Dynamic DNA Laboratories, LLC

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Comprehensive Pharmacogenetic Report Created for: Connie Comprehensive

Patient:	Connie Comprehensive	DOB:	1/1/1970
Collection Date:	1/1/2016	SSN:	123-45-6789
Ordering Physician:	Leonard McCoy	Report Generated:	6/7/2016
Provider/Facility:	Vanilla Life Tech Test Provider	Patient Phone:	123-456-789
MRN:	0123456	Requisition Number:	123456
ICD Codes:	311	Patient Ethnicity:	Caucasian
	339.12		
	413.9		
	427.32		

Current Patient Medications

Current Medication List: Warfarin, Codeine, Aspirin, Apixaban

Medications Affected by Patient Genetic Results

Codeine (Codeine; Fioricet with Codeine)	Increased Response to Codeine (CYP2D6 *1/*1 XN Rapid Metabolizer)	*Codeine is converted into its active metabolite morphine by CYP2D6. Since this patient is a rapid metabolizer, greatly increased morphine levels are expected, and the patient is at high risk of toxicity when taking codeine. 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.
Warfarin (Coumadin)	Mild Sensitivity to Warfarin (CYP2C9 *2/*2 VKORC1 -1639G>A G/G)	*Initiation Therapy: a dose decrease may be required. Consider using the warfarin dose range provided in the FDA-approved label: **3-4 mg/day.** OR consider using a personalized dose calculated by a pharmacogenetic algorithm. The estimated time to reach steady state is 8-10 days.
Apixaban (Eliquis)	Normal Response to Apixaban	**Pharmacogenetic guidance:** Apixaban is not extensively metabolized and only ~20% of the dose is metabolized primarily by CYP3A4 and CYP3A5, with minor contributions from CYP1A2 and CYP2J2. This drug is a substrate for the efflux transport proteins P-gp (ABCB1) and BCRP (ABCG2). While these enzymes and transporters are polymorphic, genetic variations are unlikely to have a clinically significant impact on apixaban exposure, and no genotype-based dosing adjustments are recommended. **Polypharmacy guidance:** Exposure to apixaban increases by 100% when co-administered with ketoconazole, a strong CYP3A/P-gp inhibitor. This translates into an increased bleeding risk (70% increase). Hence, for patients receiving 5 mg twice daily, apixaban dose should be decreased to 2.5 mg twice daily when it is coadministered with drugs that are strong dual inhibitors of CYP3A4 and P-gp (e.g., ketoconazole, itraconazole, ritonavir, and clarithromycin). In patients already taking 2.5 mg twice daily, coadministration of apixaban with strong dual inhibitors of CYP3A4 and P-gp should be avoided. No dose adjustment is recommended when co-administered with moderate inhibitors. Co-administration with rifampin, a strong CYP3A/P-gp inducer, results in halving of exposure to apixaban. There is no clinical experience at these reduced exposures. Hence, concomitant administration of strong CYP3A/P-gp inducers should be avoided.

Pharmacogenetic interpretation cannot be provided for the following patient medications that are outside the scope of this report:

Aspirin

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Guidance Levels

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

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

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

Evidence Levels

***Actionable** - Recommendations based upon publications by international pharmacogenetic expert groups, consortia or regulatory bodies (CPIC, DPWG, FDA, EMA). Recommendations are suitable for implementation in a clinical setting. Guidelines may change as new knowledge arises.
****Informative** - There are insufficient or contradictory findings documenting the impact of a given genetic polymorphism or drug interaction. Recommendations are informative and implementation in a clinical setting is optional.

Risk Management

Hyperlipidemia/Atherosclerotic Cardiovascular Disease

No increased risk of hyperlipidemia/atherosclerotic vascular disease

The patient is negative for the APOE 388 T>C (Arg112Cys) and 526 C>T (Cys158Arg) 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. Defects in APOE can increase a person's risk for developing atherosclerosis and cardiovascular disease.

No action is needed when a patient is normolipidemic.

Thrombophilia

No Increased Risk of Thrombosis

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

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

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

Hyperhomocysteinemia - Thrombosis

No Increased Risk of Hyperhomocysteinemia

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

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

MTHFR enzyme activity is normal.

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Potentially Impacted Medications				
Category	**Drug Class**	**Standard Precautions**	**Use With Caution**	**Consider Alternatives**
Anticancer Agents	Antifolates		Methotrexate (Trexall)	
Cardiovascular	Angiotensin II Receptor Antagonists	Azilsartan (Edarbi, Edarbyclor) Candesartan (Atacand) Eprosartan (Teveten) Irbesartan (Avapro) Olmesartan (Benicar) Telmisartan (Micardis) Valsartan (Diovan, Entresto)	Losartan (Cozaar, Hyzaar)	
	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	Clopidogrel (Plavix) Prasugrel (Effient) Ticagrelor (Brilinta) Vorapaxar (Zontivity)		
	Beta Blockers	Carvedilol (Coreg) Labetalol (Normodyne, Trandate) Nebivolol (Bystolic) Propranolol (Inderal) Timolol (Timoptic)		Metoprolol (Lopressor)
	Diuretics		Torsemide (Demadex)	
	Statins	Atorvastatin (Lipitor) Lovastatin (Mevacor, Altoprev, Advicor) Pitavastatin (Livalo) Pravastatin (Pravachol) Rosuvastatin (Crestor) Simvastatin (Zocor)	Fluvastatin (Lescol)	
Diabetes	Meglitinides	Repaglinide (Prandin, Prandimet)	Nateglinide (Starlix)	
	Sulfonylureas		Chlorpropamide (Diabenese) Glimepiride (Amaryl) Glipizide (Glucotrol) Glyburide (Micronase) Tolbutamide (Orinase)	

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

Category	Drug Class	Standard Precautions	Use With Caution	Consider Alternatives
Psychotropic	Anticonvulsants	Brivaracetam (Briviact) Carbamazepine (Tegretol, Carbatrol, Epitol) Eslicarbazepine (Aptiom) Ethosuximide (Zarontin) Ezogabine (Potiga) Felbamate (Felbatol) Gabapentin (Neurontin) Lacosamide (Vimpat) Lamotrigine (Lamictal) Levetiracetam (Keppra) Oxcarbazepine (Trileptal, Oxtellar XR) Perampanel (Fycompa) Phenobarbital (Luminal) Pregabalin (Lyrica) Primidone (Mysoline) Rufinamide (Banzel) Tiagabine (Gabitril) Topiramate (Topamax) Valproic Acid (Depakote, Depakene) Vigabatrin (Sabril) Zonisamide (Zonegran)	Fosphenytoin (Cerebyx) Phenytoin (Dilantin)	
	Antidementia Agents	Galantamine (Razadyne) Memantine (Namenda)	Donepezil (Aricept)	
	Antidepressants	Citalopram (Celexa) Desvenlafaxine (Pristiq) Duloxetine (Cymbalta) Escitalopram (Lexapro) Fluoxetine (Prozac, Sarafem) Levomilnacipran (Fetzima) Mirtazapine (Remeron) Nefazodone (Serzone) Sertraline (Zoloft) Vilazodone (Viibryd) Vortioxetine (Brintellix)	Amoxapine (Amoxapine) Fluvoxamine (Luvox) Maprotiline (Ludiomil)	Amitriptyline (Elavil) Clomipramine (Anafranil) Desipramine (Norpramin) Doxepin (Silenor) Imipramine (Tofranil) Nortriptyline (Pamelor) Paroxetine (Paxil, Brisdelle) Protriptyline (Vivactil) Trimipramine (Surmontil) Venlafaxine (Effexor)
	Antipsychotics	Aripiprazole (Abilify) Asenapine (Saphris) Brexpiprazole (Rexulti) Clozapine (Clozaril) Iloperidone (Fanapt) Loxapine (Loxitane, Adasuve) Lurasidone (Latuda) Olanzapine (Zyprexa) Paliperidone (Invega) Quetiapine (Seroquel) Thioridazine (Mellaril) Thiothixene (Navane) Trazodone (Oleptro) Trifluoperazine (Stelazine) Ziprasidone (Geodon)	Chlorpromazine (Thorazine) Fluphenazine (Prolixin) Perphenazine (Trilafon) Pimozide (Orap) Tetrabenazine (Xenazine)	Haloperidol (Haldol) Risperidone (Risperdal)

Category	Drug Class	Standard Precautions	Use With Caution	Consider Alternatives
	Benzodiazepines	Alprazolam (Xanax) Clobazam (Onfi) Clonazepam (Klonopin) Diazepam (Valium)		
	Other Neurological Agents	Dextromethorphan / Quinidine (Nuedexta)		
Rheumatology	Immunomodulators	Apremilast (Otezla) Leflunomide (Arava) Tofacitinib (Xeljanz)		
Transplantation	Immunosupressants	Tacrolimus (Prograf)		
Urologicals	5-Alpha Reductase Inhibitors for Benign Prostatic Hyperplasia	Dutasteride (Avodart) Finasteride (Proscar)		
	Alpha-Blockers for Benign Prostatic Hyperplasia	Alfuzosin (UroXatral) Doxazosin (Cardura) Silodosin (Rapaflo) Tamsulosin (Flomax) Terazosin (Hytrin)		
	Antispasmodics for Overactive Bladder	Darifenacin (Enablex) Fesoterodine (Toviaz) Mirabegron (Myrbetriq) Oxybutynin (Ditropan) Solifenacin (Vesicare) Tolterodine (Detrol) Trospium (Sanctura)		
	Phosphodiesterase Inhibitors for Erectile Dysfunction	Avanafil (Stendra) Sildenafil (Viagra) Tadalafil (Cialis) Vardenafil (Levitra)		

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Dosing Guidance

Amitriptyline (Elavil)	Non-Response to Amitriptyline (CYP2D6 *1/*1 XN Rapid Metabolizer)	*Consider an alternative drug, or prescribe amitriptyline at an increased dose and monitor the plasma concentration of amitriptyline and metabolites.
Atomoxetine (Strattera)	Non-Response to Atomoxetine (CYP2D6 *1/*1 XN Rapid Metabolizer)	**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.
Clomipramine (Anafranil)	Non-Response to Clomipramine (CYP2D6 *1/*1 XN Rapid Metabolizer)	*Consider an alternative drug, or prescribe clomipramine at an increased dose and monitor the plasma concentration of clomipramine and desmethylclomipramine.
Codeine (Codeine; Fioricet with Codeine)	Increased Response to Codeine (CYP2D6 *1/*1 XN Rapid Metabolizer)	*Codeine is converted into its active metabolite morphine by CYP2D6. Since this patient is a rapid metabolizer, greatly increased morphine levels are expected, and the patient is at high risk of toxicity when taking codeine. 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 *1/*1 XN Rapid Metabolizer)	*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 *1/*1 XN Rapid Metabolizer)	*Consider an alternative drug or increase doxepin dose by 100%. Adjust maintenance dose according to nordoxepin plasma concentrations.
Flecainide (Tambocor)	Altered Response to Flecainide (CYP2D6 *1/*1 XN Rapid Metabolizer)	*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 *1/*1 XN Rapid Metabolizer)	*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 *1/*1 XN Rapid Metabolizer)	*Consider an alternative drug or consider prescribing imipramine at an increased dose, then adjust dosage in response to imipramine and desipramine plasma concentrations.

Metoprolol (Lopressor)	Possible Non-Responder to Metoprolol (CYP2D6 *1/*1 XN Rapid Metabolizer)	*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 *1/*1 XN Rapid Metabolizer)	*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 *1/*1 XN Rapid Metabolizer)	**A substantially decreased antiemetic effect has been reported in CYP2D6 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 *1/*1 XN Rapid Metabolizer)	*There is a risk for decreased efficacy at standard dosage. If a standard dose is prescribed to a CYP2D6 rapid metabolizer, suboptimal plasma concentrations of the drug are likely. Consider an alternative medication.
Protriptyline (Vivactil)	Non-Response to Protriptyline (CYP2D6 *1/*1 XN Rapid Metabolizer)	*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 *1/*1 XN Rapid Metabolizer)	*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 *1/*1 XN Rapid Metabolizer)	*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 and weekly titration are recommended. If 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.
Trimipramine (Surmontil)	Non-Response to Trimipramine (CYP2D6 *1/*1 XN Rapid Metabolizer)	*Consider an alternative drug, or consider prescribing trimipramine at an increased dose, then adjust dosage in response to trimipramine plasma concentrations.
Venlafaxine (Effexor)	Non-Response to Venlafaxine (CYP2D6 *1/*1 XN Rapid Metabolizer)	*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.

Amoxapine (Amoxapine)	Possible Non-Response to Amoxapine (CYP2D6 *1/*1 XN Rapid Metabolizer)	**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.
Amphetamine (Adderall)	Poor Response to Amphetamine salts (COMT Val158Met AA Low COMT Activity)	**The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, amphetamines should be administered at the lowest effective dose, and dosage should be individually adjusted.
Celecoxib (Celebrex)	High Sensitivity to Celecoxib (CYP2C9 *2/*2 Poor Metabolizer)	*Consider starting at half the lowest recommended dose, and evaluate response the first week. Be alert to gastrointestinal adverse events. Consider alternative medication for the management of Juvenile Rheumatoid Arthritis.
Chlorpromazine (Thorazine)	Possible Non-Response to Chlorpromazine (CYP2D6 *1/*1 XN Rapid Metabolizer)	**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.
Chlorpropamide (Diabenese)	Possible Sensitivity to Chlorpropamide (CYP2C9 *2/*2 Poor Metabolizer)	**Subjects with reduced CYP2C9 activity may have increased chlorpropamide plasma drug concentrations at standard doses, leading to hypoglycemic episodes. Because there is insufficient data to whether such changes have a significant clinical impact, chlorpropamide can be prescribed according to standard label-recommended dosage and administration, with frequent monitoring of plasma glucose levels.
Clonidine (Kapvay)	Possible Altered Response to Clonidine (CYP2D6 *1/*1 XN Rapid Metabolizer)	**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.
Dexmethylphenidate (Focalin)	Poor Response to Dexmethylphenidate (COMT Val158Met AA Low COMT Activity)	**The patient's genotype result predicts a reduced therapeutic response to dexmethylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.
Dextroamphetamine (Dexedrine)	Poor Response to Dextroamphetamine (COMT Val158Met AA Low COMT Activity)	**The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, dextroamphetamine should be administered at the lowest effective dose, and dosage should be individually adjusted.

⚠ **Diclofenac (Voltaren)**	Possible Sensitivity to Diclofenac (CYP2C9 *2/*2 Poor Metabolizer)	**Diclofenac is extensively metabolized by hydroxylation and direct glucuronidation. About 50% of diclofenac is eliminated as a 4-hydroxymetabolite, a reaction mediated by CYP2C9. Other CYP enzymes including CYP2C8, CYP2C19 and CYP3A4 are also involved in the formation of a 5-hydroxymetabolite. A substantial portion of the drug is also directly glucuronidated by UGT2B7 and UGT2B4. Individuals with decreased CYP2C9 activity (i.e poor metabolizers) should be closely monitored for increased gastrointestinal adverse events when prescribed diclofenac and lower doses may be more appropriate for these patients.
⚠ **Dihydrocodeine (Synalgos-DC)**	Possible Altered Response to Dihydrocodeine (CYP2D6 *1/*1 XN Rapid Metabolizer)	*Increased conversion of dihydrocodeine to the more active metabolite dihydromorphine is expected in CYP2D6 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 *1/*1 XN Rapid Metabolizer)	**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 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 *1/*1 XN Rapid Metabolizer)	**When compared to a normal metabolizer, a 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.
⚠ **Fluphenazine (Prolixin)**	Possible Non-response to Fluphenazine (CYP2D6 *1/*1 XN Rapid Metabolizer)	**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.
⚠ **Flurbiprofen (Ansaid)**	Increased Sensitivity to Flurbiprofen (CYP2C9 *2/*2 Poor Metabolizer)	*At standard dosage, plasma concentrations of flurbiprofen are expected to be high, resulting in an increased risk of gastrointestinal toxicity. Administer flurbiprofen with caution and reduce dose if necessary.

⚠	**Fluvastatin (Lescol)**	Increased Sensitivity to Fluvastatin (CYP2C9 *2/*2 Poor Metabolizer)	***** Increased fluvastatin plasma concentrations due to reduced CYP2C9 activity may occur, resulting in myotoxicity/hepatotoxicity. Consider monitoring the patient for treatment-related adverse effects, and adjust dose as needed. Other adverse events and predisposing factors include advanced age (≥65), diabetes, hypothyroidism, renal or hepatic impairments, high statin dose, CYP2C9 inhibitors, ABCG2 inhibitors, and female gender.
⚠	**Fluvoxamine (Luvox)**	Possible Reduced Response to Fluvoxamine (CYP2D6 *1/*1 XN Rapid Metabolizer)	****** There is a risk for decreased efficacy at standard dosage. If a standard dose is prescribed to a CYP2D6 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.
⚠	**Fosphenytoin (Cerebyx)**	High Sensitivity to Fosphenytoin (CYP2C9 *2/*2 Poor Metabolizer)	***** In CYP2C9 poor metabolizers, the plasma concentrations of phenytoin are expected to increase, resulting in an increased risk of severe neurological toxicity. This risk increases further in individuals who are also CYP2C19 poor metabolizers. **Consider a standard loading dose, and reduce the maintenance dose by 50%**. Evaluate response and serum concentrations after 7-10 days. **Be alert to neurological concentration-related adverse events.**
⚠	**Glimepiride (Amaryl)**	Possible Sensitivity to Glimepiride (CYP2C9 *2/*2 Poor Metabolizer)	***** Subjects with reduced CYP2C9 activity may have increased glimepiride plasma drug concentrations at standard doses, leading to hypoglycemic episodes. Because there is insufficient data to whether such changes have a significant clinical impact, glimepiride can be prescribed according to standard label-recommended dosage and administration, with frequent monitoring of plasma glucose levels.
⚠	**Glipizide (Glucotrol)**	Possible Sensitivity to Glipizide (CYP2C9 *2/*2 Poor Metabolizer)	****** Subjects with reduced CYP2C9 activity may have increased glipizide plasma drug concentrations at standard doses, leading to hypoglycemic episodes. Because there is insufficient data to whether such changes have a significant clinical impact, glipizide can be prescribed according to standard label-recommended dosage and administration, with frequent monitoring of glucose plasma levels.
⚠	**Glyburide (Micronase)**	Possible Sensitivity to Glyburide (CYP2C9 *2/*2 Poor Metabolizer)	***** Subjects with reduced CYP2C9 activity may have increased glyburide plasma drug concentrations at standard doses, leading to hypoglycemic episodes. Because there is insufficient data to whether such changes have a significant clinical impact, glyburide can be prescribed according to standard label-recommended dosage and administration with frequent monitoring of glucose plasma levels.
⚠	**Hydrocodone (Vicodin)**	Possible Altered Response to Hydrocodone (CYP2D6 *1/*1 XN Rapid Metabolizer)	****** Increased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 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.

Ibuprofen (Advil, Motrin)	Possible Sensitivity to Ibuprofen (CYP2C9 *2/*2 Poor Metabolizer)	**Ibuprofen is extensively metabolized into hydroxylate or carboxylate metabolites by CYP2C8 and CYP2C9. Diminished ibuprofen clearance has been found in CYP2C9 poor metabolizers and those with decreased CYP2C8 activity. This change in clearance may result in elevated concentrations of the drug inadvertently leading to adverse events. Although, dosage adjustment is not necessary in a patient identified as a CYP2C9 poor metabolizer, a lower dose and a closer monitoring for increased gastrointestinal adverse events may be considered.
Indomethacin (Indocin)	Possible Sensitivity to Indomethacin (CYP2C9 *2/*2 Poor Metabolizer)	**Indomethacin is metabolized mainly by O-demethylation to its inactive metabolite O-desmethylindomethacin, a reaction catalyzed by CYP2C9. At standard dosage, plasma concentrations of indomethacin are expected to be high resulting in an increased risk of gatrointestinal toxicity. To minimize the potential risk for an adverse event, the lowest effective dose should be used for the shortest possible duration.
Lisdexamfetamine (Vyvanse)	Poor Response to Lisdexamfetamine (COMT Val158Met AA Low COMT Activity)	**The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, lisdexamfetamine should be administered at the lowest effective dose, and dosage should be individually adjusted.
Losartan (Cozaar, Hyzaar)	Possible Decreased Response to Losartan (CYP2C9 *2/*2 Poor Metabolizer)	**Losartan is metabolized to its active metabolite by CYP2C9 and CYP3A4. The patient's genotype predicts a reduced exposure to losartan's active metabolite and a possible reduced hypotensive effect. Losartan can be prescribed at label-recommended dosage and administration with additional monitoring of the patient's response.
Maprotiline (Ludiomil)	Possible Non-response to Maprotiline (CYP2D6 *1/*1 XN Rapid Metabolizer)	**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 lower dose and gradually increased in small increments according to the patient's response.**
Meloxicam (Mobic)	Increased sensitivity to Meloxicam (CYP2C9 *2/*2 Poor Metabolizer)	**CYP2C9 poor metabolizers have a higher risk of experiencing gastrointestinal toxicities when taking meloxicam at standard doses. To minimize the potential risk of adverse events in these patients, **the lowest effective dose should be used for the shortest possible duration.**

Methotrexate (Trexall)	Increased risk for methotrexate toxicity (MTHFR 677C>T TT Reduced MTHFR Activity)	**The patient carries two MTHFR 677 T alleles, resulting in a significantly reduced MTHFR activity. **Malignancy:** Leukemia or lymphoma patients who are treated with methotrexate standard regimens may have an increased risk of overall toxicity (including mucositis, thrombocytopenia, and hepatic toxicity), and an increased severity of mucositis. Consider at least a 50% reduction in methotrexate starting dose, followed by titration based on toxicity. Other genetic and clinical factors may also influence the patient's risk for toxicity and response to methotrexate treatment. **Nonmalignant conditions:** a limited number of studies found an association between the MTHFR 677 T allele and methotrexate-induced toxicity in rheumatoid arthritis patients. However, there is insufficient data to calculate dose adjustment. Monitor patient closely for increased side effects and adjust the dose accordingly. Other genetic and clinical factors may also influence the patient's risk for toxicity and response to methotrexate treatment.
Methylphenidate (Ritalin)	Poor Response to Methylphenidate (COMT Val158Met AA Low COMT Activity)	**The patient's genotype result predicts a reduced therapeutic response to methylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.
Mexiletine (Mexitil)	Altered Response to Mexiletine (CYP2D6 *1/*1 XN Rapid Metabolizer)	**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 Val158Met AA Low COMT Activity)	**The patient carries two COMT Val158Met mutations, which translates to a reduced COMT function. The patient may require lower doses of morphine for adequate pain control. The dosing regimen needs to be individualized for each patient, taking into account the patient's prior analgesic treatment experience.
Naltrexone (Vivitrol, Contrave)	Altered Response to Naltrexone (OPRM1 A118G AA Normal OPRM1 Function)	**Treatment of alcohol dependence: the patient has the wild-type genotype for OPRM1 that is associated with a poorer outcome with naltrexone therapy. Naltrexone-treated patients not carrying the 118A> G mutation are less likely to respond to this drug, and may have higher relapse rates than those who are carriers of this mutation.
Nateglinide (Starlix)	Possible Sensitivity to Nateglinide (CYP2C9 *2/*2 Poor Metabolizer)	**The patient's genotype predicts a reduced CYP2C9 activity, which may result in a slightly increased risk for hypoglycemia. Nateglinide can be prescribed at label-recommended dosage and administration with additional monitoring of the patient's response.
Oxycodone (Percocet, Oxycontin)	Possible Altered Response to Oxycodone (CYP2D6 *1/*1 XN Rapid Metabolizer)	*Increased conversion of oxycodone to the more active metabolite oxymorphone is expected in CYP2D6 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 *1/*1 XN Rapid Metabolizer)	**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 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.
Perphenazine (Trilafon)	Possible Non-Response to Perphenazine (CYP2D6 *1/*1 XN Rapid Metabolizer)	*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.
Phenytoin (Dilantin)	High Sensitivity to Phenytoin (CYP2C9 *2/*2 Poor Metabolizer)	*In CYP2C9 poor metabolizers, the plasma concentrations of phenytoin are expected to increase, resulting in an increased risk of severe neurological toxicity. This risk increases further in individuals who are also CYP2C19 poor metabolizers. **Consider a standard loading dose, and reduce the maintenance dose by 50%**. Evaluate response and serum concentrations after 7-10 days. **Be alert to neurological concentration-related adverse events.**
Pimozide (Orap)	Possible Non-Response to Pimozide (CYP2D6 *1/*1 XN Rapid Metabolizer)	*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.
Piroxicam (Feldene)	Increased Sensitivity to Piroxicam (CYP2C9 *2/*2 Poor Metabolizer)	*At standard dosage, plasma concentrations of piroxicam are expected to be high, resulting in an increased risk of gastrointestinal toxicity. Administer piroxicam with caution and reduce dose if necessary.
Propafenone (Rythmol)	Altered Response to Propafenone (CYP2D6 *1/*1 XN Rapid Metabolizer)	*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.
Tetrabenazine (Xenazine)	Unknown Sensitivity to Tetrabenazine (CYP2D6 *1/*1 XN Rapid Metabolizer)	*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 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.
Tolbutamide (Orinase)	Possible Sensitivity to Tolbutamide (CYP2C9 *2/*2 Poor Metabolizer)	*Subjects with reduced CYP2C9 activity may have increased tolbutamide plasma drug concentrations at standard doses, leading to hypoglycemic episodes. Because there is insufficient data to whether such changes have a significant clinical impact, tolbutamide can be prescribed according to standard label-recommended dosage and administration, with frequent monitoring of glucose plasma levels.

⚠ **Torsemide (Demadex)**	Possible Sensitivity to Torsemide (CYP2C9 *2/*2 Poor Metabolizer)	**The patient's genotype predicts a reduced CYP2C9 function, which may result in reduced torsemide clearance. There is insufficient data to whether such change has a significant clinical impact and whether the diuretic effects are more pronounced in patients with this phenotye. Torsemide can be prescribed at label-recommended dosage and administration with additional monitoring of the patient's response.
⚠ **Warfarin (Coumadin)**	Mild Sensitivity to Warfarin (CYP2C9 *2/*2 VKORC1 -1639G>A G/G)	*Initiation Therapy: a dose decrease may be required. Consider using the warfarin dose range provided in the FDA-approved label: **3-4 mg/day.** OR consider using a personalized dose calculated by a pharmacogenetic algorithm. The estimated time to reach steady state is 8-10 days.
✓ **Alfentanil (Alfenta)**	Normal Response to Alfentanil	****Pharmacogenetic guidance**: alfentanil is primarily metabolized by CYP3A4 and CYP3A5. Studies in healthy subjects showed that CYP3A5 genotype had no effect on the systemic or apparent oral clearances, or pharmacodynamics of alfentanil. **Polypharmacy guidance:** Alfentanil should be used with caution when prescribed to patients taking CYP3A4 inhibitors or inducers.
✓ **Alfuzosin (UroXatral)**	Normal Response to Alfuzosin	****Pharmacogenetic guidance:** No genetically-guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Alfuzosin is extensively metabolized by CYP3A4 into pharmacologically inactive metabolites. Alfuzosin is **contraindicated with strong CYP3A4 inhibitors, as the risk for QTc prolongation induced by this drug is increased at higher concentrations**. Take caution when this drug is prescribed with CYP3A4 moderate inhibitors, as drug levels may increase.
✓ **Alprazolam (Xanax)**	Normal Response to Alprazolam	****Pharmacogenetic guidance:** Alprazolam is primarily eliminated by metabolism via CYP3A4 and CYP3A5. Genetic polymorphisms of these genes are not expected to affect the efficacy or safety profiles of this drug. **Polypharmacy guidance:** The concomitant use of alprazolam with CYP3A4 inhibitors may result in increased alprazolam levels and prolonged sedation. Impairment of motor skills are also observed with some combinations. Monitor patients for exaggerated sedative effects. If possible, alprazolam should be avoided in patients receiving strong inhibitors of CYP3A4 such as ketoconazole, itraconazole and ritonavir. Drugs that induce CYP3A enzymes may decrease alprazolam levels, which results in a loss of efficacy.

✓ **Apixaban (Eliquis)**	Normal Response to Apixaban	****Pharmacogenetic guidance:** Apixaban is not extensively metabolized and only ~20% of the dose is metabolized primarily by CYP3A4 and CYP3A5, with minor contributions from CYP1A2 and CYP2J2. This drug is a substrate for the efflux transport proteins P-gp (ABCB1) and BCRP (ABCG2). While these enzymes and transporters are polymorphic, genetic variations are unlikely to have a clinically significant impact on apixaban exposure, and no genotype-based dosing adjustments are recommended. **Polypharmacy guidance:** Exposure to apixaban increases by 100% when co-administered with ketoconazole, a strong CYP3A/P-gp inhibitor. This translates into an increased bleeding risk (70% increase). Hence, for patients receiving 5 mg twice daily, apixaban dose should be decreased to 2.5 mg twice daily when it is coadministered with drugs that are strong dual inhibitors of CYP3A4 and P-gp (e.g., ketoconazole, itraconazole, ritonavir, and clarithromycin). In patients already taking 2.5 mg twice daily, coadministration of apixaban with strong dual inhibitors of CYP3A4 and P-gp should be avoided. No dose adjustment is recommended when co-administered with moderate inhibitors. Co-administration with rifampin, a strong CYP3A/P-gp inducer, results in halving of exposure to apixaban. There is no clinical experience at these reduced exposures. Hence, concomitant administration of strong CYP3A/P-gp inducers should be avoided.
✓ **Apremilast (Otezla)**	Normal Response to Apremilast	***Pharmacogenetic guidance:** Apremilast is primarily eliminated via both hydrolysis and cytochrome P450-mediated oxidative metabolism (with subsequent glucuronidation). Cytochrome P450-metabolism is mediated by CYP3A4, with minor contributions from CYP1A2 and CYP2A6. Genetic polymorphisms of these enzymes are not expected to affect the efficacy or safety profiles of apremilast. **Polypharmacy guidance:** The use of metabolizing enzyme inducers (e.g. rifampin, phenobarbital, carbamazepine, phenytoin) with apremilast is not recommended.
✓ **Aripiprazole (Abilify)**	Normal Sensitivity to Aripiprazole (CYP2D6 *1/*1 XN Rapid Metabolizer)	*No dosing adjustments are suggested in 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 the dose to 25% of the usual dose if both a CYP2D6 inhibitor and a CYP3A4 inhibitor are coadministered. Monthly dosing (intramuscular): the starting and maintenance monthly recommended dose is 400 mg. Reduce the monthly dose to 300 mg if a CYP2D6 inhibitor or a CYP3A4 inhibitor is prescribed for more than 2 weeks to patients receiving aripiprazole at 400 mg, and reduce the dose to 200 mg in patients receiving aripiprazole at 300 mg. Reduce the dose to 200 mg if a CYP2D6 inhibitor and a CYP3A4 inhibitor are both prescribed for more than 2 weeks to patients receiving aripiprazole at 400 mg, and reduce the dose to 160 mg in patients receiving aripiprazole at 300 mg.

✓ **Asenapine (Saphris)**	Normal Response to Asenapine	****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.
✓ **Atorvastatin (Lipitor)**	Normal Myopathy Risk (SLCO1B1 521T>C TT Normal Transporter Function)	**Atorvastatin plasma concentrations are not expected to increase, and unless other genetic or circumstantial risk factors are present, atorvastatin can be prescribed at standard FDA-recommended starting doses and adjusted based on disease-specific guidelines. (Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, high statin dose, comedications, and female gender.)
✓ **Atorvastatin (Lipitor)**	Normal Response to Atorvastatin (CYP3A4 *1/*1 Normal Metabolizer)	**The genotype result indicates that the patient does not carry the CYP3A4*22 allele (this allele is associated with a decreased CYP3A4 enzyme activity). The patient is expected to achieve an optimal lipid control goal with standard atorvastatin dose requirements.
✓ **Avanafil (Stendra)**	Normal Response to Avanafil	****Pharmacogenetic guidance:** no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Avanafil is extensively metabolized by CYP3A4, therefore **Avanafil should not be used with strong CYP3A4 inhibitors** such as ketoconazole, itraconazole, voriconazole, ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, and telithromycin. If taking a moderate CYP3A4 inhibitor, such as erythromycin, amprenavir, aprepitant, diltiazem, fluconazole, fosamprenavir, or verapamil, the dose should be no more than 50 mg in a 24-hour period. Inducers of CYP3A4 may decrease the concentrations of avanafil.
✓ **Azilsartan (Edarbi, Edarbyclor)**	Normal Sensitivity to Azilsartan Medoxomil (CYP2C9 *2/*2 Poor Metabolizer)	**Azilsartan medoxomil is hydrolyzed to azilsartan, its active metabolite, in the gastrointestinal tract during absorption. Azilsartan is further metabolized to inactive metabolites by CYP2C9. Azilsartan plasma concentrations are higher in presence of reduced CYP2C9 activity, but the efficacy and safety profile of this drug are not altered by this change. Consider standard label-recommended dosage and administration.

✓ **Brexpiprazole (Rexulti)**	Normal Sensitivity to Brexpiprazole (CYP2D6 *1/*1 XN Rapid Metabolizer)	*No dosing adjustments are needed in CYP2D6 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 *1/*1 Normal Metabolizer)	*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	**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.
✓ **Bupropion (Wellbutrin, Zyban, Aplenzin, Contrave)**	Normal Response to Bupropion (CYP2B6 *1/*1 Normal Metabolizer)	**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. Unless other genetic or non-genetic factors are present, individuals who are CYP2B6 normal metabolizers are not expected to have lower blood levels of hydroxybupropion. Bupropion can be prescribed at standard label-recommended dosage.
✓ **Bupropion (Wellbutrin, Zyban, Aplenzin, Contrave)**	Good Response to Bupropion (ANKK1 DRD2:Taq1A GG Unaltered DRD2 function)	**Smoking Cessation: The patient's genotype result is associated with a positive response with bupropion treatment.
✓ **Candesartan (Atacand)**	Normal Sensitivity to Candesartan Cilexetil	***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	****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.
✓ **Carisoprodol (Soma)**	Normal Sensitivity to Carisoprodol (CYP2C19 *1/*1 Normal Metabolizer)	*Carisoprodol can be prescribed at standard label-recommended dosage and administration.
✓ **Carvedilol (Coreg)**	Normal Sensitivity to Carvedilol (CYP2D6 *1/*1 XN Rapid Metabolizer)	**Carvedilol can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended with monitoring until a favorable response is achieved.
✓ **Citalopram (Celexa)**	Normal sensitivity to Citalopram (CYP2C19 *1/*1 Normal Metabolizer)	*Citalopram can be prescribed at standard label-recommended dosage and administration.
✓ **Clobazam (Onfi)**	Normal Sensitivity to Clobazam (CYP2C19 *1/*1 Normal Metabolizer)	*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	****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.
✓ **Clopidogrel (Plavix)**	Normal Response to Clopidogrel (CYP2C19 *1/*1 Normal Metabolizer)	*Clopidogrel can be prescribed at standard label-recommended dosage.
✓ **Clozapine (Clozaril)**	Normal Sensitivity to Clozapine (CYP2D6 *1/*1 XN Rapid Metabolizer)	*Clozapine can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended with monitoring until a favorable response is achieved.

✓ **Clozapine (Clozaril)**	Normal Response to Clozapine (CYP1A2 *1A/*1A Normal Metabolizer- Possible Inducibility)	**Clozapine can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended with monitoring until a favorable response is achieved. Extrinsic factors such as diet (cruciferous vegetables, heavy coffee consumption, char-grilled meats) smoking, and certain medications (omeprazole, modafinil, carbamazepine) are known to increase CYP1A2 activity.
✓ **Cyclobenzaprine (Flexeril, Amrix)**	Normal Response to Cyclobenzaprine	**Pharmacogenetic guidance:** No genetically guided drug selection or dosing recommendations are available. Cyclobenzaprine is excreted primarily as a glucuronide via the kidneys, and as an N-demethylated metabolite by CYP3A4, CYP1A2, and to a lesser extent CYP2D6. Due to the minor involvement of CYP2D6 in the metabolism of cyclobenzaprine, the polymorphism of this enzyme is not of concern in its the clinical use.
✓ **Dabigatran Etexilate (Pradaxa)**	Normal Response to Dabigatran	**Pharmacogenetic guidance:** Dabigatran is eliminated primarily unchanged by the kidneys. After oral administration, dabigatran etexilate is converted to its active form dabigatran by esterases. A small portion (20%) of dabigatran dose is also conjugated to form pharmacologically active acyl glucuronides. Dabigatran is not a substrate, inhibitor, or inducer of CYP450 enzymes. Dabigatran etexilate is a substrate of the efflux transporter P-gp (ABCB1). Common genetic polymorphism of the ABCB1 gene (2677G>T/A and 3435 C>T) do not appear to affect dabigatran exposure. **Polypharmacy guidance:** *1-Reduction in Risk of Stroke and Systemic Embolism in Non-valvular AF*: In patients with moderate renal impairment (CrCl 30-50 mL/min), concomitant use of the P-gp inhibitor dronedarone or systemic ketoconazole can be expected to produce dabigatran exposure similar to that observed in severe renal impairment. Consider reducing the dose of dabigatran to 75 mg twice daily. Dose adjustment is not necessary when coadministered with other P-gp inhibitors. In patients with CrCl<30 mL/min, avoid use of concomitant P-gp inhibitors with dabigatran. *2-Treatment of DVT and PE Reduction in the Risk of Recurrence of DVT and PE*: Avoid use of concomitant P-gp inhibitors with dabigatran in patients with CrCl <50 mL/min.
✓ **Darifenacin (Enablex)**	Normal Response to Darifenacin (CYP2D6 *1/*1 XN Rapid Metabolizer)	**Darifenacin can be prescribed at standard label-recommended dosage and administration.
✓ **Desvenlafaxine (Pristiq)**	Normal Sensitivity to Desvenlafaxine (CYP2D6 *1/*1 XN Rapid Metabolizer)	*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.
✓ **Dexlansoprazole (Dexilant, Kapidex)**	Normal Response to Dexlansoprazole (CYP2C19 *1/*1 Normal Metabolizer)	*Dexlansoprazole can be prescribed at standard label-recommended dosage and administration.

✓	**Dextromethorphan / Quinidine (Nuedexta)**	Normal Sensitivity to Dextromethorphan-Quinidine (CYP2D6 *1/*1 XN Rapid Metabolizer)	***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.
✓	**Diazepam (Valium)**	Normal Sensitivity to Diazepam (CYP2C19 *1/*1 Normal Metabolizer)	*Diazepam can be prescribed at standard label-recommended dosage and administration.
✓	**Doxazosin (Cardura)**	Normal Response to Doxazosin	****Pharmacogenetic guidance:** no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** doxazosin is metabolized by multiple enzymes. There is limited data on the effects of drugs known to influence the metabolism of doxazosin.
✓	**Duloxetine (Cymbalta)**	Normal Sensitivity to Duloxetine (CYP2D6 *1/*1 XN Rapid Metabolizer)	**Duloxetine can be prescribed at standard label-recommended dosage and administration.
✓	**Dutasteride (Avodart)**	Normal Response to Dutasteride	****Pharmacogenetic guidance:** no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Dutasteride is extensively metabolized in humans by CYP3A4 and CYP3A5. The effect of potent CYP3A4 inhibitors on dutasteride has not been studied. Because of the potential for drug-drug interactions, use caution when prescribing this drug to patients taking potent, chronic CYP3A4 enzyme inhibitors.
✓	**Edoxaban (Savaysa)**	Normal Response to Edoxaban	****Pharmacogenetic guidance:** Edoxaban is eliminated primarily as unchanged drug in urine. There is minimal metabolism via hydrolysis (mediated by carboxylesterase 1), conjugation, and oxidation by CYP3A4. Edoxaban is a substrate of the efflux transporter P-gp and its active metabolite (formed by carboxylesterase 1) is a substrate of the uptake transporter SLCO1B1. 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	***Pharmacogenetic guidance:** Eprosartan is eliminated by biliary and renal excretion, primarily as unchanged compound. Eprosartan is not metabolized by the cytochrome P450 enzymes. Genetic variability of the cytochrome P450 genes is not expected to affect the patient's response to eprosartan. No genotype-based dosing adjustments are available.
✓	**Escitalopram (Lexapro)**	Normal Sensitivity to Escitalopram (CYP2C19 *1/*1 Normal Metabolizer)	*Escitalopram can be prescribed at standard label-recommended dosage and administration.

✓ **Eslicarbazepine (Aptiom)**	Normal Response to Eslicarbazepine	****Pharmacogenetic guidance:** Genotype results obtained from the pharmacogenetic test performed in this patient cannot be used to identify patients at risk for severe cutaneous adverse reactions such as anticonvulsant hypersensitivity syndrome, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Eslicarbazepine acetate (prodrug) is converted by a reductase to its active metabolite, eslicarbazepine. Eslicarbazepine is eliminated primarily by renal excretion unchanged and as a glucuronide conjugate. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** In the presence of enzyme-inducing drugs, eslicarbazepine plasma levels are significantly decreased, and higher doses of the drug may be needed.
✓ **Esomeprazole (Nexium)**	Normal Response to Esomeprazole (CYP2C19 *1/*1 Normal Metabolizer)	*Esomeprazole can be prescribed at standard label-recommended dosage and administration.
✓ **Ethosuximide (Zarontin)**	Normal Response to Ethosuximide	****Pharmacogenetic guidance:** No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** ethosuximide is extensively metabolized by CYP3A4, and therefore this drug should be used with caution when prescribed with CYP3A4 inhibitors. Inducers of CYP3A4 increase ethosuximide clearance, and higher doses may be needed when the drug is coadministered with enzyme-inducing drugs.
✓ **Ezogabine (Potiga)**	Normal Response to Ezogabine	****Pharmacogenetic guidance:** although NAT2 rapid acetylators have a 30% increase in the exposure of ezogabine active metabolite, no dose adjustment is necessary in these individuals. **Polypharmacy guidance:** Ezogabine is extensively metabolized primarily via glucuronidation (by UGT1A4 and UGT1A1) and acetylation (by NAT2). There is no evidence of oxidative metabolism of ezogabine by cytochrome P450 enzymes, and genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Enzyme-inducing drugs such as carbamazepine and phenytoin increase ezogabine clearance by 30%, and dose increase should be considered when this drug is coadministered with enzyme-inducing antiepileptic drugs.
✓ **Felbamate (Felbatol)**	Normal Response to Felbamate	****Pharmacogenetic guidance:** No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** About 40-50% of absorbed felbamate dose appears unchanged in urine, and an additional 50% is present as metabolites and conjugates. Felbamate is a substrate of CYP3A4 and CYP2E1, but these pathways are minor for drug elimination when the drug is given as a monotherapy. This pathway is enhanced by concomitant use of enzyme-inducing antiepileptic drugs, which results in a 30 -50% decrease in felbamate plasma concentrations. Felbamate should be titrated slowly, and dose adjustment must be considered in presence of inducers.
✓ **Fentanyl (Actiq)**	Good Response to Fentanyl (OPRM1 A118G AA Normal OPRM1 Function)	**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 *1/*1 XN Rapid Metabolizer)	***There are no studies related to the exposure of fesoterodine active metabolite in rapid metabolizers. Therefore, this drug can be prescribed at standard label-recommended dosage and administration.
✓ **Finasteride (Proscar)**	Normal Response to Finasteride	****Pharmacogenetic guidance:** no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Finasteride is extensively metabolized in humans by CYP3A4. The effects of potent or moderate CYP3A4 inhibitors on finasteride have not been studied. Because of the potential for drug-drug interactions, use caution when prescribing this drug to patients taking CYP3A4 enzyme inhibitors.
✓ **Fluoxetine (Prozac, Sarafem)**	Normal Sensitivity to Fluoxetine (CYP2D6 *1/*1 XN Rapid Metabolizer)	****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 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.
✓ **Fondaparinux (Arixtra)**	Normal Response to Fondaparinux	****Pharmacogenetic guidance:** Fondaparinux is eliminated unchanged through renal excretion and is not metabolized by CYPs, and therefore genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** The concomitant use of fondaparinux with aspirin or NSAIDS may enhance the risk of hemorrhage. Discontinue agents that may enhance the risk of hemorrhage prior to initiation of therapy with fondaparinux unless essential. If co-administration is necessary, monitor patients closely for hemorrhage.
✓ **Gabapentin (Neurontin)**	Normal Response to Gabapentin	****Pharmacogenetic guidance:** no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Gabapentin is eliminated primarily through renal excretion and is not metabolized by CYPs. Genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Gabapentin can be prescribed at standard label -recommended dosage and administration.
✓ **Galantamine (Razadyne)**	Normal Sensitivity to Galantamine (CYP2D6 *1/*1 XN Rapid Metabolizer)	****Galantamine can be prescribed at standard label-recommended dosage and administration. Individualization of dose with weekly titration is recommended.
✓ **Guanfacine (Intuniv)**	Normal Response to Guanfacine	****Pharmacogenetic guidance:** Guanfacine is predominantly metabolized by CYP3A4. No genetically guided drug selection or dosing recommendations are available and guanfacine extended-release should be titrated based on the clinical response and tolerability of the individual patient. **Polypharmacy guidance**: The dose of guanfacine extended-release should be reduced to **one half of the standard dose** when co-medicated with a strong CYP3A4 inhibitor (e.g., ketoconazole, itraconazole, indinavir, ritonavir, nefazodone). When the strong CYP3A4 inhibitor is discontinued, the dose should be increased to the standard recommended dose. Guanfacine dose should be increased up to double the recommended dose when used in combination with a strong CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, St. John's wort etc.). When the CYP3A4 inducer is discontinued, the dose should be reduced to the standard recommended dose within 7-14 days.

✓ **Hydromorphone (Dilaudid, Exalgo)**	Normal Response to Hydromorphone	**No genetically guided drug selection or dosing recommendations are available. Hydromorphone is not metabolized by CYPs, and genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Hydromorphone can be prescribed at standard label-recommended dosage and administration.
✓ **Iloperidone (Fanapt)**	Normal Sensitivity to Iloperidone (CYP2D6 *1/*1 XN Rapid Metabolizer)	**Iloperidone can be prescribed at standard label-recommended dosage and administration. Iloperidone must be titrated slowly from a low starting dose to avoid orthostatic hypotension. If patients taking iloperidone experience symptoms that could indicate the occurrence of cardiac arrhythmias (e.g., dizziness, palpitations, or syncope), the prescriber should initiate further evaluation, including cardiac monitoring.
✓ **Irbesartan (Avapro)**	Normal Sensitivity to Irbesartan (CYP2C9 *2/*2 Poor Metabolizer)	**The plasma concentrations of irbesartan are increased, but its efficacy and safety profiles are not affected. Consider standard label-recommended dosage and administration.
✓ **Ketoprofen (Orudis)**	Normal Response to Ketoprofen	****Pharmacogenetic guidance:** Ketoprofen is primarily eliminated by glucuronidation (by UGT1A3, UGT1A9 and UGT2B7) and no major implication of CYP2C9 in the metabolism of this drug has been demonstrated. No genetically guided drug selection or dosing recommendations are available.
✓ **Ketorolac (Toradol)**	Normal Response to Ketorolac	****Pharmacogenetic guidance:** Ketorolac is metabolized by glucuronidation (UGT enzymes) and oxidation but the enzymes catalyzing the oxidation are not well characterized. No genetically guided drug selection or dosing recommendations are available.
✓ **Labetalol (Normodyne, Trandate)**	Normal Response to Labetalol	****Pharmacogenetic guidance:** Labetalol is extensively metabolized by UGT2B7, UGT1A1, and CYP2C19 to inactive metabolites. Preliminary studies indicate that following a single 200-mg oral dose, labetalol plasma concentrations are 2.9-fold higher in Chinese individuals with the CYP2C19 *2/*2 genotype than those with the CYP2C19 *1/*1 genotype. The clinical impact of this change is unknown. **Polypharmacy guidance:** Cimetidine increases the bioavailability of labetalol, and clinical monitoring is advised when both drugs are coadministered.
✓ **Lacosamide (Vimpat)**	Normal Sensitivity to Lacosamide (CYP2C19 *1/*1 Normal Metabolizer)	**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	****Pharmacogenetic guidance:** Genotype results obtained from the pharmacogenetic test performed in this patient cannot be used to identify patients at risk for severe cutaneous adverse reactions such as anticonvulsant hypersensitivity syndrome, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Lamotrigine is metabolized by glucuronidation, which is mediated primarily by UGT1A4 with some contribution from UGT1A1 and UGBT2B7. There are insufficient studies documenting the impact of genetic polymorphisms of these metabolizing enzymes on lamotrigine response. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Enzyme-inducing drugs increase lamotrigine clearance significantly, and higher doses of this drug are required to maintain therapeutic concentrations. Coadministration of valproic acid, an inhibitor of UGT enzymes, increases lamotrigine levels and may result in serious lamotrigine adverse effects (neurological and cutaneous). A low starting dose with a slow titration schedule is recommended when lamotrigine is added to existing valproic acid treatment.
✓ **Lansoprazole (Prevacid)**	Normal Response to Lansoprazole (CYP2C19 *1/*1 Normal Metabolizer)	*Lansoprazole can be prescribed at standard label-recommended dosage and administration.
✓ **Leflunomide (Arava)**	Normal Sensitivity to Leflunomide (CYP2C19 *1/*1 Normal Metabolizer)	**Leflunomide can be prescribed according to standard label-recommended dosage and administration. Full blood cell count (CBC) and liver function parameters should be checked no more than 6 months before beginning treatment, and every month for the initial 6 months of therapy. Blood pressure should be checked before beginning treatment and periodically thereafter.
✓ **Levetiracetam (Keppra)**	Normal Response to Levetiracetam	****Pharmacogenetic guidance:** No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Levetiracetam is minimally metabolized by non-CYP enzymes (esterases) and is primarily excreted unchanged in urine. Coadministration of enzyme-inducing antiepileptic drugs produce modest decreases in levetiracetam plasma levels.
✓ **Levomilnacipran (Fetzima)**	Normal Response to Levomilnacipran	****Pharmacogenetic guidance:** Levomilnacipran is moderately metabolized by desethylation, which is catalyzed primarily by CYP3A4, with minor contributions by CYP2C8, CYP2C19, CYP2D6, and CYP2J2. More than 58% of the dose is excreted in urine as unchanged levomilnacipran, and 18% as N -desethyl levomilnacipran. Genetic polymorphisms of CYPs are not expected to have a significant impact on levomilnacipran exposure. no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance**: the daily levomilnacipran dose should not exceed 80 mg when coadministered with strong CYP3A4 inhibitors, such as ketoconazole, itrazonazole, and ritonavir.
✓ **Levorphanol (Levo Dromoran)**	Normal Response to Levorphanol	****Pharmacogenetic guidance:** Levorphanol is metabolized by glucuronidation which is mediated by UGT2B7. There are no studies documenting the impact of genetic polymorphisms of this metabolizing enzyme on levorphanol response. And no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Enzyme inducing drugs are expected to increase levorphanol clearance significantly.

✓	**Lovastatin (Mevacor, Altoprev, Advicor)**	Normal Myopathy Risk (SLCO1B1 521T>C TT Normal Transporter Function)	**Lovastatin acid plasma concentration is not expected to be elevated. Unless other genetic or circumstantial risk factors are present, lovastatin can be prescribed at standard FDA-recommended starting doses and adjusted based on disease-specific guidelines. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, high statin dose, comedications, and female gender.
✓	**Lovastatin (Mevacor, Altoprev, Advicor)**	Normal Response to Lovastatin (CYP3A4 *1/*1 Normal Metabolizer)	**The genotype result indicates that the patient does not carry the CYP3A4*22 allele (this allele is associated with a decreased CYP3A4 enzyme activity). The patient is expected to achieve an optimal lipid control goal with standard lovastatin dose requirements.
✓	**Loxapine (Loxitane, Adasuve)**	Normal Response to Loxapine	**Pharmacogenetic guidance:** Loxapine is metabolized extensively in the liver following oral administration, with multiple metabolites formed. Loxapine metabolism occurs via hydroxylation and oxidation catalyzed by CYP1A2 along with contributions from CYP3A4, CYP2D6 and FMO. There are no studies documenting the effect of genetic polymorphisms of these metabolizing enzymes on Loxapine disposition and there are no available genetically-guided drug selection or dosing recommendations. **Polypharmacy guidance:** Loxapine is a central nervous system (CNS) depressant. The concurrent use of Loxapine with other CNS depressants (*e.g.*, alcohol, opioid analgesics, benzodiazepines, tricyclic antidepressants, general anesthetics, phenothiazines, sedative/hypnotics, muscle relaxants, and/or illicit CNS depressants) can increase the risk of respiratory depression, hypotension, profound sedation, and syncope. Therefore, consider dose reduction/modification of CNS depressants if used concomitantly with Loxapine. Loxapine has anticholinergic activity and concomitant use with other anticholinergic drugs can increase the risk of adverse reactions, including exacerbation of glaucoma and urinary retention.
✓	**Lurasidone (Latuda)**	Normal Response to Lurasidone	***Pharmacogenetic guidance:** Lurasidone is metabolized by CYP3A4. No genotype-based dosing adjustments are available. **Polypharmacy guidance:** The concomitant use of lurasidone with all CYP3A4 inhibitors may result in an increase in lurasidone plasma concentrations, which could increase or prolong adverse drug effects. **Lurasidone should not be administered with strong CYP3A4 inhibitors**. Lurasidone dose should not exceed 40 mg when administered with moderate CYP3A4 inhibitors. Monitor patients receiving lurasidone and any CYP3A4 inhibitor. **Rifampin or other strong inducers of CYP3A should not be administered with lurasidone.** If lurasidone is used concomitantly with a moderate CYP3A4 inducer, it may be necessary to increase lurasidone dose after chronic treatment (7 days or more) with the CYP3A4 inducer.

✓ **Memantine (Namenda)**	Normal Response to Memantine	****Pharmacogenetic Guidance:** Memantine is excreted predominantly unchanged in the urine. This drug undergoes partial hepatic metabolism to three inactive metabolites (N-glucuronide, 6--hydroxy metabolite, and 1-nitroso-deaminated metabolite). CYP450 enzymes do not play a significant role in the metabolism of memantine. There are no studies documenting the effects of genetic variability in metabolizing enzymes or organic cationic transporters on memantine response. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy Guidance:** Memantine is predominantly renally eliminated, and drugs that are substrates and/or inhibitors of the CYP450 system are not expected to interact with memantine. Because memantine is eliminated in part by tubular secretion, coadministration of drugs that use the same renal cationic system, including hydrochlorothiazide, triamterene, metformin, cimetidine, ranitidine, quinidine, and nicotine, could potentially result in altered plasma levels of both agents.
✓ **Meperidine (Demerol)**	Normal Response to Meperidine	****Pharmacogenetic guidance:** no genetically guided drug selection or dosing recommendations are available. Meperidine is metabolized to normeperidine by multiple CYPs, including CYP2B6, CYP3A4, and CYP2C19. The effects of genetic variants in these enzymes have not been studied. **Polypharmacy guidance:** In patients taking **strong CYP inducers**, meperidine metabolism is increased resulting in higher levels of its neurotoxic metabolite normeperidine. In presence of ritonavir, meperidine's exposure is significantly reduced while normeperidine concentrations are increased. Based on these findings, the risk of narcotic-related adverse effects from this combination appears to be minimal. However, increased concentrations of normeperidine suggest a potential for toxicity with increased dosages or long-term therapy. This combination should be avoided is possible.
✓ **Metaxalone (Skelaxin)**	Normal Response to Metaxalone	****Pharmacogenetic guidance:** Metaxalone is extensively metabolized by multiple CYP enzymes, including CYP1A2, CYP2D6, CYP2E1, and CYP3A4. Genetic polymorphisms of these enzymes are unlikely to affect its exposure to a significant extent. no genetically guided drug selection or dosing recommendations are available.
✓ **Methadone (Dolophine)**	Normal Sensitivity to Methadone (CYP2B6 *1/*1 Normal Metabolizer)	****Methadone can be prescribed at standard label-recommended dosage. No action is needed besides the standard precautions.
✓ **Methocarbamol (Robaxin)**	Normal Response to Methocarbamol	****Pharmacogenetic guidance:** Methocarbamol is metabolized via dealkylation and hydroxylation. The enzymes responsible for the metabolism of this drug have not been characterized. No genetically guided drug selection or dosing recommendations are available.
✓ **Metoclopramide (Reglan)**	Normal Response to Metoclopramide (CYP2D6 *1/*1 XN Rapid Metabolizer)	****Metoclopramide is metabolized at a faster rate in CYP2D6 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.
✓ **Milnacipran (Savella)**	Normal Response to Milnacipran	****Pharmacogenetic guidance:** milnacipran is minimally metabolized by UGT enzymes and primarily excreted unchanged in urine. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** coadministration of drugs that inhibit or induce CYP or UGT enzymes are unlikely to affect the exposure of milnacipran.

✓	**Mirabegron (Myrbetriq)**	Normal Sensitivity to Mirabegron (CYP2D6 *1/*1 XN Rapid Metabolizer)	***The exposure of mirabegron is slightly decreased in CYP2D6 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 *1/*1 XN Rapid Metabolizer)	***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	****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	****Pharmacogenetic guidance:** UGT2B7 is responsible for hepatic naproxen acyl glucuronidation, which is the primary elimination pathway for this drug (60% of total clearance). CYP2C9 and CYP1A2 are responsible for the formation of O-desmethylnaproxen but this pathway is not the primary pathway for the elimination for naproxen. Genetic polymorphism of CYP2C9 has not been found to affect the response to naproxen. No genetically guided drug selection or dosing recommendations are available.
✓	**Nebivolol (Bystolic)**	Normal Sensitivity to Nebivolol (CYP2D6 *1/*1 XN Rapid Metabolizer)	***Nebivolol can be prescribed at standard label-recommended dosage and administration. Caution is recommended during up-titration until a favorable response is achieved.
✓	**Nefazodone (Serzone)**	Normal Sensitivity to Nefazodone (CYP2D6 *1/*1 XN Rapid Metabolizer)	****Nefazodone is metabolized by CYP3A4 to its active metabolite m-chlorophenylpiperazine and other metabolites. The m-chlorophenylpiperazine metabolite which may contribute to adverse events, is further metabolized by CYP2D6. Nefazodone can be prescribed standard label recommended-dosage and administration.
✓	**Olanzapine (Zyprexa)**	Normal Sensitivity to Olanzapine (CYP2D6 *1/*1 XN Rapid Metabolizer)	****Olanzapine can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended until a favorable response is achieved.
✓	**Olanzapine (Zyprexa)**	Normal Response to Olanzapine (CYP1A2 *1A/*1A Normal Metabolizer- Possible Inducibility)	****Olanzapine can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended with monitoring until a favorable response is achieved. Extrinsic factors such as diet (cruciferous vegetables, heavy coffee consumption, char-grilled meats) smoking, and certain medications (omeprazole, modafinil, carbamazepine) are known to increase CYP1A2 activity.

✓ **Olmesartan (Benicar)**	Normal Sensitivity to Olmesartan Medoxomil	***Pharmacogenetic guidance:** Olmesartan medoxomil is hydrolyzed to olmesartan its active metabolite in the gastrointestinal tract during absorption. There is virtually no further metabolism of olmesartan. Genetic variability of the cytochrome P450 genes is not expected to affect the patient's response to olmesartan medoxomil. No genotype-based dosing adjustments are available.
✓ **Omeprazole (Prilosec)**	Normal Response to Omeprazole (CYP2C19 *1/*1 Normal Metabolizer)	*Omeprazole can be prescribed at standard label-recommended dosage and administration.
✓ **Oxcarbazepine (Trileptal, Oxtellar XR)**	Normal Response to Oxcarbazepine	****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	****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	****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 *1/*1 XN Rapid Metabolizer)	*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.
✓ **Pantoprazole (Protonix)**	Normal Response to Pantoprazole (CYP2C19 *1/*1 Normal Metabolizer)	*Pantoprazole can be prescribed at standard label-recommended dosage and administration.

✓	**Perampanel (Fycompa)**	Normal Response to Perampanel	****Pharmacogenetic guidance:** Perampanel is eliminated either unchanged or following oxidative metabolism by CYP3A4 and CYP3A5. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Enzyme-inducing drugs decrease perampanel plasma concentrations by 50-60%, and the initial dosage of the drug should be increased when it is added to a stable therapy regimen containing enzyme -inducing antiepileptic drugs. Coadministration with strong enzyme-inducers others than antiepileptic drugs (e.g., rifampin) should be avoided. Coadministration with perampanel with strong CYP3A4 inhibitors such as ketoconazole increases perampanel exposure by 20%.
✓	**Phenobarbital (Luminal)**	Normal Sensitivity to Phenobarbital (CYP2C19 *1/*1 Normal Metabolizer)	**CYP2C19 is partly involved in the metabolism of phenobarbital, and this drug can be prescribed at standard label-recommended dosage and administration.
✓	**Pitavastatin (Livalo)**	Normal Myopathy Risk (SLCO1B1 521T>C TT Normal Transporter Function)	**Pitavastatin plasma concentrations are not expected to increase, and unless other genetic or circumstantial risk factors are present, pitavastatin can be prescribed at standard FDA-recommended starting doses and adjusted based on disease-specific guidelines. The myopathy risk increases with use of the 4 mg daily dose. (Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, high statin dose, comedications, and female gender.)
✓	**Prasugrel (Effient)**	Normal Response to Prasugrel (CYP2C19 *1/*1 Normal Metabolizer)	*Prasugrel is a prodrug that is hydrolyzed in the intestine to a thiolactone, which is then converted to the active metabolite primarily by CYP3A4 and CYP2B6, and to a lesser extent by CYP2C9 and CYP2C19. Prasugrel active metabolite exposure and platelet reactivity are not affected by CYP2C19 metabolizer status. Prasugrel can be prescribed at standard label-recommended dosage.
✓	**Pravastatin (Pravachol)**	Normal Myopathy Risk (SLCO1B1 521T>C TT Normal Transporter Function)	**Pravastatin plasma concentrations are not expected to increase, and unless other genetic or circumstantial risk factors are present, pravastatin can be prescribed at standard FDA-recommended starting doses and adjusted based on disease-specific guidelines. (Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, high statin dose, comedications, and female gender.)
✓	**Pregabalin (Lyrica)**	Normal Response to Pregabalin	****Pharmacogenetic guidance:** No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Pregabalin is eliminated primarily through renal excretion and is not metabolized by CYPs. Genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Pregabalin can be prescribed at standard label-recommended dosage and administration.
✓	**Primidone (Mysoline)**	Normal Sensitivity to Primidone (CYP2C19 *1/*1 Normal Metabolizer)	**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 *1/*1 Normal Metabolizer)	**Proguanil is metabolized to an active metabolite cycloguanil by CYP2C19. The patient's genotype is associated with a normal metabolism of proguanil to cycloguanil. Proguanil can be prescribed at standard label-recommended dosage and administration.

✓ **Propranolol (Inderal)**	Normal Sensitivity to Propranolol (CYP2D6 *1/*1 XN Rapid Metabolizer)	**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	**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 *1/*1 Normal Metabolizer)	*Rabeprazole can be prescribed at standard label-recommended dosage and administration.
✓ **Ranolazine (Ranexa)**	Normal Sensitivity to Ranolazine (CYP2D6 *1/*1 XN Rapid Metabolizer)	*Ranolazine is metabolized mainly by CYP3A4, and to a lesser extent by CYP2D6. This drug can be prescribed at standard label-recommended dosage and administration. The recommended initial dose is 375 mg twice daily. After 2–4 weeks, the dose should be titrated to 500 mg twice daily, and according to the patient's response, further titrated to a recommended maximum dose of 1000 mg twice daily. If patient experiences treatment-related adverse events (e.g. dizziness, nausea, vomiting, or syncope), Down titration of ranolazine to 500 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 521T>C TT Normal Transporter Function)	**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	****Pharmacogenetic guidance:** Rivaroxaban is metabolized by CYP3A4, CYP3A5, and CYP2J2. It is also a substrate for P-gp (ABCB1) and BCRP (ABCG2) transporters. Genetic polymorphisms of these genes are not expected to affect the efficacy or safety profiles of rivaroxaban. **Polypharmacy guidance:** Avoid concomitant use of rivaroxaban with combined P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, lopinavir/ritonavir, ritonavir, indinavir, and conivaptan). Avoid concomitant use of rivaroxaban with drugs that are combined P-gp and strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, rifampin, and St. John's wort). Patients with renal impairment coadministered rivaroxaban with drugs classified as combined P-gp and moderate CYP3A4 inhibitors (e.g., diltiazem, verapamil, dronedarone, and erythromycin) have increased exposure compared with patients with normal renal function and no inhibitor use. Significant increases in rivaroxaban exposure may increase bleeding risk.
✓	**Rosuvastatin (Crestor)**	Normal Myopathy Risk (SLCO1B1 521T>C TT)	**Rosuvastatin plasma concentrations are not expected to increase, and unless other genetic or circumstantial risk factors are present, rosuvastatin can be prescribed at standard FDA-recommended starting doses and adjusted based on disease-specific guidelines. The myopathy risk increases with use of the 40 mg dose. (Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, high statin dose, comedications, and female gender.)
✓	**Rufinamide (Banzel)**	Normal Response to Rufinamide	****Pharmacogenetic guidance:** No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Rufinamide is extensively metabolized by carboxylesterases. Cytochrome P450 enzymes are not involved in its metabolism. Therefore, genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Coadministration of enzyme-inducing antiepileptic drugs produce modest decreases in rufinamide plasma levels, while coadministration of valproate increases the drug levels and requires dose adjustment. Patients stabilized on rufinamide should begin valproate therapy at a low dose, and titrate to a clinically effective dose. Similarly, patients on valproate should begin rufinamide at a lower dose.
✓	**Sertraline (Zoloft)**	Normal Sensitivity to Sertraline (CYP2C19 *1/*1 Normal Metabolizer)	*Sertraline can be prescribed at standard label-recommended dosage and administration.

✓ **Sildenafil (Viagra)**	Normal Response to Sildenafil	****Pharmacogenetic guidance:** Preliminary findings indicate that sildenafil exposure is 1.5 times higher in individuals with CYP3A5*3/*3 genotype compared to those with CYP3A5*1/*1 genotype. The clinical significance of this change is unknown. **Polypharmacy guidance:** Sildenafil is metabolized by CYP3A4 (major route) and CYP2C9 (minor route). **In patients taking strong CYP3A inhibitors, sildenafil exposure is significantly increased, and it is recommended not to exceed a maximum single dose of 25 mg in a 48-hour period.** Inducers of CYP3A may decrease the concentration of the drug.
✓ **Silodosin (Rapaflo)**	Normal Response to Silodosin	****Pharmacogenetic guidance:** silodosin is extensively metabolized by CYP3A4 into pharmacologically inactive metabolites. no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** silodosin is contraindicated with potent CYP3A4 inhibitors, as the risk for serious adverse events is increased at higher concentrations. Use caution when this drug is prescribed with CYP3A4 moderate inhibitors, as drug levels may increase.
✓ **Simvastatin (Zocor)**	Normal Myopathy Risk (SLCO1B1 521T>C TT Normal Transporter Function)	*Simvastatin plasma concentrations are not expected to be elevated, and unless other genetic or circumstantial risk factors are present, simvastatin can be prescribed at standard FDA-recommended starting doses and adjusted based on disease-specific guidelines. **The FDA recommends against the use of the 80 mg daily dose unless the patient had already tolerated this dose for 12 months without evidence of myopathy.** Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, high statin dose, comedications, and female gender.
✓ **Simvastatin (Zocor)**	Normal Response to Simvastatin (CYP3A4 *1/*1 Normal Metabolizer)	**The genotype result indicates that the patient does not carry the CYP3A4*22 allele (this allele is associated with a decreased CYP3A4 enzyme activity). The patient is expected to achieve an optimal lipid control goal with standard simvastatin dose requirements.
✓ **Solifenacin (Vesicare)**	Normal Response to Solifenacin	****Pharmacogenetic guidance:** no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Coadministration of a CYP3A4 strong inhibitor increases solifenacin serum concentrations significantly. **Therefore, it is recommended not to exceed a 5 mg daily dose of solifenacin when coadministered with strong CYP3A4 inhibitors, as the risk for QTc prolongation induced by this drug is increased at higher concentrations.** Although the effects of moderate CYP3A4 inhibitors were not examined, use caution when this drug is administered with moderate CYP3A4 inhibitors.
✓ **Sufentanil (Sufenta)**	Normal Response to Sufentanil	****Pharmacogenetic guidance:** No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Sufentanil is primarily metabolized by CYP3A4 and so should be used with caution when prescribed with CYP3A4 inhibitors or inducers.
✓ **Sulindac (Clinoril)**	Normal Response to Sulindac	****Pharmacogenetic guidance:** Sulindac is primarily eliminated by glucuronidation which is catalyzed by several isoforms including UGT1A3, UGT1A9 and UGT2B7. The role of CYP2C9 in sulindac metabolism is of minor relevance. No genetically guided drug selection or dosing recommendations are available.

✓ **Tacrolimus (Prograf)**	Typical response to Tacrolimus (CYP3A5 *3C/*3C Poor Metabolizer)	***The genotype result predicts that the patient does not express the CYP3A5 protein. Therefore, there is no risk that the patient may metabolize tacrolimus more rapidly. Careful titration of tacrolimus in response to therapeutic drug monitoring is recommended until a favorable response is achieved.
✓ **Tadalafil (Cialis)**	Normal Response to Tadalafil	****Pharmacogenetic guidance:** no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Tadalafil is extensively metabolized by CYP3A4. **Tadalafil for Use as Needed** — For patients taking concomitant potent inhibitors of CYP3A4, such as ketoconazole or ritonavir, the maximum recommended dose of vardenafil is 10 mg, not to exceed once every 72 hours. **Tadalafil for Once Daily Use** — For patients taking concomitant strong inhibitors of CYP3A4, the maximum recommended dose is 2.5 mg. Although specific interactions have not been studied, other CYP3A4 moderate inhibitors would likely increase tadalafil exposure. The exposure of tadalafil is reduced when coadministered with rifampin or other CYP3A4 inducers. This can be anticipated to decrease the efficacy of tadalafil for once-daily use, though the magnitude of decreased efficacy is unknown.
✓ **Tamsulosin (Flomax)**	Normal Response to Tamsulosin (CYP2D6 *1/*1 XN Rapid Metabolizer)	****Tamsulosin may be metabolized at a faster rate in CYP2D6 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	****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	***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	****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 *1/*1 XN Rapid Metabolizer)	***Thioridazine can be prescribed at standard label-recommended dosage and administration.
✓ **Thiothixene (Navane)**	Normal Response to Thiothixene	****Pharmacogenetic guidance:** Thiothixene is metabolized by UGTs and by cytochrome P450 enzymes (CYP1A2 and CYP3A4). No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** It is likely that strong enzyme inducers may lead to substantial decreases in thiothixene plasma concentrations with the potential for reduced effectiveness. Consider increasing the dose of thiothixene when concomitantly used with strong CYP3A4 inducers (e.g., carbamazepine).

✓ **Tiagabine (Gabitril)**	Normal Response to Tiagabine	****Pharmacogenetic guidance:** no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Tiagabine is extensively metabolized by CYP3A4, and therefore this drug should be used with caution when prescribed with CYP3A4 inhibitors. Inducers of CYP3A4 increase tiagabine clearance by 2-fold, and the initial dosage of the drug should be considered carefully when added to a stable therapy regimen containing enzyme-inducing antiepileptic drugs.
✓ **Ticagrelor (Brilinta)**	Normal Response to Ticagrelor (CYP3A5 *3C/*3C Poor Metabolizer)	******Ticagrelor can be prescribed at standard label-recommended dosage and administration. Careful monitoring is recommended until a favorable response is achieved.
✓ **Timolol (Timoptic)**	Normal Sensitivity to Timolol (CYP2D6 *1/*1 XN Rapid Metabolizer)	*****Timolol can be prescribed at standard label-recommended dosage and administration.
✓ **Tizanidine (Zanaflex)**	Normal Response to Tizanidine (CYP1A2 *1A/*1A Normal Metabolizer- Possible Inducibility)	******Tizanidine can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended with monitoring until a favorable response is achieved. Extrinsic factors such as diet (cruciferous vegetables, heavy coffee consumption, char-grilled meats) smoking, and certain medications (omeprazole, modafinil, carbamazepine) are known to increase CYP1A2 activity.
✓ **Tofacitinib (Xeljanz)**	Normal Sensitivity to Tofacitinib (CYP2C19 *1/*1 Normal Metabolizer)	******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).
✓ **Tolterodine (Detrol)**	Normal Sensitivity to Tolterodine (CYP2D6 *1/*1 XN Rapid Metabolizer)	******Tolterodine can be prescribed at standard label-recommended dosage and administration.
✓ **Topiramate (Topamax)**	Normal Response to Topiramate	****Pharmacogenetic guidance:** no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** About 50% of absorbed topiramate dose appears unchanged in urine, and an additional 50% is present as metabolites and conjugates. Topiramate metabolism by cytochrome P450 enzymes is minor for its elimination when the drug is given as a monotherapy. However, this pathway is enhanced by concomitant use of enzyme-inducing antiepileptic drugs, and may result in reduced topiramate plasma concentrations. Thus, this drug should be titrated slowly, and dose adjustment must be considered in presence of inducers. Concomitant administration of valproic acid and topiramate has been associated with hyperammonemia with and without encephalopathy.

✓ **Trazodone (Oleptro)**	Normal Response to Trazodone	****Pharmacogenetic guidance:** Trazodone is metabolized to its active metabolite m-chlorophenylpiperazine by CYP3A4. This metabolite which may contribute to adverse events, is further metabolized by CYP2D6. The impact of genetic polymorphisms of this enzyme on the clinical response to trazodone is not well documented. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance**: It is likely that CYP3A4 inhibitors may lead to substantial increases in trazodone plasma concentrations with the potential for adverse effects. If trazodone is used with a potent CYP3A4 inhibitor, the risk of cardiac arrhythmia may be increased. Therefore coadministration of trazodone with drugs that are inhibit CYP3A4 should be approached with caution.
✓ **Trifluoperazine (Stelazine)**	Normal Response to Trifluoperazine	****Pharmacogenetic guidance:** Thrifluoperazine extensively metabolized by oxidation, sulfoxidation, hydroxylation and direct glucuronidation catalyzed by UGT1A4. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** It is likely that strong enzyme inducers may lead to substantial decreases in trifluoperazine plasma concentrations with the potential for reduced effectiveness.
✓ **Trospium (Sanctura)**	Normal Response to Trospium	****Pharmacogenetic guidance:** no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** CYP enzymes do not contribute significantly to the elimination of trospium. No major drug-drug interactions are expected with CYP inhibitors or inducers.
✓ **Valproic Acid (Depakote, Depakene)**	Normal Response to Valproic acid	****Pharmacogenetic guidance:** valproic acid is extensively metabolized in the liver, which occurs primarily by glucuronidation with probable contributions of UGT1A6, UGT1A9, and UGT2B7. This drug is also metabolized by a minor CYP–dependent oxidation pathway, which includes multiple enzymes such as CYP2A6, CYP2C9, and CYP2C19. There are insufficient studies documenting the impact of genetic polymorphisms of these metabolizing enzymes on valproic acid response, and no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** enzyme-inducing drugs increase valproic acid clearance 2-fold, and higher doses of this drug are required to maintain therapeutic concentrations when added to a therapy regimen containing enzyme-inducing antiepileptic drugs.
✓ **Valsartan (Diovan, Entresto)**	Normal Sensitivity to Valsartan	***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	***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	****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	****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	***Pharmacogenetic guidance:** vorapaxar is metabolized primarily by CYP3A4, with contribution from CYP2J2. Genetic polymorphisms of these genes are not expected to affect the efficacy or safety profiles of this drug. Vorapaxar is contraindicated in people who have had a stroke, transient ischemic attack (TIA), or intracranial hemorrhage, (ICH) because of the increased bleeding risk. **Polypharmacy guidance:** Avoid concomitant use of vorapaxar with strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, lopinavir/ritonavir, ritonavir, indinavir, and conivaptan). Significant increases in vorapaxar exposure may increase bleeding risk. Avoid concomitant use with drugs that are strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, rifampin, and St. John's wort).
✓ **Voriconazole (Vfend)**	Normal Sensitivity to Voriconazole (CYP2C19 *1/*1 Normal Metabolizer)	*Voriconazole can be prescribed at standard label-recommended dosage and administration.

✓ **Vortioxetine (Brintellix)**	Normal Sensitivity to Vortioxetine (CYP2D6 *1/*1 XN Rapid Metabolizer)	***There is little evidence documenting the exposure of this drug in CYP2D6 rapid metabolizer. 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.
✓ **Ziprasidone (Geodon)**	Normal Response to Ziprasidone	****Pharmacogenetic guidance:** Ziprasidone is primarily cleared following extensive metabolism. CYP3A4 is the major CYP contributing to the oxidative metabolism of ziprasidone with minor involvement from CYP1A2. Less than one-third of ziprasidone metabolic clearance is mediated by cytochrome P450 catalyzed oxidation and approximately two-thirds via reduction involving glutathione as well as aldehyde oxidase. No genetically guided drug selection or dosing recommendations are available. Individualization of ziprasidone dose with careful weekly titration is required. Dosage adjustments should generally occur at intervals of no less than 2 days, as steady-state plasma concentrations are achieved within 1 to 3 days. In order to ensure use of the lowest effective dose, patients should ordinarily be observed for improvement for several weeks before upward dosage adjustment. When deciding among the alternative treatments available, the prescriber should consider the finding of **ziprasidone's greater capacity to prolong the QT/QTc interval** compared to several other antipsychotic drugs. **Polypharmacy guidance:** Although coadministration of strong CYP3A4 inhibitors are expected to result in modest increases in ziprasidone plasma concentrations, a closer monitoring of the patient's response and a dose reduction may be considered. Ziprasidone dose may need to be increased when used in combination with a chronic treatment of a potent CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, St. John's wort etc.).
✓ **Zonisamide (Zonegran)**	Normal Sensitivity to Zonisamide (CYP2C19 *1/*1 Normal Metabolizer)	****CYP2C19 is partly involved in the metabolism of zonisamide, and this drug can be prescribed at standard label-recommended dosage and administration.

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Pharmacogenetic Test Results			
Gene	**Genotype**	**Phenotype**	**Clinical Consequences**
ANKK1/DRD2	DRD2:Taq1A GG	Unaltered DRD2 function	Consistent with a normal dopamine receptor D2 function.
Apolipoprotein E	ε3/ε3	No Increased Risk of Hyperlipidemia/Atherosclerotic Vascular Disease	No Increased Risk of Cardiovascular Disease
COMT	Val158Met AA	Low COMT Activity	Consistent with a significantly reduced catechol O-methyltransferase (COMT) function.
CYP1A2	*1A/*1A	Normal Metabolizer- Possible Inducibility	Consistent with a typical CYP1A2 activity in absence of inducing substances. Rapid metabolism may occur in presence of inducers such as barbiturates, cruciferous vegetables, carbamazepine, rifampin and smoking.
CYP2B6	*1/*1	Normal Metabolizer	Consistent with a typical CYP2B6 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP2C19	*1/*1	Normal Metabolizer	Consistent with a typical CYP2C19 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP2C9	*2/*2	Poor Metabolizer	Consistent with a significant deficiency in CYP2C9 activity. Increased risk for side effects or loss of efficacy with drug substrates.
CYP2D6	*1/*1 XN	Rapid Metabolizer	Consistent with a significant increase in CYP2D6 activity. Potential risk for side effects or loss of efficacy with drug substrates.
CYP3A4	*1/*1	Normal Metabolizer	Consistent with a typical CYP3A4 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
CYP3A5	*3C/*3C	Poor Metabolizer	Consistent with a poor CYP3A5 activity. This phenotype is the most common in the general population. 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.
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.
MTHFR	1298A>C AA 677C>T TT	No Increased Risk of Hyperhomocysteinemia	With a normal MTHFR activity, this patient is unlikely to have elevated plasma levels of homocysteine, which is a known risk factor for cardiovascular diseases and thrombosis. Unless other risk factors are present, the patient is not expected to have an increased risk for venous thromboembolism (VTE).
OPRM1	A118G AA	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.
SLCO1B1	521T>C TT	Normal Transporter Function	Consistent with a typical SLCO1B1 transporter function. The patient's risk for statin-induced myopathy is not increased.
VKORC1	-1639G>A A/A	High Warfarin Sensitivity	VKORC1 is the site of action of warfarin. The patient may require a substantial decrease in warfarin dose.

AllelesTested: ANKK1/DRD2 DRD2:Taq1A; **Apolipoprotein E** ε2, ε4, (ε3 is reference); **COMT** Val158Met; **CYP1A2** *1C, *1D, *1F, *1K, *1L, *1V, *1W; **CYP2B6** *6, *9; **CYP2C19** *2, *3, *4, *4B, *5, *6, *7, *8, *9, *17; **CYP2C9** *2, *3, *4, *5, *6, *11; **CYP2D6** *2, *3, *4, *4M, *6, *7, *8, *9, *10, *12, *14A, *14B, *17, *29, *35, *41, *5 (gene deletion), XN (gene duplication); **CYP3A4** *1B, *2, *3, *12, *17, *22; **CYP3A5** *1D, *2, *3, *3B, *3C, *6, *7, *8, *9; **Factor II** 20210G>A; **Factor V Leiden** 1691G>A; **MTHFR** 1298A>C, 677C>T; **OPRM1** A118G; **SLCO1B1** 521T>C, 388A>G; **VKORC1** -1639G>A

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Methodology:
Laboratory specimens associated with this report were analyzed using array-based assays. Genomic DNA was extracted from the submitted specimen and amplified using the polymerase chain reaction (PCR). The polymorphisms assayed in this report were targeted through the use of oligonucleotide primers. Single nucleotide polymorphisms, whole gene deletions, and copy-number variations were determined by fluorophore-based detection of a dual-labeled probe hybridized to the complementary target sequence. These assays detect all common and most rare variants of the target genes included in this report with a known clinical significance. All assays demonstrate an analytical sensitivity and specificity >99%.

Limitations:
This test does not detect polymorphisms other than those listed. Polymorphisms not detected in this series of assays include known mutations that result in altered or inactive phenotypes. The absence of a detectable gene variant or polymorphism does not rule out the possibility that the patient has an intermediate or poor metabolizer phenotype. In rare circumstances, polymorphisms in the primer or probe binding site may affect genotyping results. This test does not identify non-genetic factors that may contribute to altered drug metabolism, including drug-drug interactions. This laboratory has been certified by the Clinical Laboratory Improvement Amendment (CLIA) of 1988 to conduct high complexity clinical testing. This is a laboratory developed test (LDT) and has not been approved by the United States Food and Drug Administration (FDA) and should not be used as the sole evidence of diagnosis. Pharmacogenomic testing does not replace the need for clinical and therapeutic monitoring.

Disclaimer: The information contained within this report is intended for use by healthcare professionals. Do not quit taking or alter the dosage of any prescription medications you are taking without first consulting your physician or pharmacist.

Laboratory Certification: CLIA # 26D2106631

Laboratory Director:

Printed Name: Christopher Gilbert, M.D.

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Patient Information Card

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

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Patient Name	DOB	Requisition ID
Connie Comprehensive	**1/1/1970**	**234444**

Pharmacogenetic Test Summary

CYP2C19	*1/*1	Normal Metabolizer
CYP2C9	*2/*2	Poor Metabolizer
CYP2D6	*1/*1 XN	Rapid Metabolizer
CYP3A4	*1/*1	Normal Metabolizer
CYP3A5	*3C/*3C	Poor Metabolizer

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

For a complete report contact Dynamic DNA Laboratories, LLC

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