Translational Software Demo
12410 SE 32nd Street, Suite 250, Bellevue WA 98005
Phone: 206-777-4063
Web: www.translationalsoftware.com
Laboratory Director: Houda Hachad, Pharm.D

Comprehensive Pharmacogenetic Report Created for: Connie Comprehensive

Patient:	Connie Comprehensive	DOB:	1/1/1970
Accession #:	234444	Gender:	Female
Collection Date:		Received Date:	
Ordered By:		Report Generated:	10/1/2015

Current Patient Medications

Current Medication List: Warfarin, Codeine, Ibuprofen, Metoprolol, Aspirin, Simvastatin

Medications Affected by Patient Genetic Results

⚠	**Ibuprofen (Advil, Motrin)**	Possible Sensitivity to Ibuprofen (CYP2C9 *3/*3 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.
⚠	**Warfarin (Coumadin)**	High Sensitivity to Warfarin (CYP2C9 *3/*3 VKORC1 -1639G>A G/G)	*Initiation Therapy: the expected therapeutic **dose is substantially lower than the usual one**. Consider using the warfarin dose range provided in the FDA-approved label: **0.5-2 mg/day.** OR consider using a personalized dose calculated by a pharmacogenetic algorithm. The estimated time to reach steady state is more than 2-4 weeks. Frequent INR monitoring is recommended.
✓	**Codeine (Codeine; Fioricet with Codeine)**	Normal Response to Codeine (CYP2D6 *1/*1 Normal Metabolizer)	*Codeine can be prescribed at standard label-recommended dosage and administration.
✓	**Metoprolol (Lopressor)**	Normal Sensitivity to Metoprolol (CYP2D6 *1/*1 Normal Metabolizer)	*Metoprolol can be prescribed at standard label-recommended dosage and administration. Selection of proper dosage requires individual titration.
✓	**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.

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

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	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
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) Codeine (Codeine; Fioricet with Codeine) Dihydrocodeine (Synalgos-DC) Fentanyl (Actiq) Hydrocodone (Vicodin) Hydromorphone (Dilaudid, Exalgo) Levorphanol (Levo Dromoran) Meperidine (Demerol) Methadone (Dolophine) Oxycodone (Percocet, Oxycontin) Oxymorphone (Opana, Numorphan) Sufentanil (Sufenta) Tapentadol (Nucynta) Tramadol (Ultram)	Morphine (MS Contin)	
	Antiaddictives		Naltrexone (Vivitrol)	
	Anti-ADHD Agents	Amphetamine (Adderall) Atomoxetine (Strattera) Clonidine (Kapvay) Dexmethylphenidate (Focalin) Dextroamphetamine (Dexedrine) Guanfacine (Intuniv) Lisdexamfetamine (Vyvanse) Methylphenidate (Ritalin)		

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Category	Drug Class	Standard Precautions	Use With Caution	Consider Alternatives
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
	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

Clopidogrel (Plavix)	Reduced Response to Clopidogrel (CYP2C19 *1/*6 Intermediate Metabolizer)	*Consider alternative therapy. Examples of alternative drugs: prasugrel (contraindicated in TIA/Stroke patients), ticagrelor, aspirin, aspirin plus dipyridamole.
Amitriptyline (Elavil)	Moderate Sensitivity to Amitriptyline (CYP2C19 *1/*6 Intermediate Metabolizer)	*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)	High Sensitivity to Celecoxib (CYP2C9 *3/*3 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.
Clobazam (Onfi)	Possible Sensitivity to Clobazam (CYP2C19 *1/*6 Intermediate Metabolizer)	*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/*6 Intermediate Metabolizer)	*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.
Diclofenac (Voltaren)	Possible Sensitivity to Diclofenac (CYP2C9 *3/*3 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.
Doxepin (Silenor)	Moderate Sensitivity to Doxepin (CYP2C19 *1/*6 Intermediate Metabolizer)	*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)	Increased Sensitivity to Flurbiprofen (CYP2C9 *3/*3 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 *3/*3 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.
Fosphenytoin (Cerebyx)	High Sensitivity to Fosphenytoin (CYP2C9 *3/*3 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 *3/*3 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 *3/*3 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 *3/*3 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.
Ibuprofen (Advil, Motrin)	Possible Sensitivity to Ibuprofen (CYP2C9 *3/*3 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.
Imipramine (Tofranil)	Moderate Sensitivity to Imipramine (CYP2C19 *1/*6 Intermediate Metabolizer)	*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 *3/*3 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.

Leflunomide (Arava)	Increased Sensitivity to Leflunomide (CYP2C19 *1/*6 Intermediate Metabolizer)	**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)	Increased sensitivity to Meloxicam (CYP2C9 *3/*3 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.**
Morphine (MS Contin)	Altered Response to Morphine (COMT Val158Met GG High/Normal COMT Activity)	**The patient does not carry the COMT Val158Met mutation. The patient may require higher doses of morphine for adequate pain control. The dosing regimen needs to be individualized for each patient, taking into account the patient's prior analgesic treatment experience.
Naltrexone (Vivitrol)	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.
Phenobarbital (Luminal)	Possible Sensitivity to Phenobarbital (CYP2C19 *1/*6 Intermediate Metabolizer)	**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)	High Sensitivity to Phenytoin (CYP2C9 *3/*3 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.**
Piroxicam (Feldene)	Increased Sensitivity to Piroxicam (CYP2C9 *3/*3 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.
Primidone (Mysoline)	Possible Sensitivity to Primidone (CYP2C19 *1/*6 Intermediate Metabolizer)	**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.

Tacrolimus (Prograf)	Insufficient Response to Tacrolimus (CYP3A5 *1/*1 Normal Metabolizer)	*The genotype result predicts that the patient expresses the CYP3A5 protein. Therefore, the patient may metabolize tacrolimus more rapidly, resulting in low tacrolimus trough levels. Studies have shown patients with this genotype may be at increased risk for acute transplant rejection while taking a standard dose of tacrolimus. Therefore, increasing starting dose 1.5 to 2 times recommended starting dose with close monitoring is strongly recommended to achieve therapeutic effect. Total starting dose should not exceed 0.3mg/kg/day.
Tetrabenazine (Xenazine)	Normal Sensitivity to Tetrabenazine (CYP2D6 *1/*1 Normal Metabolizer)	*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.
Tolbutamide (Orinase)	Possible Sensitivity to Tolbutamide (CYP2C9 *3/*3 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.
Trimipramine (Surmontil)	Moderate Sensitivity to Trimipramine (CYP2C19 *1/*6 Intermediate Metabolizer)	*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/*6 Intermediate Metabolizer)	**Voriconazole should be used with caution in patients with reduced CYP2C19 activity. Monitor closely voriconazole plasma concentrations, and adjust the dose accordingly.
Warfarin (Coumadin)	High Sensitivity to Warfarin (CYP2C9 *3/*3 VKORC1 -1639G>A G/G)	*Initiation Therapy: the expected therapeutic **dose is substantially lower than the usual one**. Consider using the warfarin dose range provided in the FDA-approved label: **0.5-2 mg/day.** OR consider using a personalized dose calculated by a pharmacogenetic algorithm. The estimated time to reach steady state is more than 2-4 weeks. Frequent INR monitoring is recommended.
Zonisamide (Zonegran)	Possible Sensitivity to Zonisamide (CYP2C19 *1/*6 Intermediate Metabolizer)	**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.

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Pharmacogenetic Test Results

Gene	Genotype	Phenotype	Clinical Consequences
Apolipoprotein E	ε3/ε3	No Increased Risk of Hyperlipidemia/Atherosclerotic Vascular Disease	No Increased Risk of Cardiovascular Disease
COMT	Val158Met GG	High/Normal COMT Activity	Consistent with a normal 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/*6	Intermediate Metabolizer	Consistent with a moderate deficiency in CYP2C19 activity. Potential risk for side effects or loss of efficacy with drug substrates.
CYP2C9	*3/*3	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	Normal Metabolizer	Consistent with a typical CYP2D6 activity. This test did not identify risks 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	*1/*1	Normal Metabolizer	Consistent with a normal CYP3A5 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
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 CC	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 G/G	Low Warfarin Sensitivity	VKORC1 is the site of action of warfarin. The patient may require an increase in warfarin dose.

AllelesTested: 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; **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

Translational Software Demo
12410 SE 32nd Street, Suite 250, Bellevue WA 98005
Phone: 206-777-4063
Web: www.translationalsoftware.com
Laboratory Director: Houda Hachad, Pharm.D

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

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

Disclaimer: The information presented on this report is provided as general educational health information. The Content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Only a physician, pharmacist or other healthcare professional should advise a patient on the use of the medications prescribed. [Lab Name] developed this test and its performance characteristics. This test has not been cleared or approved by the U.S. Food and Drug Administration. The pharmacogenetic report is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. It remains the responsibility of the health-care provider to determine the best course of treatment for a patient. Adherence to dose guidelines does not necessarily assure a successful medical outcome.

Laboratory Certification: CLIA #

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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/*6	Intermediate Metabolizer
CYP2C9	*3/*3	Poor Metabolizer
CYP2D6	*1/*1	Normal Metabolizer
CYP3A4	*1/*1	Normal Metabolizer
CYP3A5	*1/*1	Normal Metabolizer

VKORC1	-1639G>A G/G	Low Warfarin Sensitivity
MTHFR	1298A>C AA 677C>T CC	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 Translational Software Demo

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