient's clinical history, including hepatic and renal function, life style, co-administration of other drugs, and other pre-existing conditions. Drug metabolism is known to be affected by non-genetic factors. As thus DNA testing does not replace the necessity for clinical drug monitoring.

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.

Laboratory Certification: CLIA # 45D2034851

Potentially Impacted Medications

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

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

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

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
	Antipsychotics	Aripiprazole (Abilify, Aristada) Asenapine (Saphris) Brexpiprazole (Rexulti) Cariprazine (Vraylar) Iloperidone (Fanapt) Loxapine (Loxitane, Adasuve) Lurasidone (Latuda) Paliperidone (Invega) Pimavanserin (Nuplazid) Quetiapine (Seroquel) Thioridazine (Mellaril) Thiothixene (Navane) Trifluoperazine (Stelazine) Ziprasidone (Geodon)	Chlorpromazine (Thorazine) Clozapine (Clozaril) Fluphenazine (Prolixin) Olanzapine (Zyprexa) Perphenazine (Trilafon) Pimozide (Orap)	Haloperidol (Haldol) Risperidone (Risperdal)
	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)		
Transplantation	Immunosupressants		Tacrolimus (Prograf)	
Urologicals	5-Alpha Reductase Inhibitors for Benign Prostatic Hyperplasia	Dutasteride (Avodart) Finasteride (Proscar)		
	Alpha-Blockers for Benign Prostatic Hyperplasia	Alfuzosin (UroXatral) Doxazosin (Cardura) Silodosin (Rapaflo) Tamsulosin (Flomax) Terazosin (Hytrin)		
	Antispasmodics for Overactive Bladder	Darifenacin (Enablex) Fesoterodine (Toviaz) Mirabegron (Myrbetriq) Oxybutynin (Ditropan) Solifenacin (Vesicare) Tolterodine (Detrol) Trospium (Sanctura)		
	Phosphodiesterase Inhibitors for Erectile Dysfunction	Avanafil (Stendra) Sildenafil (Viagra) Tadalafil (Cialis) Vardenafil (Levitra)		

Dosing Guidance

Amitriptyline
Elavil

Non-Response to Amitriptyline (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Consider an alternative drug, or prescribe amitriptyline at an increased dose and monitor the plasma concentration of amitriptyline and metabolites.

Amitriptyline
Elavil

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

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

Atomoxetine
Strattera

Non-Response to Atomoxetine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

The patient may fail to achieve adequate plasma levels of atomoxetine if the drug is prescribed at standard recommended doses. Consider prescribing atomoxetine with careful titration and monitoring for reduced efficacy. There is insufficient data to calculate dose adjustment. Or consider an alternative medication.

Citalopram
Celexa

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

At standard label-recommended dosage, citalopram plasma concentrations levels are expected to be low which may result in a loss of efficacy. Consider an alternative medication. If citalopram is warranted, consider increasing the dose to a maximum of 150% and titrate based on the clinical response and tolerability.

Clomipramine
Anafranil

Non-Response to Clomipramine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Consider an alternative drug, or prescribe clomipramine at an increased dose and monitor the plasma concentration of clomipramine and desmethylclomipramine.

Clomipramine
Anafranil

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

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

Codeine
Codeine; Fioricet with Codeine

Increased Response to Codeine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Codeine is converted into its active metabolite morphine by CYP2D6. Since this patient is a ultra-rapid metabolizer, greatly increased morphine levels are expected, and the patient is at high risk of toxicity when taking codeine. The ultra-rapid conversion of codeine to morphine in breast feeding mothers can result in high and unsafe levels of morphine in the breast milk potentially causing life threatening respiratory depression in the breastfed infant. Avoid prescribing codeine, and consider an alternative opioid or a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids not sensitive to CYP2D6 function include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

Desipramine
Norpramin

Non-Response to Desipramine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Consider an alternative drug, or prescribe desipramine at increased dosage and observe the patient for decreased efficacy. Adjust dosage in response to desipramine and metabolites plasma concentrations and clinical response.

Doxepin
Silenor

Non-Response to Doxepin (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Consider an alternative drug or increase doxepin dose by 100%. Adjust maintenance dose according to nordoxepin plasma concentrations.

Doxepin
Silenor

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

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

Escitalopram
Lexapro

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

At standard label-recommended dosage, escitalopram plasma concentrations levels are expected to be low which may result in a loss of efficacy. Consider an alternative medication. If escitalopram is warranted, consider increasing the dose to a maximum of 150% and titrate based on the clinical response and tolerability.

Flecainide
Tambocor

Altered Response to Flecainide (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Titrate carefully and consider adjusting the dose in response to plasma concentration and ECG monitoring, OR consider an alternative drug. Examples of alternatives drugs not affected by CYP2D6 include: sotalol, disopyramide, quinidine, and amiodarone.

Haloperidol
Haldol

Non-Response to Haloperidol (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Consider an alternative drug, or prescribe haloperidol at the standard dose and adjust dosage to achieve a favorable clinical response. Be alert to decreased haloperidol plasma concentrations.

Imipramine
Tofranil

Non-Response to Imipramine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Consider an alternative drug or consider prescribing imipramine at an increased dose, then adjust dosage in response to imipramine and desipramine plasma concentrations.

Imipramine
Tofranil

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

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

Metoprolol
Lopressor

Possible Non-Responder to Metoprolol (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The patient may experience a decrease in the pharmacological effect when taking metoprolol at standard dosage. Heart Failure: Consider alternative beta-blockers such as bisoprolol or carvedilol, or prescribe metoprolol at a higher dose. Other indications: Consider alternative beta-blockers such as bisoprolol or atenolol, or prescribe metoprolol at a higher dose. If metoprolol is prescribed, titrate the dose to a maximum of 250% of the normal dose in response to efficacy and adverse events.

Nortriptyline
Pamelor

Non-Response to Nortriptyline (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Consider an alternative drug, or prescribe nortriptyline at an increased dose and monitor the plasma concentration of amitriptyline and hydroxynortriptyline.

Ondansetron
Zofran, Zuplenz

Non-Response to Ondansetron (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

A substantially decreased antiemetic effect has been reported in CYP2D6 ultra-rapid metabolizers when taking standard doses of this medication. Consider prescribing an alternative drug not metabolized by CYP2D6 such as granisetron.

Paroxetine
Paxil, Brisdelle

Reduced Response to Paroxetine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

There is a risk for decreased efficacy at standard dosage. If a standard dose is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of the drug are likely. Consider an alternative medication.

Protriptyline
Vivactil

Non-Response to Protriptyline (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Consider alternative drugs or prescribe protriptyline at increased dosage and observe the patient for decreased efficacy. Adjust dosage in response to protriptyline and metabolites plasma concentrations and clinical response.

Risperidone
Risperdal

Non-Response to Risperidone (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Consider an alternative drug, OR prescribe risperidone , be extra alert to insufficient response, and adjust dosage in response to clinical response and adverse events.

Tramadol
Ultram

Increased Response to Tramadol (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The patient is at high risk of toxicity when taking tramadol at standard dosing. Consider reducing tramadol dose by 30%. Careful monitoring for side effects (nausea, vomiting, constipation, respiratory depression, confusion, urinary retention) and weekly titration are recommended. In case of toxicity, consider alternative opioids other than codeine, or a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids not sensitive to CYP2D6 function include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

The accelerated conversion of tramadol to its active metabolite can result in high and unsafe levels of this metabolite in breast milk potentially causing life threatening respiratory depression in the breastfed infant. Use of tramadol should be avoided in breastfeeding mothers.

Trimipramine
Surmontil

Non-Response to Trimipramine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Consider an alternative drug, or consider prescribing trimipramine at an increased dose, then adjust dosage in response to trimipramine plasma concentrations.

Trimipramine
Surmontil

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

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

Venlafaxine
Effexor

Non-Response to Venlafaxine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The patient is unlikely to achieve adequate serum levels of venlafaxine and O-desmethylvenlafaxine when taking standard doses of venlafaxine. Consider an alternative drug, or increase the venlafaxine dose to a maximum of 150% of the normal dose and monitor venlafaxine and O-desmethylvenlafaxine plasma concentrations.

Voriconazole
Vfend

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

Voriconazole plasma concentrations are expected to be low if a standard dose is used, increasing the risk of loss of response and effectiveness and subsequent disease progression. Consider an alternative medication that is not dependent on CYP2C19 metabolism, such as isavuconazole, liposomal amphotericin B or posaconazole.

Amoxapine
Amoxapine

Possible Non-Response to Amoxapine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Like other tricyclic and tetracyclic antidepressants, amoxapine is metabolized by CYP2D6. However, the overall contribution of this enzyme in the metabolism of this drug is not well documented. Patients with increased CYP2D6 function may metabolize amoxapine more rapidly which can result in sub-therapeutic drug concentrations; these patients may require higher doses to achieve adequate plasma concentrations. There are no established dosing adjustments for patients with increased CYP2D6 function; therapy must be initiated cautiously and adjusted according to the patient's response.

Bupropion
Wellbutrin, Zyban, Aplenzin, Contrave

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

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

Carisoprodol
Soma

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

There is insufficient data to allow calculation of dose adjustment. If carisoprodol is prescribed, it is recommended to use a lower dose, and to carefully monitor the patient for side effects.

Chlorpromazine
Thorazine

Possible Non-Response to Chlorpromazine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Chlorpromazine is metabolized by CYP2D6, CYP3A4 and flavin-containing monooxygenases. Subjects with increased CYP2D6 function will metabolize chlorpromazine more rapidly which can result in sub-therapeutic drug concentrations. Consider a standard dose and adjust dosage according to the patient's tolerability and response. Higher doses may be necessary to achieve efficacy.

Clonidine
Kapvay

Possible Altered Response to Clonidine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Treatment with clonidine can cause dose related decreases in blood pressure and heart rate Measure heart rate and blood pressure prior to initiation of therapy, following dose increases, and periodically while on therapy. Titrate Clonidine slowly in patients with a history of hypotension, and those with underlying conditions that may be worsened by hypotension and bradycardia.

Clopidogrel
Plavix

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

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

Clozapine
Clozaril

Unknown Response to Clozapine (CYP1A2: Unknown Phenotype) — INFORMATIVE

Although the patient's CYP1A2 metabolism status cannot be predicted accurately, smoking may increase the risk of non-response to standard 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 may increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction is recommended in patients who have quit smoking.

Dexlansoprazole
Dexilant, Kapidex

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

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

Diazepam
Valium

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

CYP2C19 rapid and ultra-rapid metabolizers metabolize diazepam and nordiazepam more rapidly than normal metabolizers. However, there is insufficient data to allow calculation of dose adjustment when diazepam is prescribed. Monitor the patient's response and adjust the dose accordingly.

Dihydrocodeine
Synalgos-DC

Possible Altered Response to Dihydrocodeine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Increased conversion of dihydrocodeine to the more active metabolite dihydromorphine is expected in CYP2D6 ultra-rapid metabolizers. This may result in an exaggerated response. Adequate pain relief can be achieved by decreasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if signs of overdose (excessive sleepiness, confusion, or shallow breathing) are reported.

Dolasetron
Anzemet

Possible Altered Response to Dolasetron (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

The reduction of dolasetron to its active metabolite hydrodolasetron is mediated by a carbonyl reductase. Hydrodolasetron is further eliminated by multiple routes, including renal excretion and by glucuronidation or hydroxylation by CYP2D6. Compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower hydroxydolasetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Dolasetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Donepezil
Aricept

Possible Altered Response to Donepezil (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

When compared to a normal metabolizer, a ultra-rapid metabolizers has a 24% increase in donepezil clearance. The clinical significance of this increase is not well documented. Consider using a standard dosing regimen and adjust dosage in response to clinical response and tolerability.

Esomeprazole
Nexium

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

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

Fluphenazine
Prolixin

Possible Non-response to Fluphenazine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Fluphenazine is metabolized by CYP2D6, CYP1A2 and other enzymes. **Patients with increased CYP2D6 function will metabolize fluphenazine more rapidly which can result in sub-therapeutic drug concentrations; these patients may require higher doses to achieve adequate plasma concentrations.** There are no established dosing adjustments for patients with increased CYP2D6 function therefore, 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

Possible Reduced Response to Fluvoxamine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

There is a risk for decreased efficacy at standard dosage. If a standard dose is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of the drug are likely. There is insufficient data to calculate dose adjustments and careful titration is recommended until a favorable response is achieved. An alternative medication not metabolized by CYP2D6 can also be considered.

Granisetron
Sancuso, Sustol

Unfavorable Response to Standard Granisetron Dosing (ABCB1: Variant Allele Not Present) — INFORMATIVE

The genotype result predicts that the patient has high ABCB1 transporter expression. An increased risk of vomiting has been reported in patients with high ABCB1 transporter expression when taking standard doses of granisetron. Monitor for decreased response.

Hydrocodone
Vicodin

Possible Altered Response to Hydrocodone (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Increased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 ultra-rapid metabolizers. Usually, adequate pain relief without an increase in adverse events can be achieved by using standard or lower hydrocodone doses. Other opioids not metabolized by CYP2D6 (e.g., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if excessive side effects are reported.

Lansoprazole
Prevacid

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

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

Maprotiline
Ludiomil

Possible Non-response to Maprotiline (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Like other tricyclic and tetracyclic antidepressants, maprotiline is metabolized by CYP2D6 as well as CYP1A2. Patients with increased CYP2D6 function may metabolize maprotiline more rapidly which can result in sub-therapeutic drug concentrations; these patients may require higher doses to achieve adequate plasma concentrations. **There are no established dosing adjustments for patients with increased CYP2D6 function. Seizures have been associated with the use of maprotiline especially at high doses. Therefore, therapy must be initiated at a standard dose and gradually increased in small increments according to the patient's response.**

Methadone
Dolophine

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

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

Mexiletine
Mexitil

Altered Response to Mexiletine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Because mexiletine plasma concentrations may be decreased, consider adjusting dose in response to mexiletine plasma concentration and ECG monitoring, until a favorable response in achieved.

Morphine
MS Contin

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

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

Naltrexone
Vivitrol, Contrave

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

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

Netupitant-Palonosetron
Akynzeo

Possible Altered Response to Netupitant-Palonosetron (CYP2D6: Ultra-Rapid 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 is eliminated by multiple routes including metabolism. While CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in its metabolism to two inactive metabolites. Compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower palonosetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Palonosetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Olanzapine
Zyprexa

Unknown Response to Olanzapine (CYP1A2: Unknown Phenotype) — INFORMATIVE

There is little evidence regarding the impact of CYP1A2 genetic variants on olanzapine response. Although the patient's CYP1A2 metabolism status cannot be predicted accurately, smoking may increase the risk of non-response to standard doses, and 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.

Omeprazole
Prilosec

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

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

Oxycodone
Percocet, Oxycontin

Possible Altered Response to Oxycodone (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Increased conversion of oxycodone to the more active metabolite oxymorphone is expected in CYP2D6 ultra-rapid metabolizers. Usually, adequate pain relief without an increase in adverse events can be achieved by using standard or lower oxycodone doses. Other opioids not metabolized by CYP2D6 (e.g., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if excessive side effects are reported.

Palonosetron
Aloxi

Possible Altered Response to Palonosetron (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Palonosetron is eliminated by multiple routes including metabolism. While CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in its metabolism to two inactive metabolites. Compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower palonosetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Palonosetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Pantoprazole
Protonix

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

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

Perphenazine
Trilafon

Possible Non-Response to Perphenazine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Subjects with increased CYP2D6 function will metabolize perphenazine more rapidly, which can result in sub-therapeutic drug concentrations. Consider a dose increase with close monitoring until a favorable response is achieved.

Pimozide
Orap

Possible Non-Response to Pimozide (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

There is insufficient data to calculate dose adjustment, and if pimozide is prescribed at standard dosing, monitor response and be alert to reduced efficacy. Standard 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.

Propafenone
Rythmol

Altered Response to Propafenone (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

There is insufficient data to allow calculation of dose adjustment. Titrate carefully and adjust the dose in response to plasma concentration and ECG monitoring. OR consider alternative drug such as sotalol, disopyramide, quinidine, or amiodarone.

Propofol
Diprivan

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

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

Sertraline
Zoloft

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

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

Tacrolimus
Prograf

Insufficient Response to Tacrolimus (CYP3A5: Intermediate Metabolizer) — ACTIONABLE

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

Tetrabenazine
Xenazine

Unknown Sensitivity to Tetrabenazine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

For treating chorea associated with Huntington's disease: There is insufficient data to calculate dose adjustment, and if tetrabenazine is prescribed, 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 ultra-rapid metabolizers is not defined. The maximum daily dose in normal metabolizers is 100 mg with a maximum single dose of 37.5 mg**. If serious adverse events occur, titration should be stopped and the dose of tetrabenazine should be reduced. If the adverse event(s) do not resolve, consider withdrawal of tetrabenazine.

Tizanidine
Zanaflex

Unknown Response to Tizanidine (CYP1A2: Unknown Phenotype) — INFORMATIVE

There is little evidence regarding the impact of CYP1A2 genetic variants on tizanidine response. Although the patient's CYP1A2 metabolism status cannot be predicted accurately, 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.

Alfentanil
Alfenta

Normal Response to Alfentanil — INFORMATIVE

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

Alfuzosin
UroXatral

Normal Response to Alfuzosin — INFORMATIVE

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

Alprazolam
Xanax

Normal Response to Alprazolam — INFORMATIVE

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

Amphetamine
Adderall, Evekeo

Good Response to Amphetamine salts (COMT: High/Normal COMT Activity) — INFORMATIVE

The patient's genotype result predicts a higher likelihood of 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: Ultra-Rapid Metabolizer)
ACTIONABLE

No dosing adjustments are suggested in ultra-rapid metabolizers. Therefore, the dosing recommendations proposed are those for normal metabolizers (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 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 dosing with *Aristada* (intramuscular): 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 882 mg dose.

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.

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: Normal Metabolizer) — INFORMATIVE

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

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: Ultra-Rapid Metabolizer) — ACTIONABLE

No dosing adjustments are needed in CYP2D6 ultra-rapid metabolizers. 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: Rapid Metabolizer) — ACTIONABLE

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

Buprenorphine
Butrans, Buprenex

Normal Response to Buprenorphine — INFORMATIVE

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

Candesartan
Atacand

Normal Sensitivity to Candesartan Cilexetil — ACTIONABLE

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

Carbamazepine
Tegretol, Carbatrol, Epitol

Normal Response to Carbamazepine — INFORMATIVE

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

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.

Carvedilol
Coreg

Normal Sensitivity to Carvedilol (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

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.

Celecoxib
Celebrex

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

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

Chlorpropamide
Diabenese

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

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

Clobazam
Onfi

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

The genotype result predicts a rapid or an ultra-rapid metabolizer phenotype, which translates to an increased CYP2C19 function. Rapid and ultra-rapid metabolizers have a higher capacity to metabolize N-desmethylclobazam, the active metabolite of clobazam. However, there is insufficient data to allow calculation of dose adjustment when clobazam is prescribed. Therefore, the dosing recommendation for normal metabolizers is proposed. Clobazam can be prescribed at standard label-recommended dosage and administration. Individualize dosing within each body weight group, based on clinical efficacy and tolerability. Do not proceed with dose escalation more rapidly than weekly, because serum concentrations of clobazam and its active metabolite require 5 and 9 days, respectively, to reach steady state. Recommended daily dosing: ≤30 kg body weight: starting dose 5 mg; day 7: 10 mg and day 14: 20 mg; >30 kg body weight: starting dose 10 mg, day 7: 20 mg and day 14: 40 mg.

Clonazepam
Klonopin

Normal Response to Clonazepam — INFORMATIVE

Pharmacogenetic guidance: No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** clonazepam is extensively metabolized by CYP3A4 to an amino metabolite that is further acetylated by N-acetyltransferases. This drug should be used with caution when prescribed with CYP3A4 inhibitors or inducers.

Colchicine
Mitigare

Normal Response to Colchicine — INFORMATIVE

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.

Cyclobenzaprine
Flexeril, Amrix

Normal Response to Cyclobenzaprine — INFORMATIVE

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

Dabigatran Etexilate
Pradaxa

Normal Response to Dabigatran — INFORMATIVE

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

Darifenacin
Enablex

Normal Response to Darifenacin (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

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

Desvenlafaxine
Pristiq

Normal Sensitivity to Desvenlafaxine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Desvenlafaxine is primarily metabolized by conjugation (mediated by UGT enzymes) and, to a minor extent, through oxidative metabolism (mediated by CYP3A4). The CYP2D6 enzyme is not involved in its metabolism.

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

Deutetrabenazine
Austedo

Normal Sensitivity to Deutetrabenazine (CYP2D6: Ultra-Rapid 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 followed by a slow titration at weekly intervals by 6 mg per day based on tolerability and up to a maximum recommended daily dosage of 48 mg (24 mg twice daily).

Dexmethylphenidate
Focalin

Good Response to Dexmethylphenidate (COMT: High/Normal COMT Activity) — INFORMATIVE

The patient's genotype result predicts a higher likelihood of response to dexmethylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

Dextroamphetamine
Dexedrine

Good Response to Dextroamphetamine (COMT: High/Normal COMT Activity) — INFORMATIVE

The patient's genotype result predicts a higher likelihood of 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: Ultra-Rapid Metabolizer) — ACTIONABLE

Patients with Pseudobulbar Affect: the quinidine component of dextromethorphan-quinidine is intended to inhibit CYP2D6 so that higher exposure to dextromethorphan can be achieved compared to when dextromethorphan is given alone. There are no established dosing adjustments for patients with increased CYP2D6 function. Dextromethorphan-quinidine can be prescribed according to standard label-recommended dosage and administration with additional monitoring.

Diclofenac
Voltaren

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

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

Dolutegravir
Tivicay, Triumeq

Normal Response to Dolutegravir — ACTIONABLE

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

Doxazosin
Cardura

Normal Response to Doxazosin — INFORMATIVE

Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** doxazosin is metabolized by multiple enzymes. There is limited data on the effects of drugs known to influence the metabolism of doxazosin.

Dronabinol
Marinol

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

The patient's genotype predicts a normal CYP2C9 metabolic activity. Dronabinol can be prescribed at standard label-recommended dosage and administration.

Duloxetine
Cymbalta

Normal Sensitivity to Duloxetine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

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

Dutasteride
Avodart

Normal Response to Dutasteride — INFORMATIVE

Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Dutasteride is extensively metabolized in humans by CYP3A4 and CYP3A5. The effect of potent CYP3A4 inhibitors on dutasteride has not been studied. Because of the potential for drug-drug interactions, use caution when prescribing this drug to patients taking potent, chronic CYP3A4 enzyme inhibitors.

Edoxaban
Savaysa

Normal Response to Edoxaban — **INFORMATIVE**

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

Eprosartan
Teveten

Normal Sensitivity to Eprosartan — **ACTIONABLE**

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

Eslicarbazepine
Aptiom

Normal Response to Eslicarbazepine — **INFORMATIVE**

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

Ethosuximide
Zarontin

Normal Response to Ethosuximide — **INFORMATIVE**

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

Ezogabine
Potiga

Normal Response to Ezogabine — **INFORMATIVE**

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

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

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

The patient does not carry the OPRM1 118A>G mutation. Acute postoperative and cancer pain: the patient is expected to experience good analgesia at standard fentanyl doses. Because fentanyl has a narrow therapeutic window, it is advised to carefully titrate this drug to a tolerable dose that provides adequate analgesia with minimal side effects.

Fesoterodine
Toviaz

Normal Sensitivity to Fesoterodine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

There are no studies related to the exposure of fesoterodine active metabolite in ultra-rapid metabolizers. Therefore, this drug 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.

Flibanserin
Addyi

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

Fluoxetine is metabolized to its active metabolite norfluoxetine and to other metabolites by multiple enzymes including CYP2D6, CYP2C19, CYP2C9, and CYP3A4. Compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower fluoxetine plasma concentrations at standard dosing. However, the clininal significance of this change remains unclear. Consider prescribing fluoxetine at standard dosage and monitor the patient for decreased efficacy.

Flurbiprofen
Ansaid

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

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

Fluvastatin
Lescol

Normal Myopathy Risk (SLCO1B1: Normal Function) — INFORMATIVE

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

Fluvastatin
Lescol

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

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

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.

Fosphenytoin
Cerebyx

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

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

Gabapentin
Neurontin

Normal Response to Gabapentin — INFORMATIVE

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

Galantamine
Razadyne

Normal Sensitivity to Galantamine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

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

Glimepiride
Amaryl

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

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

Glipizide
Glucotrol

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

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

Glyburide
Micronase

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

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

Guanfacine
Intuniv

Normal Response to Guanfacine — INFORMATIVE

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

Hydromorphone
Dilaudid, Exalgo

Normal Response to Hydromorphone — INFORMATIVE

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

Ibuprofen
Advil, Motrin

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

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

Iloperidone
Fanapt

Normal Sensitivity to Iloperidone (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Iloperidone can be prescribed at standard label-recommended dosage and administration. Iloperidone must be titrated slowly from a low starting dose to avoid orthostatic hypotension. If patients taking iloperidone experience symptoms that could indicate the occurrence of cardiac arrhythmias (e.g., dizziness, palpitations, or syncope), the prescriber should initiate further evaluation, including cardiac monitoring.

Indomethacin
Indocin

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

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

Irbesartan
Avapro

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

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

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: Rapid Metabolizer) — INFORMATIVE

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

Lamotrigine
Lamictal

Normal Response to Lamotrigine — INFORMATIVE

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

Leflunomide
Arava

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

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

Lesinurad
Zurampic

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

The patient's genotype predicts a normal 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

Good Response to Lisdexamfetamine (COMT: High/Normal COMT Activity) — INFORMATIVE

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

Losartan
Cozaar, Hyzaar

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

Losartan is metabolized to its active metabolite by CYP2C9 and CYP3A4. The patient's genotype predicts a normal exposure to losartan and its active metabolite. Losartan can be prescribed at label-recommended dosage and administration.

Lovastatin
Mevacor, Altoprev, Advicor

Normal Myopathy Risk (SLCO1B1: Normal Function) — INFORMATIVE

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.

Lovastatin
Mevacor, Altoprev, Advicor

Normal Response to Lovastatin (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 lovastatin dose requirements.

Loxapine
Loxitane, Adasuve

Normal Response to Loxapine — INFORMATIVE

Pharmacogenetic guidance: Loxapine is metabolized extensively in the liver following oral administration, with multiple metabolites formed. Loxapine metabolism occurs via hydroxylation and oxidation catalyzed by CYP1A2 along with contributions from CYP3A4, CYP2D6 and FMO. There are no studies documenting the effect of genetic polymorphisms of these metabolizing enzymes on Loxapine disposition and there are no available genetically-guided drug selection or dosing recommendations. **Polypharmacy guidance:** Loxapine is a central nervous system (CNS) depressant. The concurrent use of Loxapine with other CNS depressants (*e.g.*, alcohol, opioid analgesics, benzodiazepines, tricyclic antidepressants, general anesthetics, phenothiazines, sedative/hypnotics, muscle relaxants, and/or illicit CNS depressants) can increase the risk of respiratory depression, hypotension, profound sedation, and syncope. Therefore, consider dose reduction/modification of CNS depressants if used concomitantly with Loxapine. Loxapine has anticholinergic activity and concomitant use with other anticholinergic drugs can increase the risk of adverse reactions, including exacerbation of glaucoma and urinary retention.

Lurasidone
Latuda

Normal Response to Lurasidone — ACTIONABLE

Pharmacogenetic guidance: Lurasidone is metabolized by CYP3A4. No genotype-based dosing adjustments are available. **Polypharmacy guidance:** The concomitant use of lurasidone with all CYP3A4 inhibitors may result in an increase in lurasidone plasma concentrations, which could increase or prolong adverse drug effects. **Lurasidone should not be administered with strong CYP3A4 inhibitors**. Lurasidone dose should not exceed 40 mg when administered with moderate CYP3A4 inhibitors. Monitor patients receiving lurasidone and any CYP3A4 inhibitor. **Rifampin or other strong inducers of CYP3A should not be administered with lurasidone.** If lurasidone is used concomitantly with a moderate CYP3A4 inducer, it may be necessary to increase lurasidone dose after chronic treatment (7 days or more) with the CYP3A4 inducer.

Meloxicam
Mobic

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

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

Memantine
Namenda

Normal Response to Memantine — INFORMATIVE

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

Meperidine
Demerol

Normal Response to Meperidine — INFORMATIVE

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

Metaxalone
Skelaxin

Normal Response to Metaxalone — INFORMATIVE

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

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.

Methotrexate
Trexall

Normal risk for methotrexate toxicity (MTHFR: Normal MTHFR Activity) — INFORMATIVE

The patient does not carry the MTHFR 677 T allele, and unless other risk factors are present, the patient is not expected to have an increased risk for methotrexate toxicity. Consider using label-recommended dosage and administration.

Methylphenidate
Ritalin, Aptensio XR, Concerta, Metadate ER, Quillivant ER

Good Response to Methylphenidate (COMT: High/Normal COMT Activity) — INFORMATIVE

The patient's genotype result predicts a higher likelihood of 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.

Metoclopramide
Reglan

Normal Response to Metoclopramide (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Metoclopramide is metabolized at a faster rate in CYP2D6 ultra-rapid metabolizers, which may result in lower serum concentrations of the drug, but the clinical impact of this change is unknown. Metoclopramide can be prescribed at standard label-recommended dosage and administration.

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.

Milnacipran
Savella

Normal Response to Milnacipran — INFORMATIVE

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

Mirabegron
Myrbetriq

Normal Sensitivity to Mirabegron (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The exposure of mirabegron is slightly decreased in CYP2D6 ultra-rapid metabolizers. However, this change is not clinically significant, and no changes in the pharmacological or toxic effects of the drug are expected. Therefore, mirabegron can be prescribed at standard label-recommended dosage and administration.

Mirtazapine
Remeron

Normal Sensitivity to Mirtazapine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Mirtazapine can be prescribed at standard label-recommended dosage and administration. If higher doses are prescribed, there is an increased risk of cardiovascular adverse events. Therefore, careful titration is recommended until a favorable response is achieved.

Nabumetone
Relafen

Normal Response to Nabumetone — INFORMATIVE

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

Naproxen
Aleve

Normal Sensitivity to Naproxen — INFORMATIVE

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

Nateglinide
Starlix

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

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.

Nateglinide
Starlix

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

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

Nebivolol
Bystolic

Normal Sensitivity to Nebivolol (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

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

Nefazodone
Serzone

Normal Sensitivity to Nefazodone (CYP2D6: Ultra-Rapid 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.

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.

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.

Oxymorphone
Opana, Numorphan

Normal Response to Oxymorphone — INFORMATIVE

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

Paliperidone
Invega

Normal Sensitivity to Paliperidone (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Paliperidone is metabolized to a limited extent by CYP2D6, and changes in CYP2D6 activity are not expected to alter the response to this drug. Paliperidone can be prescribed at standard label-recommended dosage and administration.

Perampanel
Fycompa

Normal Response to Perampanel — INFORMATIVE

Pharmacogenetic guidance: Perampanel is eliminated either unchanged or following oxidative metabolism by CYP3A4 and CYP3A5. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Enzyme-inducing drugs decrease perampanel plasma concentrations by 50-60%, and the initial dosage of the drug should be increased when it is added to a stable therapy regimen containing enzyme-inducing antiepileptic drugs. Coadministration with strong enzyme-inducers others than antiepileptic drugs (e.g., rifampin) should be avoided. Coadministration with perampanel with strong CYP3A4 inhibitors such as ketoconazole increases perampanel exposure by 20%.

Phenobarbital
Luminal

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

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

Phenytoin
Dilantin

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

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

Pimavanserin
Nuplazid

Normal Response to Pimavanserin — INFORMATIVE

Pharmacogenetic guidance: Pimavanserin is predominantly metabolized by CYP3A4 and CYP3A5 and to a lesser extent by CYP2J2, CYP2D6, and other CYP and FMO enzymes. CYP3A4 is the major enzyme responsible for the formation of its major active metabolite (AC-279). There are no available genetically-guided drug selection or dosing recommendations.
Polypharmacy guidance: Pimavanserin prolongs the QT interval and its use should be avoided in patients with known QT prolongation or in combination with other drugs known to prolong QT interval including Class 1A antiarrhythmics (e.g., quinidine, procainamide) or Class 3 antiarrhythmics (e.g., amiodarone, sotalol), certain antipsychotic medications (e.g., ziprasidone, chlorpromazine, thioridazine), and certain antibiotics (e.g., gatifloxacin, moxifloxacin). Concomitant use of pimavanserin with CYP3A4 inhibitor increases pimavanserin exposure and a dose reduction of 50% is needed when this drug is coadministered with strong CYP3A inhibitors. Coadministration of pimavanserin with strong CYP3A inducers may result in reduced efficacy and a dose increase may be needed.

Piroxicam
Feldene

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

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

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: Rapid Metabolizer) — INFORMATIVE

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

Proguanil
Malarone

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

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

Propranolol
Inderal

Normal Sensitivity to Propranolol (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

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

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: Rapid Metabolizer) — **INFORMATIVE**

Rabeprazole can be prescribed at standard 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: Ultra-Rapid 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 mg 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.

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.

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.

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.

Tadalafil
Cialis

Normal Response to Tadalafil — INFORMATIVE

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

Tamsulosin
Flomax

Normal Response to Tamsulosin (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Tamsulosin may be metabolized at a faster rate in CYP2D6 ultra-rapid metabolizers, potentially resulting in decreased serum concentrations of tamsulosin. However, there is insufficient data related to the clinical impact of this potential change. Therefore, 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: Ultra-Rapid 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: Ultra-Rapid Metabolizer) — ACTIONABLE

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

Tofacitinib
Xeljanz

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

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

Tolbutamide
Orinase

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

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

Tolterodine
Detrol

Normal Sensitivity to Tolterodine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

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

Topiramate
Topamax

Normal Response to Topiramate — INFORMATIVE

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

Torsemide
Demadex

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

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

Trazodone
Oleptro

Normal Response to Trazodone — INFORMATIVE

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

Trifluoperazine
Stelazine

Normal Response to Trifluoperazine — INFORMATIVE

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

Trospium
Sanctura

Normal Response to Trospium — INFORMATIVE

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

Valbenazine
Ingrezza

Normal Sensitivity to Valbenazine (CYP2D6: Ultra-Rapid 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.

Vigabatrin
Sabril

Normal Response to Vigabatrin — INFORMATIVE

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

Vilazodone
Viibryd

Normal Response to Vilazodone — **INFORMATIVE**

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

Vorapaxar
Zontivity

Normal Response to Vorapaxar — **ACTIONABLE**

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

Vortioxetine
Trintellix

Normal Sensitivity to Vortioxetine (CYP2D6: Ultra-Rapid Metabolizer) — **ACTIONABLE**

There is little evidence documenting the exposure of this drug in CYP2D6 ultra-rapid metabolizers. Vortioxetine plasma concentrations may decrease, but the clinical relevance of this change is not documented. 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.

Warfarin
Coumadin

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

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

Ziprasidone
Geodon

Normal Response to Ziprasidone — **INFORMATIVE**

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

Zonisamide
Zonegran

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

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

GENE CARD FOR XXXX XXXXXX

This gene card can be provided to the patients to assist their pharmacist for personalizing medications.
The card can be cut out along the dashed line and carried with the patient.

REPORT DETAILS

Name: XXXX XXXXXX
DOB: XX/XX/1970
ACC #: XXXXXX

Pharmacogenetic Test Summary

ABCB1	3435C>T C/C	Variant Allele Not Present
ANKK1/DRD2	DRD2:Taq1A G/G	Unaltered DRD2 function
Apolipoprotein E	ε3/ε3	Normal APOE function
COMT	Val158Met G/G	High/Normal COMT Activity
CYP1A2	*1L/*1L	Unknown Phenotype
CYP2B6	*1/*6	Intermediate Metabolizer
CYP2C19	*1/*17	Rapid Metabolizer
CYP2C9	*1/*1	Normal Metabolizer
CYP2D6	*1/*2 XN	Ultra-Rapid Metabolizer
CYP3A4	*1/*1	Normal Metabolizer
CYP3A5	*1/*6	Intermediate Metabolizer
Factor II	20210G>A GG	Normal Thrombosis Risk
Factor V Leiden	1691G>A GG	Normal Thrombosis Risk
MTHFR	1298A>C AC	Reduced MTHFR Activity
MTHFR	677C>T CC	Normal MTHFR Activity
OPRM1	A118G A/A	Normal OPRM1 Function
SLCO1B1	521T>C T/T	Normal Function
VKORC1	-1639G>A G/G	Low Warfarin Sensitivity

For a complete report contact Ayass BioScience LLC
www.AyassBioscience.com