PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Sample 5 S550	**SPECIMEN TYPE:**	Buccal	Doctor, Doctor
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Report Overview

A medication has potentially reduced efficacy, increased toxicity or the patient has an increased risk for the indicated condition.	**ACTIONABLE** Recommendations based upon publications by international pharmacogenetic expert groups, consortia or regulatory bodies (CPIC, DPWG, FDA. EMA). Recommendations are suitable for implementation in a clinical setting. Guidelines may change as knowledge arises.
Guidelines exist for adjusting dosage, increased vigilance or the patient has a moderate risk for the indicated condition.	
The medication can be prescribed according to standard regimens or the patient's risk for the indicated condition is not increased.	**INFORMATIVE** There are insufficient or contradictory findings documenting the impact of a given genetic polymorphism or drug interaction. Recommendations are informative and implementation in a clinical setting is optional.

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Risk Management

Hyperhomocysteinemia - Depression

No Increased Risk of Hyperhomocysteinemia

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

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

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

Thrombophilia

No Increased Risk of Thrombosis

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

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

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

Hyperhomocysteinemia - Thrombosis

No Increased Risk of Hyperhomocysteinemia

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

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

The patient's MTHFR activity is slightly reduced.

Hyperlipidemia/Atherosclerotic Cardiovascular Disease

No increased risk of cardiovascular disease

The patient is a non carrier of the risk alleles in LPA gene for both the variants (rs3798220 and rs10455872).

The patient's genotype is associated with normal lipoprotein levels. The patient has no increased risk of atherosclerosis and cardiovascular disease as compared to the general population unless other risk factors are present.

No action is needed for this patient unless other genetic and non genetic risk factors (e.g. high blood pressure, smoking, diabetes, obesity, high blood cholesterol and excessive alcohol use) are present.

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Current Patient Medications

Plavix, Starlix, Tamoxifen, Lipitor, Codeine, Ritalin, Amphetamine, Zonegran, Paxil, Flomax

Plavix
Clopidogrel

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

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

Ritalin
Methylphenidate

Decreased Response to Methylphenidate (COMT: Intermediate COMT Activity) — 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.

Amphetamine
Adderall

Good Response to Amphetamine salts (COMT: Intermediate COMT Activity) — INFORMATIVE

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

Codeine
Codeine; Fioricet with Codeine

Normal Response to Codeine (CYP2D6: Normal Metabolizer) — ACTIONABLE

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

Flomax
Tamsulosin

Normal Response to Tamsulosin (CYP2D6: Normal Metabolizer) — ACTIONABLE

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

Lipitor
Atorvastatin

Normal Myopathy Risk (SLCO1B1: Normal Function) — INFORMATIVE

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

Lipitor
Atorvastatin

Normal Response to Atorvastatin (CYP3A4: Normal Metabolizer) — INFORMATIVE

The genotype result indicates that the patient does not carry the CYP3A4*22 allele (this allele is associated with a decreased CYP3A4 enzyme activity). The patient is expected to achieve an optimal lipid control goal with standard atorvastatin dose requirements.

Paxil
Paroxetine

Normal Sensitivity to Paroxetine (CYP2D6: Normal Metabolizer) — ACTIONABLE

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

Starlix
Nateglinide

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

The patient carries two copies of SLCO1B1 rs4149056 T allele, which is associated with normal transporter function. Nateglinide can be prescribed at label-recommended standard dosage and administration.

Starlix
Nateglinide

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

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

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✓ **Zonegran**
Zonisamide

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

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

Medications outside the scope of the report: Tamoxifen

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Potentially Impacted Medications

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Anticancer Agents	**Antifolates**	Methotrexate (Trexall)		
Cardiovascular	**Angiotensin II Receptor Antagonists**	Azilsartan (Edarbi, Edarbyclor) Candesartan (Atacand) Eprosartan (Teveten) Irbesartan (Avapro) Losartan (Cozaar, Hyzaar) Olmesartan (Benicar) Telmisartan (Micardis) Valsartan (Diovan, Entresto)		
	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	Atenolol (Tenormin) Bisoprolol (Zebeta) Carvedilol (Coreg) Labetalol (Normodyne, Trandate) Metoprolol (Lopressor) Nebivolol (Bystolic) Propranolol (Inderal) Timolol (Timoptic)		
	Diuretics	Torsemide (Demadex)		
	Statins	Atorvastatin (Lipitor) Lovastatin (Mevacor, Altoprev, Advicor) Pitavastatin (Livalo) Pravastatin (Pravachol) Rosuvastatin (Crestor) Simvastatin (Zocor)	Fluvastatin (Lescol)	
Diabetes	**Meglitinides**	Nateglinide (Starlix) Repaglinide (Prandin, Prandimet)		
	Sulfonylureas	Chlorpropamide (Diabenese) Glimepiride (Amaryl) Glipizide (Glucotrol) Glyburide (Micronase) Tolbutamide (Orinase)		

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Gastrointestinal	Antiemetics	Dolasetron (Anzemet) Metoclopramide (Reglan) Ondansetron (Zofran, Zuplenz) Palonosetron (Aloxi)		
	Proton Pump Inhibitors	Rabeprazole (Aciphex)	Dexlansoprazole (Dexilant, Kapidex) Esomeprazole (Nexium) Lansoprazole (Prevacid) Omeprazole (Prilosec) Pantoprazole (Protonix)	
Infections	Antifungals		Voriconazole (Vfend)	
	Antimalarials	Proguanil (Malarone)		
Pain	Fibromyalgia Agents	Milnacipran (Savella)		
	Muscle Relaxants	Cyclobenzaprine (Flexeril, Amrix) Metaxalone (Skelaxin) Methocarbamol (Robaxin)	Carisoprodol (Soma) Tizanidine (Zanaflex)	
	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) Hydromorphone (Dilaudid, Exalgo) Levorphanol (Levo Dromoran) Meperidine (Demerol) Morphine (MS Contin) Oxycodone (Percocet, Oxycontin) Oxymorphone (Opana, Numorphan) Sufentanil (Sufenta) Tapentadol (Nucynta) Tramadol (Ultram)	Fentanyl (Actiq) Hydrocodone (Vicodin)	
	Antiaddictives	Naltrexone (Vivitrol, Contrave)		
	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
Psychotropic	**Anticonvulsants**	Brivaracetam (Briviact) Carbamazepine (Tegretol, Carbatrol, Epitol) Eslicarbazepine (Aptiom) Ethosuximide (Zarontin) Ezogabine (Potiga) Felbamate (Felbatol) Gabapentin (Neurontin) Lacosamide (Vimpat) Lamotrigine (Lamictal) Levetiracetam (Keppra) Oxcarbazepine (Trileptal, Oxtellar XR) Perampanel (Fycompa) Phenobarbital (Luminal) Pregabalin (Lyrica) Primidone (Mysoline) Rufinamide (Banzel) Tiagabine (Gabitril) Topiramate (Topamax) Valproic Acid (Depakote, Depakene) Vigabatrin (Sabril) Zonisamide (Zonegran)	Fosphenytoin (Cerebyx) Phenytoin (Dilantin)	
	Antidementia Agents	Donepezil (Aricept) Galantamine (Razadyne) Memantine (Namenda)		
	Antidepressants	Amoxapine (Amoxapine) Desipramine (Norpramin) Desvenlafaxine (Pristiq) Duloxetine (Cymbalta) Fluoxetine (Prozac, Sarafem) Fluvoxamine (Luvox) Levomilnacipran (Fetzima) Maprotiline (Ludiomil) Mirtazapine (Remeron) Nefazodone (Serzone) Nortriptyline (Pamelor) Paroxetine (Paxil, Brisdelle) Protriptyline (Vivactil) Trazodone (Oleptro) Venlafaxine (Effexor) Vilazodone (Viibryd) Vortioxetine (Trintellix)	Sertraline (Zoloft)	Amitriptyline (Elavil) Citalopram (Celexa) Clomipramine (Anafranil) Doxepin (Silenor) Escitalopram (Lexapro) Imipramine (Tofranil) Trimipramine (Surmontil)

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
	Antipsychotics	Aripiprazole (Abilify) Asenapine (Saphris) Brexpiprazole (Rexulti) Chlorpromazine (Thorazine) Fluphenazine (Prolixin) Haloperidol (Haldol) Iloperidone (Fanapt) Loxapine (Loxitane, Adasuve) Lurasidone (Latuda) Paliperidone (Invega) Perphenazine (Trilafon) Pimavanserin (Nuplazid) Pimozide (Orap) Quetiapine (Seroquel) Risperidone (Risperdal) Thioridazine (Mellaril) Thiothixene (Navane) Trifluoperazine (Stelazine) Ziprasidone (Geodon)	Clozapine (Clozaril) Olanzapine (Zyprexa) Tetrabenazine (Xenazine)	
	Benzodiazepines	Alprazolam (Xanax) Clobazam (Onfi) Clonazepam (Klonopin)	Diazepam (Valium)	
	Other Neurological Agents	Dextromethorphan / Quinidine (Nuedexta) Flibanserin (Addyi)		
Rheumatology	Anti-Gout Agents	Colchicine (Mitigare) Febuxostat (Uloric) Lesinurad (Zurampic)		
	Immunomodulators	Apremilast (Otezla) Leflunomide (Arava) Tofacitinib (Xeljanz)		
Transplantation	Immunosupressants	Tacrolimus (Prograf)		
Urologicals	5-Alpha Reductase Inhibitors for Benign Prostatic Hyperplasia	Dutasteride (Avodart) Finasteride (Proscar)		
	Alpha-Blockers for Benign Prostatic Hyperplasia	Alfuzosin (UroXatral) Doxazosin (Cardura) Silodosin (Rapaflo) Tamsulosin (Flomax) Terazosin (Hytrin)		
	Antispasmodics for Overactive Bladder	Darifenacin (Enablex) Fesoterodine (Toviaz) Mirabegron (Myrbetriq) Oxybutynin (Ditropan) Solifenacin (Vesicare) Tolterodine (Detrol) Trospium (Sanctura)		
	Phosphodiesterase Inhibitors for Erectile Dysfunction	Avanafil (Stendra) Sildenafil (Viagra) Tadalafil (Cialis) Vardenafil (Levitra)		

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Dosing Guidance

Amitriptyline
Elavil

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

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

Citalopram
Celexa

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

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

Clomipramine
Anafranil

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

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

Doxepin
Silenor

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

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

Escitalopram
Lexapro

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

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

Imipramine
Tofranil

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

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

Trimipramine
Surmontil

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

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

Carisoprodol
Soma

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

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

Celecoxib
Celebrex

Possible Sensitivity to Celecoxib (CYP2C9: Intermediate Metabolizer) — INFORMATIVE

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

Clopidogrel
Plavix

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

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

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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.

Dexlansoprazole
Dexilant, Kapidex

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

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

Dexmethylphenidate
Focalin

Decreased Response to Dexmethylphenidate (COMT: Intermediate COMT Activity) — 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.

Diazepam
Valium

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

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

Diclofenac
Voltaren

Possible Sensitivity to Diclofenac (CYP2C9: Intermediate Metabolizer) — 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.

Esomeprazole
Nexium

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

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

Fentanyl
Actiq

Altered Response to Fentanyl (OPRM1: Altered OPRM1 Function) — INFORMATIVE

The patient carries one copy of the OPRM1 118A>G mutation. Acute postoperative and cancer pain: the patient's genotype has been shown to be associated with reduced analgesia at standard fentanyl doses. Therefore, the patient may require higher doses of this drug. Because fentanyl has a narrow therapeutic window, it is advised to carefully titrate this drug to a tolerable dose that provides adequate analgesia with minimal side effects.

Flurbiprofen
Ansaid

Possible Sensitivity to Flurbiprofen (CYP2C9: Intermediate Metabolizer) — 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.

Fluvastatin
Lescol

Possible Sensitivity to Fluvastatin (CYP2C9: Intermediate Metabolizer) — 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.

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Fosphenytoin
Cerebyx

Moderate Sensitivity to Fosphenytoin (CYP2C9: Intermediate Metabolizer) — 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.

Hydrocodone
Vicodin

Altered Response to Hydrocodone (OPRM1: Altered OPRM1 Function) — INFORMATIVE

Acute postoperative and cancer pain: the patient's genotype has been shown to be associated with reduced analgesia and increased opioid side effects at standard or high hydrocodone doses. If the patient fails to respond to increased hydrocodone doses, an alternative opioid may be considered.

Indomethacin
Indocin

Possible Sensitivity to Indomethacin (CYP2C9: Intermediate Metabolizer) — 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.

Lansoprazole
Prevacid

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

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

Meloxicam
Mobic

Possible Sensitivity to Meloxicam (CYP2C9: Intermediate Metabolizer) — 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.

Methylphenidate
Ritalin

Decreased Response to Methylphenidate (COMT: Intermediate COMT Activity) — 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.

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.

Omeprazole
Prilosec

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

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

Pantoprazole
Protonix

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

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

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Phenytoin
Dilantin

Moderate Sensitivity to Phenytoin (CYP2C9: Intermediate Metabolizer) — **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: Intermediate Metabolizer) — **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.

Sertraline
Zoloft

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

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

Tetrabenazine
Xenazine

Normal Sensitivity to Tetrabenazine (CYP2D6: Normal Metabolizer) — **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.

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.

Voriconazole
Vfend

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

Voriconazole plasma concentrations may be low when standard dosage is used, increasing the risk of loss of response and effectiveness. Closely monitor voriconazole plasma concentrations, and adjust the dose accordingly.

Warfarin
Coumadin

Mild Sensitivity to Warfarin (CYP2C9 *1/*3 VKORC1 -1639G>A G/G) — **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.

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Sample 5 S550	**SPECIMEN TYPE:**	Buccal	**Doctor, Doctor**
ACC #:	S550	**COLLECTION DATE:**	9/7/2016	
DOB:	1/1/1900	**RECEIVED DATE:**	9/8/2016	
SEX:	M	**REPORT DATE:**	2/6/2017	

Caution: It is important to note that the combination of genetic metabolizer and non-genetic factors, such as, but not limited to: body size, age, inhibition caused by interference of drugs or food, liver function, and kidney function produce the overall response to a given drug dose.

Methods: This specimen was analyzed for gene mutations by real-time PCR (TaqMan SNP Genotyping, Thermo Fisher) developed by Phi Life Sciences, LLC. These assays were validated following the 1988 CLIA standards. Performance characteristics were validated by Phi Life Sciences Laboratory with analytical specificity and sensitivity of >99% for detection of the variants above.

Lab Disclaimer: The FDA has neither cleared nor approved these assays, nor is FDA pre-market review required. These tests are used for clinical purposes and should not be regarded as investigational or for research only. Diagnosis and treatment decisions are the sole responsibility of the practitioner and does not replace the need for clinical and therapeutic drug monitoring. Hence, the interpretation and commentary are provided to the practitioner for educational purposes only and should not be taken as diagnostic or treatment recommendations. For further assistance with interpretation of these results, please contact Phi Life Sciences' Clinical Support at 888-576-5445.

Testing Performed By: Phi Life Sciences, LLC, CLIA No. 42D2114196, 645 Meeting St, Suite 3, Charleston, SC 29403.

Laboratory Director: Catherine Li, MD

Translational Software Disclaimer: The information presented on this report is provided as general educational health information. The content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Only a physician, pharmacist or other healthcare professional should advise a patient on the use of the medications prescribed.

The pharmacogenetic assay involves use of reporting software and genotype-phenotype associations performed by Translational Software (www.translationalsoftware.com). The software has not been evaluated by the Food and Drug Administration. The software, and the report generated by the software, is not intended to diagnose, treat, cure, or prevent any disease. A qualified designee within the lab uses Translational Software to generate and subsequently review the report. The pharmacogenetic report is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. It remains the responsibility of the health-care provider to determine the best course of treatment for a patient. Adherence to dose guidelines does not necessarily assure a successful medical outcome.

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Patient Information Card

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

REPORT DETAILS

Name: Sample 5 S550
DOB: 1/1/1900
ACC #: S550

Pharmacogenetic Test Summary

COMT	Val158Met AG	Intermediate COMT Activity
CYP1A2	*1A/*1F	Normal Metabolizer - Higher Inducibility
CYP2C19	*1/*17	Rapid Metabolizer
CYP2C9	*1/*3	Intermediate Metabolizer
CYP2D6	*1/*3	Normal Metabolizer
CYP3A4	*1/*1	Normal Metabolizer
CYP3A5	*3/*3	Poor Metabolizer
Factor II	20210G>A GG	Normal Thrombosis Risk
Factor V Leiden	1691G>A GG	Normal Thrombosis Risk
LPA	rs10455872 A/A	Wild-type for rs10455872
LPA	rs3798220 T/T	Wild-type for rs3798220
MTHFR	677C>T CC	Normal MTHFR Activity
MTHFR	1298A>C AC	Reduced MTHFR Activity
OPRM1	A118G AG	Altered OPRM1 Function
SLC6A4	463T>G A/A	Homozygous for A Allele
SLCO1B1	521T>C TT	Normal Function
VKORC1	-1639G>A G/G	Low Warfarin Sensitivity