ScriptAssured pharmacogenetics

Drug Metabolism Test Results

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Comprehensive Pharmacogenetic Report for G********** T**********

Patient:	G********** T**********	Accession #:	R0001104
DOB:	1/1/1980	Collection Date:	9/18/2015
Gender:	Unknown	Received Date:	9/21/2015
Ordered By:	David Gallegos	Report Generated:	11/18/2015
		Specimen Type:	Buccal Swab

Test Details

Gene	Genotype	Phenotype	Alleles Tested
Apolipoprotein E	ε3/ε4	Increased Risk of Hyperlipidemia/Atherosclerotic Vascular Disease	ε2, ε4, (ε3 is reference)
COMT	Val158Met AG	Intermediate COMT Activity	Val158Met
CYP2C19	*1/*2	Intermediate Metabolizer	*2, *3, *4, *4B, *5, *6, *7, *8, *9, *10, *17
CYP2C9	*1/*3	Intermediate Metabolizer	*2, *3, *4, *5, *6, *8, *11, *13, *27
CYP2D6	*1/*4	Normal Metabolizer	*2, *3, *4, *4M, *6, *7, *8, *9, *10, *12, *14A, *14B, *15, *17, *29, *41, *44, *5 (gene deletion), XN (gene duplication)
CYP3A4	*1/*1	Normal Metabolizer	*1B, *2, *3, *6, *12, *16, *17, *22
CYP3A5	*3/*3	Poor Metabolizer	*2, *3, *3B, *3C, *3K, *3L, *5, *6, *7, *8, *9
Factor II Factor V Leiden	20210G>A GG 1691G>A GG	No Increased Risk of Thrombosis	20210G>A, 1691G>A
MTHFR	1298A>C AA 677C>T CT	No Increased Risk of Hyperhomocysteinemia	1298A>C, 677C>T
SLCO1B1	521T>C TT	Normal Transporter Function	521T>C
VKORC1	-1639G>A G/G	Low Warfarin Sensitivity	-1639G>A

Methodology
Deoxyribonucleic acid (DNA) was isolated from buccal swabs and the alleles were characterized using Taqman® SNP Genotyping Assays. If applicable, copy number variation in CYP2D6 was assessed using a TaqMan® Copy Number Assay. The specific alleles detected by the assays are indicated in the accompanying table and include all common and most rare variants with known clinically significant effects on drug metabolism and are reported at analytical sensitivity and specificity exceeding 99%. Technical specifications are available upon request. Drug-Gene associations performed by Translational Software.

Limitations
The interpretation of these results is meant to assist the ordering clinician with managing a patient's drug regimen and is not intended to be used as a treatment recommendation. Only qualified healthcare professionals should provide advice to patients regarding the use of prescribed or OTC medications. Patient treatment and diagnosis is the sole responsibility of the ordering clinician. It is strongly recommended that these results be communicated to the patient in a setting that includes appropriate counseling. This test is not comprehensive and cannot detect novel genetic variants that may exist in the tested genes or elsewhere in the genome and which could confer functional characteristics that influence the actual phenotype of the tested individual. Absence of a detectable mutation does not exclude the possibility that the patient has a different drug metabolism phenotype due to harboring untested phenotypically important polymorphisms, drug-drug interactions, co-morbidities, lifestyle habits or other non-genetic factors. This report does not address drug allergies or drug-drug interactions.

Laboratory Accreditation
This test was developed and its performance characteristics determined by Sorenson Genomics – Identigene. It has not been cleared or approved by the US Food and Drug Administration (FDA). FDA does not require this test to go through premarket FDA review. This test is for clinical purposes and should be used in conjunction with a physician's diagnosis and prescribed treatment plan. This test should not be regarded as investigational or for research. This laboratory is accredited by the College of American Pathologists (CAP) and is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high-complexity clinical laboratory testing. Testing was performed by Sorenson Genomics – Identigene, 2495 S West Temple, Salt Lake City, UT 84115.

Laboratory Certification: CLIA # 46D2011013; CAP #7526925

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Risk Management

Hyperlipidemia/Atherosclerotic Cardiovascular Disease

Increased risk of hyperlipidemia/atherosclerotic vascular disease

The patient is positive for the APOE 388 T>C (Arg112Cys) mutation and negative for the 526 C>T (Cys158Arg) mutation. The patient's genotype is ε3/ε4 (frequency: 15-28%). The APOE E3 is the normal APOE. The APOE E4 confers a limitation of HDL binding to its receptor, and is associated with increased plasma cholesterol, LDL, and triglycerides.

The ε4 allele is associated with an increased risk of hyperlipidemia/atherosclerotic vascular disease, and individuals that are heterozygous for this allele may have higher total cholesterol levels and elevated LDL cholesterol levels.

Consider dietary adjustment (very low fat diet) and statins (or HMG-CoA reductase inhibitors).

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

No Increased Risk of Hyperhomocysteinemia

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

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

The patient's MTHFR activity is slightly reduced.

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Potentially Impacted Medications				
Category	**Drug Class**	**Standard Precautions**	**Use With Caution**	**Consider Alternatives**
		Medication can be prescribed according to standard regimens	Guidelines exist for adjusting dosage or increased vigilance	Medication has potentially reduced efficacy or increased toxicity
Anticancer Agents	Antifolates		Methotrexate (Trexall)	
Cardiovascular	Angiotensin II Receptor Antagonists	Irbesartan (Avapro)		
	Antianginal Agents	Ranolazine (Ranexa)		
	Antiarrhythmics	Flecainide (Tambocor) Mexiletine (Mexitil) Propafenone (Rythmol)		
	Anticoagulants	Apixaban (Eliquis) Dabigatran Etexilate (Pradaxa) Edoxaban (Savaysa) Fondaparinux (Arixtra) Rivaroxaban (Xarelto)	Warfarin (Coumadin)	
	Antiplatelets	Prasugrel (Effient) Ticagrelor (Brilinta) Vorapaxar (Zontivity)		Clopidogrel (Plavix)
	Beta Blockers	Carvedilol (Coreg) Labetalol (Normodyne, Trandate) Metoprolol (Lopressor) Nebivolol (Bystolic) Propranolol (Inderal) Timolol (Timoptic)		
	Statins	Atorvastatin (Lipitor) Lovastatin (Mevacor) Pitavastatin (Livalo) Pravastatin (Pravachol) Rosuvastatin (Crestor) Simvastatin (Zocor)	Fluvastatin (Lescol)	
Diabetes	Sulfonylureas	Glimepiride (Amaryl) Glipizide (Glucotrol) Glyburide (Micronase) Tolbutamide (Orinase)		
Gastrointestinal	Antiemetics	Dolasetron (Anzemet) Metoclopramide (Reglan) Ondansetron (Zofran) Palonosetron (Aloxi)		
	Proton Pump Inhibitors	Dexlansoprazole (Dexilant, Kapidex) Esomeprazole (Nexium) Lansoprazole (Prevacid) Omeprazole (Prilosec) Pantoprazole (Protonix) Rabeprazole (Aciphex)		
Infections	Antifungals		Voriconazole (Vfend)	

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Category	Drug Class	Standard Precautions	Use With Caution	Consider Alternatives
		Medication can be prescribed according to standard regimens	Guidelines exist for adjusting dosage or increased vigilance	Medication has potentially reduced efficacy or increased toxicity
Pain	Fibromyalgia Agents	Milnacipran (Savella)		
	Muscle Relaxants	Carisoprodol (Soma) Cyclobenzaprine (Flexeril, Amrix) Metaxalone (Skelaxin) Methocarbamol (Robaxin)		
	NSAIDs	Ibuprofen (Advil, Motrin) Ketoprofen (Orudis) Ketorolac (Toradol) Nabumetone (Relafen) Naproxen (Aleve) Sulindac (Clinoril)	Celecoxib (Celebrex) Diclofenac (Voltaren) Flurbiprofen (Ansaid) Indomethacin (Indocin) Meloxicam (Mobic) Piroxicam (Feldene)	
	Opioids	Alfentanil (Alfenta) Buprenorphine (Butrans, Buprenex) Codeine (Codeine; Fioricet with Codeine) Dihydrocodeine (Synalgos-DC) Fentanyl (Actiq) Hydrocodone (Vicodin) Hydromorphone (Dilaudid, Exalgo) Levorphanol (Levo Dromoran) Meperidine (Demerol) Morphine (MS Contin) Oxycodone (Percocet, Oxycontin) Oxymorphone (Opana, Numorphan) Sufentanil (Sufenta) Tapentadol (Nucynta) Tramadol (Ultram)		
	Anti-ADHD Agents	Amphetamine (Adderall) Atomoxetine (Strattera) Clonidine (Kapvay) Dextroamphetamine (Dexedrine) Guanfacine (Intuniv) Lisdexamfetamine (Vyvanse)	Dexmethylphenidate (Focalin) Methylphenidate (Ritalin)	

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Category	Drug Class	Standard Precautions	Use With Caution	Consider Alternatives
		Medication can be prescribed according to standard regimens	Guidelines exist for adjusting dosage or increased vigilance	Medication has potentially reduced efficacy or increased toxicity
Psychotropic	Anticonvulsants	Carbamazepine (Tegretol, Carbatrol) Eslicarbazepine (Aptiom) Ethosuximide (Zarontin) Ezogabine (Potiga) Felbamate (Felbatol) Gabapentin (Neurontin) Lacosamide (Vimpat) Lamotrigine (Lamictal) Levetiracetam (Keppra) Oxcarbazepine (Trileptal) Perampanel (Fycompa) Pregabalin (Lyrica) Rufinamide (Banzel) Tiagabine (Gabitril) Topiramate (Topamax) Valproic Acid (Depakote, Depakene) Vigabatrin (Sabril)	Fosphenytoin (Cerebyx) Phenobarbital (Luminal) Phenytoin (Dilantin) Primidone (Mysoline) Zonisamide (Zonegran)	
	Antidementia Agents	Donepezil (Aricept) Galantamine (Razadyne) Memantine (Namenda)		
	Antidepressants	Amoxapine (Amoxapine) Citalopram (Celexa) Desipramine (Norpramin) Desvenlafaxine (Pristiq) Duloxetine (Cymbalta) Escitalopram (Lexapro) Fluoxetine (Prozac, Sarafem) Fluvoxamine (Luvox) Levomilnacipran (Fetzima) Maprotiline (Ludiomil) Mirtazapine (Remeron) Nefazodone (Serzone) Nortriptyline (Pamelor) Paroxetine (Paxil, Brisdelle) Protriptyline (Vivactil) Sertraline (Zoloft) Venlafaxine (Effexor) Vilazodone (Viibryd) Vortioxetine (Brintellix)	Amitriptyline (Elavil) Clomipramine (Anafranil) Doxepin (Silenor) Imipramine (Tofranil) Trimipramine (Surmontil)	

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Category	Drug Class	Standard Precautions	Use With Caution	Consider Alternatives
		Medication can be prescribed according to standard regimens	Guidelines exist for adjusting dosage or increased vigilance	Medication has potentially reduced efficacy or increased toxicity
	Antipsychotics	Aripiprazole (Abilify) Asenapine (Saphris) Chlorpromazine (Thorazine) Clozapine (Clozaril) Fluphenazine (Prolixin) Haloperidol (Haldol) Iloperidone (Fanapt) Lurasidone (Latuda) Olanzapine (Zyprexa) Paliperidone (Invega) Perphenazine (Trilafon) Pimozide (Orap) Quetiapine (Seroquel) Risperidone (Risperdal) Thioridazine (Mellaril) Thiothixene (Navane) Trazodone (Oleptro) Trifluoperazine (Stelazine) Ziprasidone (Geodon)	Tetrabenazine (Xenazine)	
	Benzodiazepines	Alprazolam (Xanax) Clonazepam (Klonopin) Diazepam (Valium)	Clobazam (Onfi)	
Rheumatology	Immunomodulators	Apremilast (Otezla) Tofacitinib (Xeljanz)	Leflunomide (Arava)	
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)

Moderate Sensitivity to Amitriptyline (CYP2C19 *1/*2 Intermediate Metabolizer) Evidence Level: **Actionable**

Amitriptyline should be used with caution in patients with reduced CYP2C19 activity. Consider a lower starting dose, and increase dosing over several days until an optimal response is achieved.

Celecoxib (Celebrex)

Possible Sensitivity to Celecoxib (CYP2C9 *1/*3 Intermediate Metabolizer) Evidence Level: **Informative**

Celecoxib can be prescribed at standard label-recommended dosage and administration. Evaluate response the first week and be alert to gastrointestinal adverse events.

Clobazam (Onfi)

Possible Sensitivity to Clobazam (CYP2C19 *1/*2 Intermediate Metabolizer) Evidence Level: **Actionable**

In CYP2C19 intermediate metabolizers, plasma levels of the active metabolite N-desmethylclobazam were 2-fold higher than those found in CYP2C19 normal metabolizers. The dose adjustment for intermediate metabolizers is not well established, and therefore the recommendation for poor metabolizers is proposed. The starting dose should be 5 mg/day, and dose titration should proceed slowly according to weight. Patients should be titrated initially to 10 mg /day (≤30 kg body weight) or 20 mg/day (>30 kg body weight). If necessary and based upon clinical response, an additional titration to the maximum doses 20 mg/day (≤30 kg body weight) or 40 mg/day (>30 kg body weight) may be started on day 21.

Clomipramine (Anafranil)

Moderate Sensitivity to Clomipramine (CYP2C19 *1/*2 Intermediate Metabolizer) Evidence Level: **Actionable**

Clomipramine should be used with caution in patients with reduced CYP2C19 activity. Consider a lower starting dose, and increase dosing over several days until an optimal response is achieved.

Clopidogrel (Plavix)

Reduced Response to Clopidogrel (CYP2C19 *1/*2 Intermediate Metabolizer) Evidence Level: **Actionable**

Consider alternative therapy. Examples of alternative drugs: prasugrel (contraindicated in TIA/Stroke patients), ticagrelor, aspirin, aspirin plus dipyridamole.

Dexmethylphenidate (Focalin)

Decreased Response to Dexmethylphenidate (COMT Val158Met AG Intermediate COMT Activity) Evidence Level: **Informative**

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

Diclofenac (Voltaren)

Possible Sensitivity to Diclofenac (CYP2C9 *1/*3 Intermediate Metabolizer) Evidence Level: **Informative**

Diclofenac is extensively metabolized by hydroxylation and direct glucuronidation. About 50% of diclofenac is eliminated as a 4-hydroxymetabolite, a reaction mediated by CYP2C9. Other CYP enzymes including CYP2C8, CYP2C19 and CYP3A4 are also involved in the formation of a 5-hydroxymetabolite. A substantial portion of the drug is also directly glucuronidated by UGT2B7 and UGT2B4. Individuals with decreased CYP2C9 activity (i.e intermediate metabolizers) should be closely monitored for increased gastrointestinal adverse events when prescribed diclofenac and lower doses may be more appropriate for these patients.

Doxepin (Silenor)

Moderate Sensitivity to Doxepin (CYP2C19 *1/*2 Intermediate Metabolizer) Evidence Level: **Actionable**

Doxepin should be used with caution in patients with reduced CYP2C19 activity. Consider a lower starting dose, and increase dosing over several days until an optimal response is achieved.

Flurbiprofen (Ansaid)

Possible Sensitivity to Flurbiprofen (CYP2C9 *1/*3 Intermediate Metabolizer) Evidence Level: **Informative**

The patient may have high plasma levels of the drug. Flurbiprofen can be prescribed at standard label-recommended dosage and administration with closer monitoring for gastrointestinal side effects.

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Fluvastatin (Lescol)

Possible Sensitivity to Fluvastatin (CYP2C9 *1/*3 Intermediate Metabolizer) Evidence Level: **Actionable**

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.

Fosphenytoin (Cerebyx)

Moderate Sensitivity to Fosphenytoin (CYP2C9 *1/*3 Intermediate Metabolizer) Evidence Level: **Actionable**

The genotype results indicate that the patient is a CYP2C9 substrate intermediate metabolizer. Plasma concentrations of phenytoin are likely to increase, resulting in an increased risk of mild to moderate neurological toxicity. Consider a standard loading dose, and reduce the maintenance dose by 25%. Evaluate response and serum concentrations after 7-10 days. Be alert to neurological concentration-related adverse events.

Imipramine (Tofranil)

Moderate Sensitivity to Imipramine (CYP2C19 *1/*2 Intermediate Metabolizer) Evidence Level: **Actionable**

Imipramine should be used with caution in patients with reduced CYP2C19 activity. Consider a lower starting dose, and increase dosing over several days until an optimal response is achieved.

Indomethacin (Indocin)

Possible Sensitivity to Indomethacin (CYP2C9 *1/*3 Intermediate Metabolizer) Evidence Level: **Informative**

Indomethacin is metabolized mainly by O-demethylation to its inactive metabolite O-desmethylindomethacin, a reaction catalyzed by CYP2C9. At standard doses, indomethacin plasma concentrations may be higher in individuals with decreased CYP2C9 function. Although indomethacin can be prescribed at standard label recommended-dosage and administration, a closer monitoring for signs of gastrointestinal toxicity during long-term administration is recommended.

Leflunomide (Arava)

Increased Sensitivity to Leflunomide (CYP2C19 *1/*2 Intermediate Metabolizer) Evidence Level: **Informative**

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

Meloxicam (Mobic)

Possible Sensitivity to Meloxicam (CYP2C9 *1/*3 Intermediate Metabolizer) Evidence Level: **Informative**

Meloxicam plasma concentrations may be higher in individual with decreased CYP2C9 function. A reduction in meloxicam dosage may be needed with a closer monitoring for signs of gastrointestinal toxicity during long-term administration.

Methotrexate (Trexall)

Increased risk for methotrexate toxicity (MTHFR 677C>T CT Reduced MTHFR Activity) Evidence Level: **Informative**

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

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Methylphenidate (Ritalin)

Decreased Response to Methylphenidate (COMT Val158Met AG Intermediate COMT Activity) Evidence Level: **Informative**

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

Phenobarbital (Luminal)

Possible Sensitivity to Phenobarbital (CYP2C19 *1/*2 Intermediate Metabolizer) Evidence Level: **Informative**

CYP2C19 is partly involved in the metabolism of phenobarbital, and although CYP2C19 intermediate metabolizers have a lower clearance of phenobarbital than normal metabolizers, no significant changes in clinical outcome has been reported with this antiepileptic drug. Therefore, phenobarbital can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

Phenytoin (Dilantin)

Moderate Sensitivity to Phenytoin (CYP2C9 *1/*3 Intermediate Metabolizer) Evidence Level: **Actionable**

The genotype results indicate that the patient is a CYP2C9 substrate intermediate metabolizer. Plasma concentrations of phenytoin are likely to increase, resulting in an increased risk of mild to moderate neurological toxicity. Consider a standard loading dose, and reduce the maintenance dose by 25%. Evaluate response and serum concentrations after 7-10 days. Be alert to neurological concentration-related adverse events.

Piroxicam (Feldene)

Possible Sensitivity to Piroxicam (CYP2C9 *1/*3 Intermediate Metabolizer) Evidence Level: **Informative**

Piroxicam plasma concentrations may be higher in individual with decreased CYP2C9 function. Although piroxicam can be prescribed at standard label-recommended dosage and administration, a closer monitoring for signs of gastrointestinal toxicity during long-term administration is recommended.

Primidone (Mysoline)

Possible Sensitivity to Primidone (CYP2C19 *1/*2 Intermediate Metabolizer) Evidence Level: **Informative**

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

Tetrabenazine (Xenazine)

Normal Sensitivity to Tetrabenazine (CYP2D6 *1/*4 Normal Metabolizer) Evidence Level: **Actionable**

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.

Trimipramine (Surmontil)

Moderate Sensitivity to Trimipramine (CYP2C19 *1/*2 Intermediate Metabolizer) Evidence Level: **Actionable**

Trimipramine should be used with caution in patients with reduced CYP2C19 activity. Consider a lower starting dose, and increase dosing over several days until an optimal response is achieved.

Voriconazole (Vfend)

Moderate Sensitivity to Voriconazole (CYP2C19 *1/*2 Intermediate Metabolizer) Evidence Level: **Actionable**

Voriconazole should be used with caution in patients with reduced CYP2C19 activity. Monitor closely voriconazole plasma concentrations, and adjust the dose accordingly.

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Warfarin (Coumadin)

Mild sensitivity to warfarin (CYP2C9 *1/*3 VKORC1 -1639G>A G/G) Evidence Level: **Actionable**

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.

Zonisamide (Zonegran)

Possible Sensitivity to Zonisamide (CYP2C19 *1/*2 Intermediate Metabolizer) Evidence Level: **Informative**

CYP2C19 is partly involved in the metabolism of zonisamide, and although preliminary studies show that CYP2C19 intermediate metabolizers have a slightly lower (15%) zonisamide clearance than normal metabolizers, no significant change in the clinical outcome has been reported with this antiepileptic drug. Therefore, zonisamide can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

Report Legend

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.

Please access the gene monographs via the report portal at https://provider.scriptassured.com/portal/login to learn more about the genes analyzed and their protein products. There you can find information on Clinical Utility, Assay Interpretation, Genotype-Phenotype Relationships, Clinical Implications, Inhibitors, Inducers, and lists of References relevant at the time of report generation.

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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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(800) 591-9044

Patient Name	DOB	Requisition ID
G******** T************	**1/1/1980**	**R0001104**

Pharmacogenetic Test Summary

CYP2C19	*1/*2	Intermediate Metabolizer
CYP2C9	*1/*3	Intermediate Metabolizer
CYP2D6	*1/*4	Normal Metabolizer
CYP3A4	*1/*1	Normal Metabolizer
CYP3A5	*3/*3	Poor Metabolizer

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

For a complete report contact Sorenson Genomics

Fold