ADVANCED LAB 3
1800 McDonough Rd Suite 209, Hoffman Estates, IL 60192
(847) 873-8012
**Lab Director:** Dr. Harsukh Gevariya
**CLIA: 14D2245475 NPI # 1073267795**

| PATIENT INFORMATION | SPECIMEN DETAILS | | PROVIDER INFORMATION |
|---|---|---|---|
| **NAME:** SAMPLE REPORT | **SPECIMEN TYPE:** | Buccal Swab | **ORDERING PHYSICIAN:** |
| **ACC #:** SAMPLE REPORT | **COLLECTION DATE:** | 5/16/2023 | **PROVIDER:** |
| **DOB:** SAMPLE REPORT | **RECEIVED DATE:** | 5/17/2023 | |
| **SEX:** SAMPLE REPORT | **REPORT DATE:** | 5/19/2023 | |

# PGx Comprehensive Report

## Current Patient Medications

**All provided patient medications:** Glipizide, Metformin, Gabapentin, Tramadol, Crestor, Lorazepam, Levothyroxine, Flexeril, Savella, Aspirin, Lisinopril, Januvia, Sertraline

**Patient medications with NO clinical content:** Metformin, Lorazepam, Levothyroxine, Aspirin, Lisinopril, Januvia

### Crestor | ROSUVASTATIN

**Increased Rosuvastatin Exposure (SLCO1B1: Decreased Function)**

ACTIONABLE

The patient's genotype is associated with possible increased rosuvastatin exposure. Rosuvastatin can be prescribed at standard label-recommended dosage and administration, but patients may be at an increased myopathy risk with doses >20 mg.

### Flexeril | CYCLOBENZAPRINE

Normal Response to Cyclobenzaprine

INFORMATIVE

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

### Gabapentin | NEURONTIN®

Normal Response to Gabapentin

INFORMATIVE

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

### Glipizide | GLUCOTROL®

Normal Exposure to Glipizide

INFORMATIVE

**Pharmacogenetic guidance**: Glipizide is metabolized by CYP2C9. While this clearance pathway is diminished in subjects with reduced CYP2C9 activity, such a change has not been shown to be clinically significant. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance**: Co-administration of glipizide with a strong CYP2C9 inhibitor may result in higher glipizide concentrations possibly leading to hypoglycemia. Co-administration with a strong CYP2C9 inducer may result in lower glipizide concentrations and a lack of efficacy.

### Savella | MILNACIPRAN

Normal Response to Milnacipran

INFORMATIVE

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

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## Sertraline | ZOLOFT®

**ACTIONABLE**

The patient's genotype is associated with an increased exposure to sertraline and may possibly increase risk of adverse effects. Sertraline can be initiated at standard label-recommended dosage. Consider slow up-titration and lower than standard maintenance doses.

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The patient's genotype is associated with a significantly increased exposure to sertraline and may increase risk of adverse effects. Consider a lower initial dose and slow up-titration with a 50% reduction of the standard label-recommended maintenance dose or consider an alternative medication not predominantly metabolized by CYP2C19.

The patient's genotype is associated with an increased exposure to sertraline and may possibly increase risk of adverse effects. Sertraline can be initiated at standard label-recommended dosage. Consider slow up-titration and lower than standard label-recommended maintenance doses.

The patient's genotype is associated with a significantly increased exposure to sertraline and may increase risk of adverse effects. Consider a lower initial dose and slow up-titration with a 25% reduction of the standard label-recommended maintenance dose or consider an alternative medication not predominantly metabolized by CYP2B6.

The patient's genotype is associated with an increased exposure to sertraline and may increase risk of adverse effects. Sertraline can be initiated at standard label-recommended dosage. Consider slow up-titration and lower than standard label-recommended maintenance doses.

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The patient's genotype is associated with an increased exposure to sertraline and may increase risk of adverse effects. Consider a lower initial dose and slow up-titration with a 50% reduction of the standard label-recommended maintenance dose or consider an alternative medication not predominantly metabolized by CYP2C19.

## Tramadol | ULTRAM®

Normal Exposure to Tramadol Active Metabolite (CYP2D6: Normal Metabolizer)

**ACTIONABLE**

The patient genotype is associated with normal conversion of tramadol to its active metabolite (O-desmethyltramadol), which may result in standard pharmacological and/or toxic effects.

Tramadol can be prescribed at standard label-recommended age- or weight-based dosing and monitoring.

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## GUIDANCE LEVELS

A medication has potentially reduced efficacy, increased toxicity or the patient has an increased risk for the indicated condition.

Guidelines exist for adjusting dosage, increased vigilance or the patient has a moderate risk for the indicated condition.

The medication can be prescribed according to standard regimens or the patient's risk for the indicated condition is not increased.

## 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 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. |

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# Condition Risk Factors

## Type III Hyperlipoproteinemia
Not Associated with Type III Hyperlipoproteinemia

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

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

No action is needed when a patient is normolipidemic.

## Hyperhomocysteinemia - Depression
No Increased Risk of Hyperhomocysteinemia

The patient carries one copy of the MTHFR c.665C>T variant (heterozygous). MTHFR enzyme activity is reduced (60% of normal activity).

Patients diagnosed with depression often have low folate levels and homocysteine is a highly sensitive marker of folate status. Functional folate deficiency is indicated by elevated homocysteine. The patient's small reduction in MTHFR activity is not a risk factor for hyperhomocysteinemia.

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

## Thrombophilia
Normal Risk of Thrombosis

The patient does not carry the F5 c.1601G>A variant (also known as Factor V Leiden) or the F2 c.*97G>A variant (also known as Factor II 20210G>A).

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.

Assess thrombotic risk based on other genetic and/or circumstantial risk factors such as smoking, obesity, malignancy, prolonged immobilization or surgery.

**Estrogen-containing contraceptive and hormone replacement therapy:** unless other genetic and/or circumstantial risk factors are present, consider standard prescribing and monitoring practices.

## Hyperhomocysteinemia - Thrombosis
No Increased Risk of Hyperhomocysteinemia

The patient carries one copy of the MTHFR c.665C>T variant (heterozygous) and does not carry the MTHFR c.1286A>C variant. MTHFR enzyme activity is reduced (60% of normal activity).

Based on results for the MTHFR c.665C>T variant, the patient has a small reduction in MTHFR activity, which is not a risk factor for hyperhomocysteinemia. Hyperhomocysteinemia is associated with a risk for venous thromboembolism (VTE). Unless other risk factors are present, the patient is not expected to have an increased risk for VTE.

The patient's MTHFR activity is slightly reduced.

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# Potentially Impacted Medications

| CATEGORY | DRUG CLASS | STANDARD PRECAUTIONS | USE WITH CAUTION | CONSIDER ALTERNATIVES |
|---|---|---|---|---|
| **Anesthesia** | Injectable Anesthetics | *Propofol (Diprivan®)* | | |
| **Anticancer Agents** | Anti-Estrogens | Tamoxifen (Nolvadex®, Soltamox®) | | |
| | Antifolates | | Methotrexate (Trexall®) | |
| | Aromatase Inhibitors | *Anastrozole (Arimidex®)*<br>*Exemestane (Aromasin®)*<br>*Letrozole (Femara®)* | | |
| | Protein Kinase Inhibitors | Erdafitinib (Balversa®)<br>Gefitinib (Iressa®) | | |
| **Antihistamines** | Histamine (H1) Receptor Antagonists | Meclizine (Antivert®) | | |
| **Cardiovascular** | Angiotensin II Receptor Antagonists | Azilsartan (Edarbi®, Edarbyclor®)<br>*Candesartan (Atacand®)*<br>*Eprosartan (Teveten®)*<br>Irbesartan (Avapro®)<br>Losartan (Cozaar®, Hyzaar®)<br>*Olmesartan (Benicar®)*<br>*Telmisartan (Micardis®)*<br>*Valsartan (Diovan®, Entresto®)* | | |
| | Antianginal Agents | Ranolazine (Ranexa®) | | |
| | Antiarrhythmics | *Amiodarone (Nexterone®, Pacerone®)*<br>*Disopyramide (Norpace®)*<br>Flecainide (Tambocor®)<br>Mexiletine (Mexitil®)<br>Propafenone (Rythmol®)<br>*Quinidine (Quinidine®)*<br>*Sotalol (Betapace®, Sorine®, Sotylize®)* | | |
| | Anticoagulants | *Apixaban (Eliquis®)*<br>*Betrixaban (Bevyxxa®)*<br>*Dabigatran Etexilate (Pradaxa®)*<br>*Edoxaban (Savaysa®)*<br>*Fondaparinux (Arixtra®)*<br>*Rivaroxaban (Xarelto®)*<br>Warfarin (Coumadin®) | | |
| | Antiplatelets | Clopidogrel (Plavix®)<br>*Prasugrel (Effient®)*<br>*Ticagrelor (Brilinta®)*<br>*Vorapaxar (Zontivity®)* | | |

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|---|---|---|---|---|
| | Beta Blockers | *Atenolol (Tenormin®)*<br>*Bisoprolol (Zebeta®)*<br>Carvedilol (Coreg®)<br>*Labetalol (Normodyne®, Trandate®)*<br>Metoprolol (Lopressor®)<br>Nebivolol (Bystolic®)<br>Propranolol (Inderal®)<br>Timolol (Blocadren®) | | |
| | Cardiac myosin inhibitor | Mavacamten (Camzyos®) | | |
| | Diuretics | Torsemide (Demadex®) | | |
| | Statins | | Fluvastatin (Lescol®)<br>Pravastatin (Pravachol®)<br>**Rosuvastatin (Crestor®)** | Atorvastatin (Lipitor®)<br>Lovastatin (Mevacor®, Altoprev®, Advicor®)<br>Pitavastatin (Livalo®)<br>Simvastatin (Zocor®) |
| **Diabetes** | Meglitinides | Nateglinide (Starlix®)<br>Repaglinide (Prandin®, Prandimet®) | | |
| | Sulfonylureas | *Chlorpropamide (Diabinese®)*<br>*Glimepiride (Amaryl®)*<br>***Glipizide (Glucotrol®)***<br>*Glyburide (Micronase®)*<br>*Tolbutamide (Orinase®)* | | |
| **Gastrointestinal** | Antiemetics | *Aprepitant (Emend-oral®)*<br>Dolasetron (Anzemet®)<br>Dronabinol (Marinol®)<br>*Fosaprepitant (Emend-IV®)*<br>Fosnetupitant / Palonosetron (Akynzeo-IV®)<br>*Granisetron (Sancuso®, Sustol®)*<br>Metoclopramide (Reglan®)<br>Netupitant / Palonosetron (Akynzeo-oral®)<br>Ondansetron (Zofran®, Zuplenz®)<br>Palonosetron (Aloxi®)<br>*Rolapitant (Varubi®)* | | |
| | Proton Pump Inhibitors | Esomeprazole (Nexium®)<br>Rabeprazole (Aciphex®) | Dexlansoprazole (Dexilant®, Kapidex®)<br>Lansoprazole (Prevacid®)<br>Omeprazole (Prilosec®)<br>Pantoprazole (Protonix®) | |
| **Gaucher Disease** | Endocrine-Metabolic Agents | Eliglustat (Cerdelga®)<br>*Imiglucerase (Cerezyme®)*<br>*Miglustat (Zavesca®)*<br>*Taliglucerase alfa (Elelyso®)*<br>*Velaglucerase alfa (Vpriv®)* | | |

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|---|---|---|---|---|
| **Gynecology** | **Endometriosis Pain Agents** | Elagolix (Orilissa®) | | |
| **Hematology** | **Hemostatic Agents** | Avatrombopag (Doptelet®)<br>Eltrombopag (Promacta®)<br>Lusutrombopag (Mulpleta®) | | |
| **Infections** | **Antifungals** | *Amphotericin B (AmBisome®, Abelcet®)*<br>*Anidulafungin (Eraxis®)*<br>*Caspofungin (Cancidas®)*<br>*Fluconazole (Diflucan®)*<br>*Isavuconazonium (Cresemba®)*<br>*Itraconazole (Sporanox®)*<br>*Micafungin (Mycamine®)*<br>*Posaconazole (Noxafil®)*<br>Voriconazole (Vfend®) | | |
| | **Anti-HIV Agents** | *Dolutegravir (Tivicay®, Triumeq®)*<br>*Doravirine (Pifeltro®)*<br>Efavirenz (Sustiva®)<br>*Etravirine (Edurant®)*<br>*Raltegravir (Isentress®, Dutrebis®)*<br>*Rilpivirine (Intelence®)* | | |
| | **Antimalarials** | *Proguanil (Malarone®)* | | |
| **Multiple Sclerosis** | **Disease-Modifying Agents** | Siponimod (Mayzent®) | | |
| **Pain** | **Fibromyalgia Agents** | ***Milnacipran (Savella®)*** | | |
| | **Muscle Relaxants** | Carisoprodol (Soma®)<br>***Cyclobenzaprine (Flexeril®, Amrix®)***<br>*Metaxalone (Skelaxin®)*<br>*Methocarbamol (Robaxin®)* | Tizanidine (Zanaflex®) | |
| | **NSAIDs** | Celecoxib (Celebrex®)<br>*Diclofenac (Voltaren®)*<br>Flurbiprofen (Ansaid®)<br>Ibuprofen (Advil®, Motrin®)<br>*Indomethacin (Indocin®)*<br>*Ketoprofen (Orudis®)*<br>*Ketorolac (Toradol®)*<br>Meloxicam (Mobic®)<br>*Nabumetone (Relafen®)*<br>*Naproxen (Aleve®)*<br>Piroxicam (Feldene®)<br>*Sulindac (Clinoril®)* | | |

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|---|---|---|---|---|
| | Opioids | *Alfentanil (Alfenta®)*<br>Benzhydrocodone (Apadaz®)<br>*Buprenorphine (Butrans®, Buprenex®)*<br>Codeine (Codeine; Fioricet® with Codeine)<br>Dihydrocodeine (Synalgos-DC®)<br>*Fentanyl (Actiq®)*<br>Hydrocodone (Vicodin®)<br>*Hydromorphone (Dilaudid®, Exalgo®)*<br>*Levorphanol (Levo Dromoran®)*<br>*Meperidine (Demerol®)*<br>Methadone (Dolophine®)<br>Morphine (MS Contin®)<br>Oliceridine (Olinvyk)<br>Oxycodone (Percocet®, Oxycontin®)<br>*Oxymorphone (Opana®, Numorphan®)*<br>*Sufentanil (Sufenta®)*<br>*Tapentadol (Nucynta®)*<br>**Tramadol (Ultram®)** | | |
| **Psychotropic** | Antiaddictives | Bupropion (Wellbutrin®, Zyban®, Aplenzin®, Contrave®)<br>Lofexidine (Lucemyra®) | | |
| | Anti-ADHD Agents | *Clonidine (Kapvay®)*<br>*Guanfacine (Intuniv®)* | Amphetamine (Adderall®, Evekeo®)<br>Atomoxetine (Strattera®)<br>Dexmethylphenidate (Focalin®)<br>Dextroamphetamine (Dexedrine®)<br>Lisdexamfetamine (Vyvanse®)<br>Methylphenidate (Ritalin®, Aptensio XR®, Concerta®, Metadate ER®, Quillivant ER®) | |

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

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|---|---|---|---|---|
| | Antipsychotics | Aripiprazole (Abilify®, Aristada®)<br>*Asenapine (Saphris®)*<br>Brexpiprazole (Rexulti®)<br>*Cariprazine (Vraylar®)*<br>Chlorpromazine (Thorazine®)<br>*Fluphenazine (Prolixin®)*<br>Haloperidol (Haldol®)<br>Iloperidone (Fanapt®)<br>*Loxapine (Loxitane®, Adasuve®)*<br>*Lurasidone (Latuda®)*<br>Paliperidone (Invega®)<br>Perphenazine (Trilafon®)<br>*Pimavanserin (Nuplazid®)*<br>Pimozide (Orap®)<br>*Quetiapine (Seroquel®)*<br>Risperidone (Risperdal®)<br>Thioridazine (Mellaril®)<br>*Thiothixene (Navane®)*<br>*Trifluoperazine (Stelazine®)*<br>*Ziprasidone (Geodon®)* | Clozapine (Clozaril®)<br>Olanzapine (Zyprexa®) | |
| | Benzodiazepines | *Alprazolam (Xanax®)*<br>Clobazam (Onfi®)<br>*Clonazepam (Klonopin®)*<br>Diazepam (Valium®) | | |
| | Other Neurological Agents | Deutetrabenazine (Austedo®)<br>Dextromethorphan / Quinidine (Nuedexta®)<br>Flibanserin (Addyi®)<br>Valbenazine (Ingrezza®) | Tetrabenazine (Xenazine®) | |
| **Pulmonology** | Asthma/COPD | *Arformoterol (Brovana®)*<br>*Indacaterol (Arcapta Neohaler®, Utibron®)* | | |
| **Rheumatology** | Anti-Hyperuricemics and Anti-Gout Agents | *Colchicine (Mitigare®)*<br>*Febuxostat (Uloric®)* | | |
| | Immunomodulators | *Apremilast (Otezla®)*<br>Leflunomide (Arava®)<br>*Tofacitinib (Xeljanz®)* | | |
| **Sjogren's Syndrome** | Cholinergic Agonists | Cevimeline (Evoxac®) | | |
| **Sleep Disorder Agents** | Narcoleptic Agents | Pitolisant (Wakix®) | | |
| **Transplantation** | Immunosuppressants | Tacrolimus (Prograf®) | | |
| **Urologicals** | 5-Alpha Reductase Inhibitors for Benign Prostatic Hyperplasia | *Dutasteride (Avodart®)*<br>*Finasteride (Proscar®)* | | |

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| CATEGORY | DRUG CLASS | STANDARD PRECAUTIONS | USE WITH CAUTION | CONSIDER ALTERNATIVES |
|---|---|---|---|---|
| | **Alpha-Blockers for Benign Prostatic Hyperplasia** | *Alfuzosin (UroXatral®)*<br>*Doxazosin (Cardura®)*<br>*Silodosin (Rapaflo®)*<br>Tamsulosin (Flomax®)<br>*Terazosin (Hytrin®)* | | |
| | **Antispasmodics for Overactive Bladder** | Darifenacin (Enablex®)<br>Fesoterodine (Toviaz®)<br>Mirabegron (Myrbetriq®)<br>*Oxybutynin (Ditropan®)*<br>*Solifenacin (Vesicare®)*<br>Tolterodine (Detrol®)<br>*Trospium (Sanctura®)* | | |
| | **Phosphodiesterase Inhibitors for Erectile Dysfunction** | *Avanafil (Stendra®)*<br>*Sildenafil (Viagra®)*<br>*Tadalafil (Cialis®)*<br>*Vardenafil (Levitra®)* | | |

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# Dosing Guidance

## Atorvastatin
*Lipitor®*

**Increased Atorvastatin Exposure (SLCO1B1: Decreased Function)** — ACTIONABLE

The patient's genotype is associated with possible increased atorvastatin exposure. Patients may be at an increased myopathy risk.

Consider starting atorvastatin at doses ≤40 mg. If doses >40 mg are needed, consider combination therapy (e.g., atorvastatin plus a non-statin guideline directed therapy).

- Cooper-DeHoff RM, Niemi M, Ramsey LB, Luzum JA, Tarkiainen EK, Straka RJ, Gong L, Tuteja S, Wilke RA, Wadelius M, Larson EA, Roden DM, Klein TE, Yee SW, Krauss RM, Turner RM, Palaniappan L, Gaedigk A, Giacomini KM, Caudle KE, Voora D. The Clinical Pharmacogenetics Implementation Consortium Guideline for SLCO1B1, ABCG2, and CYP2C9 genotypes and Statin-Associated Musculoskeletal Symptoms. Clin Pharmacol Ther 2022 May;111(5):1007-1021.
- Lipitor [package insert]. New York, NY: Pfizer Inc.; 2020.

## Lovastatin
*Mevacor®, Altoprev®, Advicor®*

**Increased Lovastatin Exposure (SLCO1B1: Decreased Function)** — ACTIONABLE

The patient's genotype is associated with possible increased lovastatin exposure. Patients may be at an increased myopathy risk.
Consider an alternative statin based on disease-specific guidelines. If lovastatin use is warranted, consider limiting dose to ≤20 mg per day.

- Cooper-DeHoff RM, Niemi M, Ramsey LB, Luzum JA, Tarkiainen EK, Straka RJ, Gong L, Tuteja S, Wilke RA, Wadelius M, Larson EA, Roden DM, Klein TE, Yee SW, Krauss RM, Turner RM, Palaniappan L, Gaedigk A, Giacomini KM, Caudle KE, Voora D. The Clinical Pharmacogenetics Implementation Consortium Guideline for SLCO1B1, ABCG2, and CYP2C9 genotypes and Statin-Associated Musculoskeletal Symptoms. Clin Pharmacol Ther 2022 May;111(5):1007-1021.

## Pitavastatin
*Livalo®*

**Increased Pitavastatin Exposure (SLCO1B1: Decreased Function)** — ACTIONABLE

The patient's genotype is associated with possible increased pitavastatin exposure. Patients may be at an increased myopathy risk with doses >1 mg per day.

Consider starting pitavastatin at doses ≤2 mg. If doses >2 mg are needed, consider an alternative statin or combination therapy (e.g., pitavastatin plus a non-statin guideline directed medical therapy).

- Cooper-DeHoff RM, Niemi M, Ramsey LB, Luzum JA, Tarkiainen EK, Straka RJ, Gong L, Tuteja S, Wilke RA, Wadelius M, Larson EA, Roden DM, Klein TE, Yee SW, Krauss RM, Turner RM, Palaniappan L, Gaedigk A, Giacomini KM, Caudle KE, Voora D. The Clinical Pharmacogenetics Implementation Consortium Guideline for SLCO1B1, ABCG2, and CYP2C9 genotypes and Statin-Associated Musculoskeletal Symptoms. Clin Pharmacol Ther 2022 May;111(5):1007-1021.

## Simvastatin
*Zocor®*

**Increased Simvastatin Exposure (SLCO1B1: Decreased Function)** — ACTIONABLE

The patient's genotype is associated with possible increased simvastatin exposure. Patients may be at an increased myopathy risk with doses >20 mg.

Consider an alternative statin. If simvastatin use is warranted, consider limiting dose to <20 mg.

- Cooper-DeHoff RM, Niemi M, Ramsey LB, Luzum JA, Tarkiainen EK, Straka RJ, Gong L, Tuteja S, Wilke RA, Wadelius M, Larson EA, Roden DM, Klein TE, Yee SW, Krauss RM, Turner RM, Palaniappan L, Gaedigk A, Giacomini KM, Caudle KE, Voora D. The Clinical Pharmacogenetics Implementation Consortium Guideline for SLCO1B1, ABCG2, and CYP2C9 genotypes and Statin-Associated Musculoskeletal Symptoms. Clin Pharmacol Ther 2022 May;111(5):1007-1021.
- Zocor [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; 2021.

## Amphetamine
*Adderall®, Evekeo®*

**Poor Response to Amphetamine salts (COMT: Low COMT Activity)** — INFORMATIVE

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.

- Mattay VS, Goldberg TE, Fera F, Hariri AR, Tessitore A, Egan MF, Kolachana B, Callicott JH, Weinberger DR. Catechol O-methyltransferase val158-met genotype and individual variation in the brain response to amphetamine. Proc Natl Acad Sci U S A 2003 May;100(10):6186-91.
- Hamidovic A, Dlugos A, Palmer AA, de Wit H. Catechol-O-methyltransferase val158met genotype modulates sustained attention in both the drug-free state and in response to amphetamine. Psychiatr Genet 2010 Jun;20(3):85-92.

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## Atomoxetine
*Strattera®*

**Normal Atomoxetine Exposure (CYP2D6: Normal Metabolizer)** — **ACTIONABLE**

The genotype result indicates that the patient is likely to have an insufficient response due to inadequate drug exposure following standard dosing as compared with poor metabolizers.

**Consider the following dosing strategy:**

- Initiate treatment at 40 mg/day, then increase to 80 mg/day after 3 days.
- If after 2 weeks, optimal clinical response is not observed and adverse events are not present, consider a dose increase to 100 mg/day.
- If after an additional 2 weeks, optimal clinical response is not observed, consider therapeutic drug monitoring 1-2 hours post dose. If the plasma concentration is < 200 ng/mL, consider a proportional dose increase to approach 400 ng/mL. Doses > 100 mg/day may be needed to achieve a target therapeutic concentration (therapeutic range: 200-1,000 ng/mL). Note: doses above 120 mg/day have not been evaluated.


- Brown JT, Bishop JR, Sangkuhl K, Nurmi EL, Mueller DJ, Dinh JC, Gaedigk A, Klein TE, Caudle KE, McCracken JT, de Leon J, Leeder JS. Clinical Pharmacogenetics Implementation Consortium Guideline for Cytochrome P450 (CYP)2D6 Genotype and Atomoxetine Therapy. Clin Pharmacol Ther 2019 Jul;106(1):94-102.
- Atomoxetine [package insert]. Parsippany, NJ: Teva Pharmaceuticals; 2022.


## Clozapine
*Clozaril®*

**Non-Response to Clozapine (CYP1A2: Normal Metabolizer - Higher Inducibility)** — **INFORMATIVE**

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


- Bolla E, Bortolaso P, Ferrari M, Poloni N, Callegari C, Marino F, Lecchini S, Vender S, Cosentino M. Are CYP1A2*1F and *1C associated with clozapine tolerability?: a preliminary investigation. Psychiatry Res 2011 Oct;189(3):483.
- Ferrari M, Bolla E, Bortolaso P, Callegari C, Poloni N, Lecchini S, Vender S, Marino F, Cosentino M. Association between CYP1A2 polymorphisms and clozapine-induced adverse reactions in patients with schizophrenia. Psychiatry Res 2012 Dec;200(2-3):1014-7.
- Ozdemir V, Kalow W, Okey AB, Lam MS, Albers LJ, Reist C, Fourie J, Posner P, Collins EJ, Roy R. Treatment-resistance to clozapine in association with ultrarapid CYP1A2 activity and the C-->A polymorphism in intron 1 of the CYP1A2 gene: effect of grapefruit juice and low-dose fluvoxamine. J Clin Psychopharmacol 2001 Dec;21(6):603-7.
- Koonrungsesomboon N, Khatsri R, Wongchompoo P, Teekachunhatean S. The impact of genetic polymorphisms on CYP1A2 activity in humans: a systematic review and meta-analysis. Pharmacogenomics J 2018 12;18(6):760-768.


## Dexlansoprazole
*Dexilant®, Kapidex®*

**Normal or Possible Slightly Decreased Exposure to Dexlansoprazole (CYP2C19: Normal Metabolizer)** — **INFORMATIVE**

The patient's genotype is predictive of normal metabolism but may be associated with a slightly decreased dexlansoprazole clinical exposure following standard dosing. Be alert for insufficient response, consider prescribing dexlansoprazole at standard label-recommended dosage and administration. May consider increasing the recommended dose for certain indications by 50-100% to optimize therapeutic efficacy.


- Lima JJ, Thomas CD, Barbarino J, Desta Z, Van Driest SL, El Rouby N, Johnson JA, Cavallari LH, Shakhnovich V, Thacker DL, Scott SA, Schwab M, Uppugunduri CRS, Formea CM, Franciosi JP, Sangkuhl K, Gaedigk A, Klein TE, Gammal RS, Furuta T. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C19 and Proton Pump Inhibitor Dosing. Clin Pharmacol Ther. 2020 Aug 8.


## Dexmethylphenidate
*Focalin®*

**Poor Response to Dexmethylphenidate (COMT: Low COMT Activity)** — **INFORMATIVE**

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.


- Cheon KA, Jun JY, Cho DY. Association of the catechol-O-methyltransferase polymorphism with methylphenidate response in a classroom setting in children with attention-deficit hyperactivity disorder. Int Clin Psychopharmacol 2008 Sep;23(5):291-8.
- Kereszturi E, Tarnok Z, Bognar E, Lakatos K, Farkas L, Gadoros J, Sasvari-Szekely M, Nemoda Z. Catechol-O-methyltransferase Val158Met polymorphism is associated with methylphenidate response in ADHD children. Am J Med Genet B Neuropsychiatr Genet 2008 Dec;147B(8):1431-5.


## Dextroamphetamine
*Dexedrine®*

**Poor Response to Dextroamphetamine (COMT: Low COMT Activity)** — **INFORMATIVE**

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.


- Mattay VS, Goldberg TE, Fera F, Hariri AR, Tessitore A, Egan MF, Kolachana B, Callicott JH, Weinberger DR. Catechol O-methyltransferase val158-met genotype and individual variation in the brain response to amphetamine. Proc Natl Acad Sci U S A 2003 May;100(10):6186-91.

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## Fluvastatin
*Lescol®*

**Increased Fluvastatin Exposure (SLCO1B1: Decreased Function; CYP2C9: Normal Metabolizer)** — **ACTIONABLE**

The patient's genotype is associated with possible increased fluvastatin exposure. Fluvastatin can be prescribed at standard label-recommended dosage and administration, but patients may be at an increased risk for myopathy with doses >40 mg per day.


- Cooper-DeHoff RM, Niemi M, Ramsey LB, Luzum JA, Tarkiainen EK, Straka RJ, Gong L, Tuteja S, Wilke RA, Wadelius M, Larson EA, Roden DM, Klein TE, Yee SW, Krauss RM, Turner RM, Palaniappan L, Gaedigk A, Giacomini KM, Caudle KE, Voora D. The Clinical Pharmacogenetics Implementation Consortium Guideline for SLCO1B1, ABCG2, and CYP2C9 genotypes and Statin-Associated Musculoskeletal Symptoms. Clin Pharmacol Ther 2022 May;111(5):1007-1021.


## Lansoprazole
*Prevacid®*

**Normal or Possible Slightly Decreased Exposure to Lansoprazole (CYP2C19: Normal Metabolizer)** — **ACTIONABLE**

The patient's genotype is predictive of normal metabolism but may be associated with a slightly decreased lansoprazole clinical exposure following standard dosing. Be alert for insufficient response, consider prescribing lansoprazole at standard label-recommended dosage and administration. May consider increasing the recommended dose for certain indications by 50-100% to optimize therapeutic efficacy.


- Lima JJ, Thomas CD, Barbarino J, Desta Z, Van Driest SL, El Rouby N, Johnson JA, Cavallari LH, Shakhnovich V, Thacker DL, Scott SA, Schwab M, Uppugunduri CRS, Formea CM, Franciosi JP, Sangkuhl K, Gaedigk A, Klein TE, Gammal RS, Furuta T. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C19 and Proton Pump Inhibitor Dosing. Clin Pharmacol Ther. 2020 Aug 8.


## Lisdexamfetamine
*Vyvanse®*

**Poor Response to Lisdexamfetamine (COMT: Low COMT Activity)** — **INFORMATIVE**

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.


- Mattay VS, Goldberg TE, Fera F, Hariri AR, Tessitore A, Egan MF, Kolachana B, Callicott JH, Weinberger DR. Catechol O-methyltransferase val158-met genotype and individual variation in the brain response to amphetamine. Proc Natl Acad Sci U S A 2003 May;100(10):6186-91.
- Hamidovic A, Dlugos A, Palmer AA, de Wit H. Catechol-O-methyltransferase val158met genotype modulates sustained attention in both the drug-free state and in response to amphetamine. Psychiatr Genet 2010 Jun;20(3):85-92.


## Methotrexate
*Trexall®*

**Increased Risk for Methotrexate Toxicity (MTHFR: Reduced MTHFR Activity)** — **INFORMATIVE**

The patient carries one copy of the MTHFR c.665C>T variant resulting in a reduced MTHFR activity. **Malignancy:** Leukemia or lymphoma patients who are treated with methotrexate standard regimens might have an increased likelihood of treatment interruptions due to methotrexate toxicity. Monitor the 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. **Nonmalignant conditions:** a limited number of studies found an association between individuals carrying the MTHFR c.665C>T variant 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.


- De Mattia E, Toffoli G. C677T and A1298C MTHFR polymorphisms, a challenge for antifolate and fluoropyrimidine-based therapy personalisation. Eur J Cancer 2009 May;45(8):1333-51.
- Choi YJ, Park H, Lee JS, Lee JY, Kim S, Kim TW, Park JS, Kim JE, Yoon DH, Suh C. Methotrexate elimination and toxicity: MTHFR 677C>T polymorphism in patients with primary CNS lymphoma treated with high-dose methotrexate. Hematol Oncol 2017 Dec;35(4):504-509.
- Zhao M, Liang L, Ji L, Chen D, Zhang Y, Zhu Y, Ongaro A. MTHFR gene polymorphisms and methotrexate toxicity in adult patients with hematological malignancies: a meta-analysis. Pharmacogenomics 2016 06;17(9):1005-17.


## Methylphenidate
*Ritalin®, Aptensio XR®, Concerta®, Metadate ER®, Quillivant ER®*

**Poor Response to Methylphenidate (COMT: Low COMT Activity)** — **INFORMATIVE**

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.


- Cheon KA, Jun JY, Cho DY. Association of the catechol-O-methyltransferase polymorphism with methylphenidate response in a classroom setting in children with attention-deficit hyperactivity disorder. Int Clin Psychopharmacol 2008 Sep;23(5):291-8.

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## Olanzapine
*Zyprexa®*

**Non-Response to Olanzapine (CYP1A2: Normal Metabolizer - Higher Inducibility)** **INFORMATIVE**

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


- Perera V, Gross AS, Polasek TM, Qin Y, Rao G, Forrest A, Xu J, McLachlan AJ. Considering CYP1A2 phenotype and genotype for optimizing the dose of olanzapine in the management of schizophrenia. Expert Opin Drug Metab Toxicol 2013 Sep;9(9):1115-37.
- Laika B, Leucht S, Heres S, Schneider H, Steimer W. Pharmacogenetics and olanzapine treatment: CYP1A2*1F and serotonergic polymorphisms influence therapeutic outcome. Pharmacogenomics J 2010 Feb;10(1):20-9.
- Koonrungsesomboon N, Khatsri R, Wongchompoo P, Teekachunhatean S. The impact of genetic polymorphisms on CYP1A2 activity in humans: a systematic review and meta-analysis. Pharmacogenomics J 2018 12;18(6):760-768.


## Omeprazole
*Prilosec®*

**Normal or Possible Slightly Decreased Exposure to Omeprazole (CYP2C19: Normal Metabolizer)** **ACTIONABLE**

The patient's genotype is predictive of normal metabolism but may be associated with a slightly decreased omeprazole clinical exposure following standard dosing. Be alert for insufficient response, consider prescribing omeprazole at standard label-recommended dosage and administration. May consider increasing the recommended dose for certain indications by 50-100% to optimize therapeutic efficacy.


- Lima JJ, Thomas CD, Barbarino J, Desta Z, Van Driest SL, El Rouby N, Johnson JA, Cavallari LH, Shakhnovich V, Thacker DL, Scott SA, Schwab M, Uppugunduri CRS, Formea CM, Franciosi JP, Sangkuhl K, Gaedigk A, Klein TE, Gammal RS, Furuta T. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C19 and Proton Pump Inhibitor Dosing. Clin Pharmacol Ther. 2020 Aug 8.


## Pantoprazole
*Protonix®*

**Normal or Possible Slightly Decreased Exposure to Pantoprazole (CYP2C19: Normal Metabolizer)** **ACTIONABLE**

The patient's genotype is predictive of normal metabolism but may be associated with a slightly decreased pantoprazole clinical exposure following standard dosing. Be alert for insufficient response, consider prescribing pantoprazole at standard label-recommended dosage and administration. May consider increasing the recommended dose for certain indications by 50-100% to optimize therapeutic efficacy.


- Lima JJ, Thomas CD, Barbarino J, Desta Z, Van Driest SL, El Rouby N, Johnson JA, Cavallari LH, Shakhnovich V, Thacker DL, Scott SA, Schwab M, Uppugunduri CRS, Formea CM, Franciosi JP, Sangkuhl K, Gaedigk A, Klein TE, Gammal RS, Furuta T. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C19 and Proton Pump Inhibitor Dosing. Clin Pharmacol Ther. 2020 Aug 8.


## Pravastatin
*Pravachol®*

**Increased Pravastatin Exposure (SLCO1B1: Decreased Function)** **ACTIONABLE**

The patient's genotype is associated with possible increased pravastatin exposure. Pravastatin can be prescribed at standard label-recommended dosage and administration, but patients may be at an increased myopathy risk with doses >40 mg per day.


- Cooper-DeHoff RM, Niemi M, Ramsey LB, Luzum JA, Tarkiainen EK, Straka RJ, Gong L, Tuteja S, Wilke RA, Wadelius M, Larson EA, Roden DM, Klein TE, Yee SW, Krauss RM, Turner RM, Palaniappan L, Gaedigk A, Giacomini KM, Caudle KE, Voora D. The Clinical Pharmacogenetics Implementation Consortium Guideline for SLCO1B1, ABCG2, and CYP2C9 genotypes and Statin-Associated Musculoskeletal Symptoms. Clin Pharmacol Ther 2022 May;111(5):1007-1021.


## Rosuvastatin
*Crestor®*

**Increased Rosuvastatin Exposure (SLCO1B1: Decreased Function)** **ACTIONABLE**

The patient's genotype is associated with possible increased rosuvastatin exposure. Rosuvastatin can be prescribed at standard label-recommended dosage and administration, but patients may be at an increased myopathy risk with doses >20 mg.


- Cooper-DeHoff RM, Niemi M, Ramsey LB, Luzum JA, Tarkiainen EK, Straka RJ, Gong L, Tuteja S, Wilke RA, Wadelius M, Larson EA, Roden DM, Klein TE, Yee SW, Krauss RM, Turner RM, Palaniappan L, Gaedigk A, Giacomini KM, Caudle KE, Voora D. The Clinical Pharmacogenetics Implementation Consortium Guideline for SLCO1B1, ABCG2, and CYP2C9 genotypes and Statin-Associated Musculoskeletal Symptoms. Clin Pharmacol Ther 2022 May;111(5):1007-1021.
- Crestor [package insert]. Wilmington, DE: AstraZeneca; 2020.


## Tetrabenazine
*Xenazine®*

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

**For treating chorea associated with Huntington's disease:** Individualization of dose with careful weekly titration is required. The first week's starting dose is 12.5 mg daily; second week, 25 mg (12.5 mg twice daily); then slowly titrate at weekly intervals by 12.5 mg to a tolerated dose. **The maximum daily dose in CYP2D6 normal metabolizers is 100 mg, with a maximum single dose of 37.5 mg**. If serious adverse events occur, titration should be stopped and the dose of tetrabenazine should be reduced. If the adverse event(s) do not resolve, consider withdrawal of tetrabenazine.


- Xenazine [package insert]. Deerfield, IL: Lundbeck Inc.; 2017.

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## Tizanidine

*Zanaflex®*

### Possible Non-Response to Tizanidine (CYP1A2: Normal Metabolizer - Higher Inducibility)

**INFORMATIVE**

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


- Backman JT, Schröder MT, Neuvonen PJ. Effects of gender and moderate smoking on the pharmacokinetics and effects of the CYP1A2 substrate tizanidine. Eur J Clin Pharmacol 2008 Jan;64(1):17-24.
- Granfors MT, Backman JT, Neuvonen M, Ahonen J, Neuvonen PJ. Fluvoxamine drastically increases concentrations and effects of tizanidine: a potentially hazardous interaction. Clin Pharmacol Ther 2004 Apr;75(4):331-41.
- Al-Ghazawi M, Alzoubi M, Faidi B. Pharmacokinetic comparison of two 4 mg tablet formulations of tizanidine. Int J Clin Pharmacol Ther 2013 Mar;51 (3):255-62.
- Koonrungsesomboon N, Khatsri R, Wongchompoo P, Teekachunhatean S. The impact of genetic polymorphisms on CYP1A2 activity in humans: a systematic review and meta-analysis. Pharmacogenomics J 2018 12;18(6):760-768.

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# Test Details

| Gene | Results | Phenotype | Clinical Consequences |
|---|---|---|---|
| **APOE** | ε3/ε3 | **Normal APOE function** | Not associated with type III hyperlipoproteinemia - No increased risk of cardiovascular disease |
| **COMT** | Val158Met A/A | **Low COMT Activity** | Consistent with a significantly reduced catechol O-methyltransferase (COMT) function. |
| **CYP1A2** | *1A/*1F | **Normal Metabolizer - Higher Inducibility** | Consistent with a typical CYP1A2 activity in absence of inducing substances. Rapid Metabolism occurs 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 enzyme activity. |
| **CYP2C9** | *1/*1 | **Normal Metabolizer** | Consistent with a typical CYP2C9 enzyme activity. |
| **CYP2D6** | *1/*1 | **Normal Metabolizer** | Consistent with a typical CYP2D6 enzyme activity. |
| **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** | *3/*3 | **Poor Metabolizer** | Consistent with an absence of CYP3A5 enzyme expression (Non-Expresser). This phenotype is the most common in the general population. |
| **F2**<br>**F5** | rs1799963 GG<br>rs6025 CC | **Normal Risk of Thrombosis** | Unless other genetic or circumstantial risk factors are present, the patient is not expected to have an increased risk for thrombosis. |
| **MTHFR** | c.665C>T GA | **Reduced MTHFR Activity** | The patient carries one copy of the MTHFR c.665C>T variant (heterozygous) and the patient's MTHFR activity is reduced slightly. This is not associated with an increased risk of hyperhomocysteinemia. |
| **MTHFR** | c.1286A>C TT<br>c.665C>T GA | **No Increased Risk of Hyperhomocysteinemia** | The patient is heterozygous for the MTHFR c.665C>T variant and does not carry the MTHFR c.1286A>C variant. The MTHFR function is reduced slightly, but it is not associated with an increased risk for hyperhomocysteinemia. |
| **SLCO1B1** | *1/*5 | **Decreased Function** | Consistent with a decreased SLCO1B1 transporter function. Exercise caution when certain SLCO1B1 drug substrates are prescribed. |
| **VKORC1** | -1639G>A G/A | **Intermediate Warfarin Sensitivity** | Consistent with a moderately decreased VKORC1 expression. Exercise caution with coumarin anticoagulants. |

**Alleles Tested: APOE** ε2, ε4, (ε3 is reference); **COMT** Val158Met; **CYP1A2** *1C, *1D, *1E, *1F, *1J, *1K, *1L, *1V, *1W; **CYP2B6** *5, *6, *7, *9, *18, *18.002, *22; **CYP2C19** *2, *3, *4A, *4B, *5, *6, *7, *8, *9, *10, *17; **CYP2C9** *2, *3, *4, *5, *6, *11; **CYP2D6** *2, *3, *4, *4M, *6, *7, *8, *9, *10, *12, *14, *17, *29, *41, *114, *5 (gene deletion), XN (gene duplication); **CYP3A4** *2, *3, *12, *17, *22; **CYP3A5** *3, *6, *7, *8, *9; **F2** rs1799963; **F5** rs6025; **MTHFR** c.1286A>C, c.665C>T; **SLCO1B1** *5; **VKORC1** -1639G>A