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PATIENT INFORMATION

NAME: Sample Report
DOB: 1/1/2018
SEX:
ACC #: DNA123456ZA

SPECIMEN DETAILS

SPECIMEN TYPE: Buccal Swab
ORDERED BY:
REPORT DATE: 7/10/2019

Medcheck Report

Current Patient Medications

Simvastatin, Methylphenidate, Amitriptyline, Codeine

Amitriptyline

Decreased Amitriptyline Exposure (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The patient is predicted to be a CYP2D6 ultra-rapid metabolizer which is likely to result in a significantly increased metabolism of amitriptyline to less active compounds and a subsequent decrease in amitriptyline exposure leading to therapy failure.

Psychiatric Conditions: Consider an alternative medication. If Amitriptyline is warranted, consider increasing the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Neuropathic Pain: Consider an alternative medication. If amitriptyline is warranted titrate dose according to the patient's clinical response and tolerability.

Codeine

Increased Response to Codeine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Codeine is converted into its active metabolite morphine by CYP2D6. Since this patient is a ultra-rapid metabolizer, greatly increased morphine levels are expected, and the patient is at high risk of toxicity when taking codeine. The ultra-rapid conversion of codeine to morphine in breast feeding mothers can result in high and unsafe levels of morphine in the breast milk potentially causing life threatening respiratory depression in the breastfed infant. Avoid prescribing codeine, and consider an alternative opioid or a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids not sensitive to CYP2D6 function include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

Simvastatin

Intermediate Myopathy Risk (SLCO1B1: Decreased Function) — ACTIONABLE

Simvastatin plasma concentrations are expected to be elevated. **Consider avoiding simvastatin**, and prescribe an alternative statin or another hypolipidemic drug, or consider prescribing simvastatin at a lower starting dose (20 mg/day). Routine creatine kinase (CK) monitoring is also advised. **The FDA recommends against the 80 mg daily dose.** Although the association between the SLCO1B1 521T>C variant and myopathy risk is not clearly established for other statins such as atorvastatin, pitavastatin, rosuvastatin, and pravastatin, caution is advised if high doses of these statins are used in this patient. Fluvastatin plasma levels are not affected by the SLCO1B1 521T>C variant.

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.

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

⚠ Antipsychotic-Induced Tardive Dyskinesia

Moderate Risk of Antipsychotic-Induced Tardive Dyskinesia

The patient carries one copy of the Taq1A variant (heterozygous for the A1 allele).

The genotype results predict that the patient may have reduced dopamine receptor DRD2 density and hypodopaminergic functioning. The patient has moderate risk for tardive dyskinesia when treated with antipsychotics.

Monitor the patient for any signs of tardive dyskinesia.

⚠ Antipsychotic-Induced Hyperprolactinemia

Moderate Risk of Antipsychotic-induced Hyperprolactinemia

The patient carries one copy of the Taq1A variant (heterozygous for the A1 allele).

The genotype results predict that the patient may have reduced dopamine receptor DRD2 density and hypodopaminergic functioning. The patient has moderate risk of hyperprolactinemia when treated with antipsychotics.

Monitor patient closely for signs of hyperprolactinemia. An evaluation of the risk-benefit profile of the antipsychotic medication may be required.

⚠ Antipsychotic-Induced Weight Gain

Moderate Risk of Antipsychotic-Induced Weight Gain

The patient carries one copy of the Taq1A variant (heterozygous for the A1 allele).

The genotype results predict that the patient may have reduced dopamine receptor DRD2 density and hypodopaminergic functioning. The patient has moderate risk for weight gain when treated with antipsychotics.

Monitor patient closely for signs of weight gain.

✓ 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 MTHFR c.665C>T variant (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
Anesthesia	Injectable Anesthetics		Propofol	
Anticancer Agents	Antifolates		Methotrexate	
Cardiovascular	Angiotensin II Receptor Antagonists	Azilsartan Irbesartan Losartan		
	Antianginal Agents	Ranolazine		
	Antiarrhythmics		Mexiletine Propafenone	Flecainide
	Anticoagulants	Warfarin		
	Antiplatelets			Clopidogrel
	Beta Blockers	Carvedilol Nebivolol Propranolol Timolol		Metoprolol
	Diuretics	Torsemide		
	Statins	Fluvastatin	Atorvastatin Lovastatin Pitavastatin Pravastatin Rosuvastatin	Simvastatin
Diabetes	Meglitinides	Nateglinide Repaglinide		
	Sulfonylureas	Chlorpropamide Glimepiride Glipizide Glyburide Tolbutamide		
Gastrointestinal	Antiemetics	Dronabinol Metoclopramide	Dolasetron Fosnetupitant-Palonosetron Netupitant-Palonosetron Palonosetron	Ondansetron
	Proton Pump Inhibitors	Dexlansoprazole Esomeprazole Lansoprazole Omeprazole Pantoprazole Rabeprazole		
Gaucher Disease	Endocrine-Metabolic Agents			Eliglustat
Gynecology	Endometriosis Pain Agents	Elagolix		
Hematology	Hemostatic Agents	Avatrombopag Eltrombopag Lusutrombopag		

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Infections	Antifungals	Voriconazole		
	Antimalarials	Proguanil		
Multiple Sclerosis	Disease-Modifying Agents	Siponimod		
Pain	Muscle Relaxants	Carisoprodol	Tizanidine	
	NSAIDs	Celecoxib Diclofenac Flurbiprofen Ibuprofen Indomethacin Meloxicam Piroxicam		
	Opioids	Fentanyl Morphine	Benzhydrocodone Dihydrocodeine Hydrocodone Methadone Oxycodone	Codeine Tramadol
Psychotropic	Antiaddictives	Lofexidine	Bupropion Naltrexone	
	Anti-ADHD Agents	Amphetamine Dextroamphetamine Lisdexamfetamine	Atomoxetine Clonidine Dexmethylphenidate Methylphenidate	
	Anticonvulsants	Brivaracetam Fosphenytoin Lacosamide Phenytoin	Phenobarbital Primidone Zonisamide	
	Antidementia Agents	Galantamine	Donepezil	
	Antidepressants	Citalopram Desvenlafaxine Duloxetine Escitalopram Fluoxetine Mirtazapine Nefazodone Sertraline Vortioxetine	Amoxapine Fluvoxamine Maprotiline Protriptyline	Amitriptyline Clomipramine Desipramine Doxepin Imipramine Nortriptyline Paroxetine Trimipramine Venlafaxine
	Antipsychotics	Aripiprazole Brexpiprazole Iloperidone Paliperidone Quetiapine Thioridazine	Chlorpromazine Clozapine Fluphenazine Olanzapine Perphenazine Pimozide	Haloperidol Risperidone Zuclopenthixol
	Benzodiazepines	Diazepam	Clobazam Lorazepam Oxazepam	
	Mood Stabilizers		Lithium	

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
	Other Neurological Agents	Deutetrabenazine Dextromethorphan / Quinidine Flibanserin Valbenazine	Tetrabenazine	
	Anti-Hyperuricemics and Anti-Gout Agents	Allopurinol Lesinurad		
Rheumatology	Immunomodulators	Tofacitinib	Leflunomide	
	Other Antirheumatic Agents		Sulfasalazine	
Sjogren's Syndrome	Cholinergic Agonists	Cevimeline		
Transplantation	Immunosuppressants	Tacrolimus		
Urologicals	Alpha-Blockers for Benign Prostatic Hyperplasia	Tamsulosin		
	Antispasmodics for Overactive Bladder	Darifenacin Fesoterodine Mirabegron Tolterodine		

Dosing Guidance

Amitriptyline

Decreased Amitriptyline Exposure (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The patient is predicted to be a CYP2D6 ultra-rapid metabolizer which is likely to result in a significantly increased metabolism of amitriptyline to less active compounds and a subsequent decrease in amitriptyline exposure leading to therapy failure.

Psychiatric Conditions: Consider an alternative medication. If Amitriptyline is warranted, consider increasing the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Neuropathic Pain: Consider an alternative medication. If amitriptyline is warranted titrate dose according to the patient's clinical response and tolerability.

Clomipramine

Decreased Clomipramine Exposure (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

The patient is predicted to be a CYP2D6 ultra-rapid metabolizer which is is likely to result in a significantly increased metabolism of clomipramine to less active compounds and a subsequent decrease in clomipramine exposure leading to therapy failure.

Psychiatric Conditions: Consider an alternative medication. If clomipramine is warranted, consider increasing the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Clopidogrel

Reduced Response to Clopidogrel (CYP2C19: Intermediate Metabolizer) — ACTIONABLE

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

Codeine

Increased Response to Codeine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Codeine is converted into its active metabolite morphine by CYP2D6. Since this patient is a ultra-rapid metabolizer, greatly increased morphine levels are expected, and the patient is at high risk of toxicity when taking codeine. The ultra-rapid conversion of codeine to morphine in breast feeding mothers can result in high and unsafe levels of morphine in the breast milk potentially causing life threatening respiratory depression in the breastfed infant. Avoid prescribing codeine, and consider an alternative opioid or a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids not sensitive to CYP2D6 function include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

Desipramine

Decreased Desipramine Exposure (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

The patient is predicted to be a CYP2D6 ultra-rapid metabolizer which is likely to result in a significantly increased metabolism of desipramine to less active compounds and a subsequent decrease in desipramine exposure leading to therapy failure.

Psychiatric Conditions: Consider an alternative medication. If desipramine is warranted, consider increasing the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Doxepin

Decreased Doxepin Exposure (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

The patient is predicted to be a CYP2D6 ultra-rapid metabolizer which is likely to result in a significantly increased metabolism of doxepin to less active compounds and a subsequent decrease in doxepin exposure leading to therapy failure.

Psychiatric Conditions: Consider an alternative medication. If doxepin is warranted, consider increasing the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Insomnia: Doxepin can be prescribed according to the standard recommended dosage and administration. Monitor patient closely for decreased efficacy.

Eliglustat

Possible Non-Response to Eliglustat (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

CYP2D6 ultra-rapid metabolizers may not reach adequate concentrations of eliglustat to achieve a therapeutic effect. Eliglustat should not be prescribed in patients who are CYP2D6 ultra-rapid metabolizers. An alternative medication may be considered.

Flecainide

Altered Response to Flecainide (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Titrate carefully and consider adjusting the dose in response to plasma concentration and ECG monitoring, OR consider an alternative drug. Examples of alternatives drugs not affected by CYP2D6 include: sotalol, disopyramide, quinidine, and amiodarone.

Haloperidol

Non-Response to Haloperidol (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Consider an alternative drug, or prescribe haloperidol at the standard dose and adjust dosage to achieve a favorable clinical response. Be alert to decreased haloperidol plasma concentrations.

Imipramine

Decreased Imipramine Exposure (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

The patient is predicted to be a CYP2D6 ultra-rapid metabolizer which is is likely to result in a significantly increased metabolism of imipramine to less active compounds and a subsequent decrease in imipramine exposure leading to therapy failure.

Psychiatric Conditions: Consider an alternative medication. If imipramine is warranted, consider increasing the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Metoprolol

Possible Non-Responder to Metoprolol (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The patient may experience a decrease in the pharmacological effect when taking metoprolol at standard dosage. Heart Failure: Consider alternative beta-blockers such as bisoprolol or carvedilol, or prescribe metoprolol at a higher dose. Other indications: Consider alternative beta-blockers such as bisoprolol or atenolol, or prescribe metoprolol at a higher dose. If metoprolol is prescribed, titrate the dose to a maximum of 250% of the normal dose in response to efficacy and adverse events.

Nortriptyline

Decreased Nortriptyline Exposure (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The patient is predicted to be a CYP2D6 ultra-rapid metabolizer which is likely to result in a significantly increased metabolism of nortriptyline to less active compounds and a subsequent decrease in nortriptyline exposure leading to therapy failure.

Psychiatric Conditions: Consider an alternative medication. If nortriptyline is warranted, consider increasing the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Ondansetron

Non-Response to Ondansetron (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

A substantially decreased antiemetic effect has been reported in CYP2D6 ultra-rapid metabolizers when taking standard doses of this medication. Consider prescribing an alternative drug not metabolized by CYP2D6 such as granisetron.

Paroxetine

Reduced Response to Paroxetine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

There is a risk for decreased efficacy at standard dosage. If a standard dose is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of the drug are likely. Consider an alternative medication.

Risperidone

Non-Response to Risperidone (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Consider an alternative drug, OR prescribe risperidone , be extra alert to insufficient response, and adjust dosage in response to clinical response and adverse events.

Simvastatin

Intermediate Myopathy Risk (SLCO1B1: Decreased Function) — ACTIONABLE

Simvastatin plasma concentrations are expected to be elevated. **Consider avoiding simvastatin**, and prescribe an alternative statin or another hypolipidemic drug, or consider prescribing simvastatin at a lower starting dose (20 mg/day). Routine creatine kinase (CK) monitoring is also advised. **The FDA recommends against the 80 mg daily dose.** Although the association between the SLCO1B1 521T>C variant and myopathy risk is not clearly established for other statins such as atorvastatin, pitavastatin, rosuvastatin, and pravastatin, caution is advised if high doses of these statins are used in this patient. Fluvastatin plasma levels are not affected by the SLCO1B1 521T>C variant.

Tramadol

Increased Response to Tramadol (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The patient is at high risk of toxicity when taking tramadol at standard dosing. Consider reducing tramadol dose by 30%. Careful monitoring for side effects (nausea, vomiting, constipation, respiratory depression, confusion, urinary retention) and weekly titration are recommended. In case of toxicity, consider alternative opioids other than codeine, or a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids not sensitive to CYP2D6 function include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

The accelerated conversion of tramadol to its active metabolite can result in high and unsafe levels of this metabolite in breast milk potentially causing life threatening respiratory depression in the breastfed infant. Use of tramadol should be avoided in breastfeeding mothers.

Trimipramine

Decreased Trimipramine Exposure (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

The patient is predicted to be a CYP2D6 ultra-rapid metabolizer which is likely to result in a significantly increased metabolism of trimipramine to less active compounds and a subsequent decrease in trimipramine exposure leading to therapy failure.

Psychiatric Conditions: Consider an alternative medication. If trimipramine is warranted, consider increasing the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Venlafaxine

Non-Response to Venlafaxine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The patient is unlikely to achieve adequate serum levels of venlafaxine and O-desmethylvenlafaxine when taking standard doses of venlafaxine. Consider an alternative drug, or increase the venlafaxine dose to a maximum of 150% of the normal dose and monitor venlafaxine and O-desmethylvenlafaxine plasma concentrations.

Zuclopenthixol

Non-Response to Zuclopenthixol (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Based on the genotype result, this this patient may be at risk of therapy failure when taking zuclopenthixol at standard dosage. Consider using this drug with close monitoring of plasma concentrations and titrate dose in response to the clinical effect, or consider an alternative medication. Unless contraindicated, alternative medications include flupenthixol, clozapine, olanzapine or quetiapine.

Amoxapine

Possible Decreased Amoxapine Exposure (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Like other tricyclic and tetracyclic antidepressants, amoxapine is metabolized by CYP2D6. However, the overall contribution of this enzyme in the metabolism of this drug is not well documented. Patients with increased CYP2D6 function may metabolize amoxapine more rapidly which can result in sub-therapeutic drug concentrations; these patients may require higher doses to achieve adequate plasma concentrations. There are no established dosing adjustments for patients with increased CYP2D6 function; therapy must be initiated cautiously and adjusted according to the patient's response.

Atomoxetine

Possible Atomoxetine Underexposure Leading to Decreased Response (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The genotype result indicates that the patient is likely to have an insufficient response due to inadequate drug exposure following standard dosing. Consider the following dosing strategy:

- Initiate treatment at 40 mg/day, increase to 80 mg/day after 3 days and maintain dose.
- 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 2 weeks, optimal clinical response is not observed and adverse events are not present, consider therapeutic drug monitoring 1-2 hours post dose. If the plasma concentration is less than 200 ng/ml consider a dose increase to a target of 400 ng/ml. Doses greater than 100 mg/day may be needed to achieve a targeted therapeutic concentration. (Therapeutic range: 200-1000 ng/ml).

Atorvastatin

Increased Myopathy Risk (SLCO1B1: Decreased Function) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated atorvastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high atorvastatin doses in this patient should be avoided. If atorvastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

Atorvastatin

Altered Response to Atorvastatin (CYP3A4: Intermediate Metabolizer) — INFORMATIVE

The genotype result indicates that the patient carries the CYP3A4*22 allele (this allele is associated with lower CYP3A4 enzyme activity). Preliminary studies have shown that patients carrying the CYP3A4*22 allele may achieve an optimal lipid control goal with lower atorvastatin dose requirements.

Benzhydrocodone

Possible Altered Response to Benzhydrocodone (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Benzhydrocodone is a prodrug of hydrocodone and is converted to active hydrocodone by intestinal enzymes. Increased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 ultrarapid metabolizers. Usually, adequate pain relief without an increase in adverse events can be achieved by using standard or lower doses. Other opioids not metabolized by CYP2D6 (e.g., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if excessive side effects are reported.

Bupropion

Possibly Decreased Response to Bupropion (CYP2B6: Intermediate Metabolizer) — INFORMATIVE

Bupropion is metabolized to its active metabolite hydroxybupropion by CYP2B6. This metabolite contributes to the therapeutic effects of bupropion when used as a smoking cessation agent or as an antidepressant. Individuals who are CYP2B6 intermediate metabolizers may or may not have lower blood levels of hydroxybupropion which may or may not result in a reduced response to bupropion treatment. Bupropion can be prescribed at standard label-recommended dosage with careful monitoring of the patient's response. Therapeutic monitoring of hydroxybupropion levels may be considered to guide dosing adjustment.

Bupropion

Decreased Response to Bupropion for Smoking Cessation (ANKK1: Altered DRD2 function) — INFORMATIVE

Smoking Cessation: The patient's genotype result is associated with a positive response to nicotine replacement therapy and a lesser response to bupropion treatment.

Chlorpromazine

Possible Non-Response to Chlorpromazine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Chlorpromazine is metabolized by CYP2D6, CYP3A4 and flavin-containing monooxygenases. Subjects with increased CYP2D6 function will metabolize chlorpromazine more rapidly which can result in sub-therapeutic drug concentrations. Consider a standard dose and adjust dosage according to the patient's tolerability and response. Higher doses may be necessary to achieve efficacy.

Clobazam

Possible Sensitivity to Clobazam (CYP2C19: Intermediate Metabolizer) — 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.

Clonidine

Possible Altered Response to Clonidine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Treatment with clonidine can cause dose related decreases in blood pressure and heart rate Measure heart rate and blood pressure prior to initiation of therapy, following dose increases, and periodically while on therapy. Titrate Clonidine slowly in patients with a history of hypotension, and those with underlying conditions that may be worsened by hypotension and bradycardia.

Clozapine

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.

Dexmethylphenidate

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.

Dihydrocodeine

Possible Altered Response to Dihydrocodeine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Increased conversion of dihydrocodeine to the more active metabolite dihydromorphine is expected in CYP2D6 ultra-rapid metabolizers. This may result in an exaggerated response. Adequate pain relief can be achieved by decreasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if signs of overdose (excessive sleepiness, confusion, or shallow breathing) are reported.

Dolasetron

Possible Altered Response to Dolasetron (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

The reduction of dolasetron to its active metabolite hydrodolasetron is mediated by a carbonyl reductase. Hydrodolasetron is further eliminated by multiple routes, including renal excretion and by glucuronidation or hydroxylation by CYP2D6. Compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower hydroxydolasetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Dolasetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Donepezil

Possible Altered Response to Donepezil (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

When compared to a normal metabolizer, a ultra-rapid metabolizers has a 24% increase in donepezil clearance. The clinical significance of this increase is not well documented. Consider using a standard dosing regimen and adjust dosage in response to clinical response and tolerability.

Fluphenazine

Possible Non-response to Fluphenazine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Fluphenazine is metabolized by CYP2D6, CYP1A2 and other enzymes. **Patients with increased CYP2D6 function will metabolize fluphenazine more rapidly which can result in sub-therapeutic drug concentrations; these patients may require higher doses to achieve adequate plasma concentrations.** There are no established dosing adjustments for patients with increased CYP2D6 function therefore, therapy must be initiated cautiously with oral or parenteral fluphenazine hydrochloride. When the pharmacological effects and an appropriate dosage are apparent, an equivalent dose of fluphenazine decanoate (IM or SC) may be administered and subsequent dosage adjustments may be necessary.

Fluvoxamine

Possible Reduced Response to Fluvoxamine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

There is a risk for decreased efficacy at standard dosage. If a standard dose is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of the drug are likely. There is insufficient data to calculate dose adjustments and careful titration is recommended until a favorable response is achieved. An alternative medication not metabolized by CYP2D6 can also be considered.

Fosnetupitant-Palonosetron

Possible Altered Response to Fosnetupitant-Palonosetron (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Fosnetupitant: Fosnetupitant is converted to netupitant via metabolic hydrolysis. Netupitant is extensively metabolized to three major metabolites (desmethyl, N-oxide and a hydroxy-methyl derivatives). Metabolism is mediated primarily by CYP3A4 and to a lesser extent by CYP2C9 and CYP2D6. No genetically guided drug selection or dosing recommendations are available for this drug. Fosnetupitant can be prescribed at standard label-recommended dosage and administration.
Palonosetron: Palonosetron is eliminated by multiple routes including metabolism. While CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in its metabolism to two inactive metabolites. Compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower palonosetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Palonosetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Hydrocodone

Possible Altered Response to Hydrocodone (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Increased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 ultra-rapid metabolizers. Usually, adequate pain relief without an increase in adverse events can be achieved by using standard or lower hydrocodone doses. Other opioids not metabolized by CYP2D6 (e.g., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if excessive side effects are reported.

Leflunomide

Increased Sensitivity to Leflunomide (CYP2C19: Intermediate Metabolizer) — 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.

Lithium

Decreased Response to Lithium (BDNF: Homozygous for rs6265 C Allele) — INFORMATIVE

BDNF encodes the brain-derived neurotrophic factor involved in neuroprotection and neuroplasticity. The patient is homozygous for the C allele of BDNF variant rs6265. This genotype is associated with a poor response to lithium treatment for bipolar disorder.

Lorazepam

Possible Altered Response to Lorazepam (UGT2B15: Intermediate Metabolizer) — INFORMATIVE

Lorazepam clearance may be reduced in this patient. However, there is insufficient evidence whether this change results in a significant clinical effect. Consider monitoring the patient for increased sedation and adjust dosing accordingly.

Lovastatin

Increased Myopathy Risk (SLCO1B1: Decreased Function) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated lovastatin acid plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high lovastatin doses in this patient should be avoided. If lovastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

Lovastatin

Altered Response to Lovastatin (CYP3A4: Intermediate Metabolizer) — INFORMATIVE

The genotype result indicates that the patient carries the CYP3A4*22 allele (this allele is associated with lower CYP3A4 enzyme activity). Preliminary studies have shown that patients carrying the CYP3A4*22 allele may achieve an optimal lipid control goal with lower lovastatin dose requirements.

Maprotiline

Possible Decreased Maprotiline Exposure (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Like other tricyclic and tetracyclic antidepressants, maprotiline is metabolized by CYP2D6 as well as CYP1A2. Patients with increased CYP2D6 function may metabolize maprotiline more rapidly which can result in sub-therapeutic drug concentrations; these patients may require higher doses to achieve adequate plasma concentrations. **There are no established dosing adjustments for patients with increased CYP2D6 function. Seizures have been associated with the use of maprotiline especially at high doses. Therefore, therapy must be initiated at a standard dose and gradually increased in small increments according to the patient's response.**

Methadone

Possible Sensitivity to Methadone (CYP2B6: Intermediate Metabolizer) — INFORMATIVE

Based on currently available evidence, S-methadone plasma concentrations may increase, resulting in higher risk of cardiac arrhythmias and QTc prolongation. Consider lower starting doses of methadone, and adjust dosing based on the clinical response.

Methotrexate

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.

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.

Mexiletine

Altered Response to Mexiletine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Because mexiletine plasma concentrations may be decreased, consider adjusting dose in response to mexiletine plasma concentration and ECG monitoring, until a favorable response in achieved.

Naltrexone

Altered Response to Naltrexone (OPRM1: Normal OPRM1 Function) — INFORMATIVE

Treatment of alcohol dependence: the patient has the OPRM1 118AA wild-type genotype that is associated with a poorer outcome with naltrexone therapy. Naltrexone-treated patients not carrying the OPRM1 118A>G G allele are less likely to respond to this drug, and may have higher relapse rates than those who are carriers of this allele. This association has not been reported consistently across studies.

Netupitant-Palonosetron

Possible Altered Response to Netupitant-Palonosetron (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Netupitant: Netupitant is extensively metabolized to three major metabolites (desmethyl, N-oxide and a hydroxy-methyl derivatives). Metabolism is mediated primarily by CYP3A4 and to a lesser extent by CYP2C9 and CYP2D6. No genetically guided drug selection or dosing recommendations are available for this drug. Netupitant can be prescribed at standard label-recommended dosage and administration.
Palonosetron: Palonosetron is eliminated by multiple routes including metabolism. While CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in its metabolism to two inactive metabolites. Compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower palonosetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Palonosetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Olanzapine

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.

Oxazepam

Possible Altered Response to Oxazepam (UGT2B15: Intermediate Metabolizer) — INFORMATIVE

Oxazepam clearance may be reduced in this patient. However, there is insufficient evidence whether this change results in a significant clinical effect. Consider monitoring the patient for increased sedation and adjust dosing accordingly.

Oxycodone

Possible Altered Response to Oxycodone (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Increased conversion of oxycodone to the more active metabolite oxymorphone is expected in CYP2D6 ultra-rapid metabolizers. Usually, adequate pain relief without an increase in adverse events can be achieved by using standard or lower oxycodone doses. Other opioids not metabolized by CYP2D6 (e.g., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if excessive side effects are reported.

Palonosetron

Possible Altered Response to Palonosetron (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Palonosetron is eliminated by multiple routes including metabolism. While CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in its metabolism to two inactive metabolites. Compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower palonosetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Palonosetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Perphenazine

Possible Non-Response to Perphenazine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Subjects with increased CYP2D6 function will metabolize perphenazine more rapidly, which can result in sub-therapeutic drug concentrations. Consider a dose increase with close monitoring until a favorable response is achieved.

Phenobarbital

Possible Sensitivity to Phenobarbital (CYP2C19: Intermediate Metabolizer) — 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.

Pimozide

Possible Non-Response to Pimozide (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

There is insufficient data to calculate dose adjustment, and if pimozide is prescribed at standard dosing, monitor response and be alert to reduced efficacy. Standard starting dose: 1 to 2 mg/day (adult) or 0.05 mg/kg/day (children). Doses may be increased to a maximum of 10 mg/day or 0.2 mg/kg/day.

Pitavastatin

Increased Myopathy Risk (SLCO1B1: Decreased Function) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated pitavastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high pitavastatin doses in this patient should be avoided. If pitavastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

Pravastatin

Increased Myopathy Risk (SLCO1B1: Decreased Function) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated pravastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high pravastatin doses in this patient should be avoided. If pravastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

Primidone

Possible Sensitivity to Primidone (CYP2C19: Intermediate Metabolizer) — 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.

Propafenone

Altered Response to Propafenone (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

There is insufficient data to allow calculation of dose adjustment. Titrate carefully and adjust the dose in response to plasma concentration and ECG monitoring. OR consider an alternative drug such as sotalol, disopyramide, quinidine, or amiodarone.

Dose adjustments with co-medications: concurrent use of propafenone along with CYP3A4 inhibitors and CYP2D6 inhibitors may significantly increase the plasma concentration of propafenone and thereby increase the risk of proarrhythmia and other adverse events. Therefore, avoid simultaneous use of propafenone with both a CYP2D6 inhibitor and a CYP3A4 inhibitor.

Propofol

Possible Altered Propofol Response (CYP2B6: Intermediate Metabolizer) — INFORMATIVE

Preliminary studies indicate that the patient's genotype may be associated with higher propofol exposure at standard dosing. This CYP2B6 genotype along with other factors such as old age (>65 years) and associated comorbidities may contribute to delayed emergence from anesthesia. There is insufficient data to allow calculation of dose adjustment; careful monitoring during post-surgery is recommended. The dosing regimen needs to be individualized for each patient, considering the patient's prior propofol dose requirements, age and comorbidities.

Protriptyline

Possible Decreased Protriptyline Exposure (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Like other tricyclic and tetracyclic antidepressants, protriptyline is metabolized by CYP2D6. Patients with increased CYP2D6 function may metabolize protriptyline more rapidly which can result in sub-therapeutic drug concentrations; these patients may require higher doses to achieve adequate plasma concentrations. There are no established dosing adjustments for patients with increased CYP2D6 function. Therefore, therapy must be initiated at a standard dose and gradually increased in small increments according to the patient's response.

Rosuvastatin

Increased Myopathy Risk (SLCO1B1 521T>C T/C; ABCG2 421C>A C/C) — INFORMATIVE

The patient does not carry a polymorphism in the ABCG2 gene that is associated with a higher rosuvastatin plasma exposure. The patient carries a polymorphism in the SLCO1B1 gene that is associated with an increased risk of myopathy. Rosuvastatin plasma concentrations are expected to increase, and the patient's risk of rosuvastatin-induced myopathy is elevated. Other factors that may increase this risk further include: uncontrolled hypothyroidism, renal impairment, diabetes, and comedications with ABCG2 or SLCO1B1 inhibitors. For patient age of 20-60 years, the maximum recommended dose range to reduce the risk of high statin exposure: 20-40 mg/day (highest dose). Start with usual doses 10-20 mg/day. It is possible to increase dose to 40 mg/day in non-Asian patients if no other risk factors are present and the patient is closely monitored for adverse events. For patient age of >60 years, the maximum recommended dose range to reduce the risk of high statin exposure: 20 mg/day. Start with usual doses 10-20 mg/day or 5 mg/day in Asian patients.

Sulfasalazine

Decreased Response to Sulfasalazine For the Treatment of Rheumatoid Arthritis (ABCG2: Normal Function) — INFORMATIVE

Rheumatoid Arthritis: The patient carries two copies of ABCG2 rs2231142 C allele. Preliminary data suggests that this genotype may be associated with decreased plasma levels of sulfasalazine which may decrease the likelihood of response to this drug.

Tetrabenazine

Unknown Sensitivity to Tetrabenazine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

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

Tizanidine

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.

Zonisamide

Possible Sensitivity to Zonisamide (CYP2C19: Intermediate Metabolizer) **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.

dnalife

PATIENT INFORMATION

NAME: Sample Report
DOB: 1/1/2018
SEX:
ACC #: DNA123456ZA

SPECIMEN DETAILS

SPECIMEN TYPE: Buccal Swab
ORDERED BY:
REPORT DATE: 7/10/2019

Test Details

Gene	Genotype	Phenotype	Clinical Consequences
ABCG2	421C>A C/C	**Normal Function**	Consistent with a normal ABCG2 transporter function. The patient's risk for statin-induced adverse events is normal.
ADRA2A	C-1291G C/G	**Heterozygous for the G Allele**	Carriers of the G allele of ADRA2A C-1291G variant, show greater reduction of inattentive symptoms when administered Methylphenidate or Dexmethylphenidate.
ANKK1/DRD2	DRD2:Taq1A C/T	**Altered DRD2 function**	Consistent with a reduced dopamine receptor D2 function.
BDNF	434C>T C/C	**Homozygous for rs6265 C Allele**	Consistent with normal activity-dependent secretion of BDNF from neurons and normal BDNF signaling.
COMT	Val158Met A/G	**Intermediate COMT Activity**	Consistent with a 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/*6	**Intermediate Metabolizer**	Consistent with a moderate deficiency in CYP2B6 activity. Potential risk for side effects or loss of efficacy with drug substrates.
CYP2C19	*1/*2	**Intermediate Metabolizer**	Consistent with a moderate deficiency in CYP2C19 activity. Potential risk for side effects or loss of efficacy with drug substrates.
CYP2C9	*1/*1	**Normal Metabolizer**	Consistent with a typical CYP2C9 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP2D6	*2/*2 XN	**Ultra-Rapid Metabolizer**	Consistent with a significant increase in CYP2D6 activity. Potential risk for side effects or loss of efficacy with drug substrates.
CYP3A4	*3/*22	**Intermediate Metabolizer**	Consistent with a moderate deficiency in 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 a poor CYP3A5 activity. This phenotype is the most common in the general population. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
CYP4F2	1347G>A G/G	**Homozygous for the G allele (rs2108622)**	
F2 **F5**	rs1799963 GG 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.
MC4R	g.60215554C>A C/A	**Heterozygous for A Allele (rs489693)**	Altered MC4R function
MTHFR	c.665C>T GA	**Reduced MTHFR Activity**	The patient carries one MTHFR C677T mutation (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 c.665C>T GA	**No Increased Risk of Hyperhomocysteinemia**	The patient MTHFR function is reduced slightly. This is not associated with an increased risk for venous thromboembolism.
OPRM1	A118G A/A	**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 T/C	**Decreased Function**	Consistent with a decreased SLCO1B1 transporter function. The patient's risk for statin-induced myopathy is intermediate.
UGT2B15	*1/*2	**Intermediate Metabolizer**	Consistent with a moderately decreased UGT2B15 glucuronidation function. Potential risk for side effects with drug substrates.

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PATIENT INFORMATION

NAME: Sample Report
DOB: 1/1/2018
SEX:
ACC #: DNA123456ZA

SPECIMEN DETAILS

SPECIMEN TYPE: Buccal Swab
ORDERED BY:
REPORT DATE: 7/10/2019

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.

Alleles Tested: ABCG2 421C>A; **ADRA2A** C-1291G; **ANKK1/DRD2** DRD2:Taq1A; **BDNF** 434C>T; **COMT** Val158Met; **CYP1A2** *1F, *1K; **CYP2B6** *16, *6, *9, *11, *18; **CYP2C19** *2, *3, *4, *4B, *6, *7, *8, *9, *10, *17; **CYP2C9** *2, *3, *4, *5, *6, *8, *11, *27; **CYP2D6** *2, *3, *4, *4M, *6, *7, *8, *9, *10, *12, *14A, *14B, *17, *29, *35, *41, *5 (gene deletion), XN (gene duplication); **CYP3A4** *3, *12, *17, *22; **CYP3A5** *3, *3C, *6, *7; **CYP4F2** 1347G>A; **Factor II** rs1799963; **Factor V Leiden** rs6025; **MC4R** g.60215554C>A; **MTHFR** c.1286A>C, c.665C>T; **OPRM1** A118G; **SLCO1B1** 521T>C; **UGT2B15** *2; **VKORC1** -1639G>A

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%.

Lab Disclaimer: DNAlysis Biotechnology developed the Genotype test. The performance characteristics of this test were determined by DNAlysis Biotechnology. It has not been cleared or approved by the U.S. Food and Drug Administration.

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.

Approved By: Laboratory Manager
Thenusha Naidoo
MS 0000990

PATIENT INFORMATION

NAME: Sample Report
DOB: 1/1/2018
SEX:
ACC #: DNA123456ZA

SPECIMEN DETAILS

SPECIMEN TYPE: Buccal Swab
ORDERED BY:
REPORT DATE: 7/10/2019

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 Report
DOB: 1/1/2018
ACC #: DNA123456ZA

Pharmacogenetic Test Summary

ABCG2	421C>A C/C	Normal Function
ADRA2A	C-1291G C/G	Heterozygous for the G Allele
ANKK1/DRD2	DRD2:Taq1A C/T	Altered DRD2 function
BDNF	434C>T C/C	Homozygous for rs6265 C Allele
COMT	Val158Met A/G	Intermediate COMT Activity
CYP1A2	*1A/*1F	Normal Metabolizer - Higher Inducibility
CYP2B6	*1/*6	Intermediate Metabolizer
CYP2C19	*1/*2	Intermediate Metabolizer
CYP2C9	*1/*1	Normal Metabolizer
CYP2D6	*2/*2 XN	Ultra-Rapid Metabolizer
CYP3A4	*3/*22	Intermediate Metabolizer
CYP3A5	*3/*3	Poor Metabolizer
CYP4F2	1347G>A G/G	Homozygous for the G allele (rs2108622)
Factor II	rs1799963 GG	Normal Thrombosis Risk
Factor V Leiden	rs6025 CC	Normal Thrombosis Risk
MC4R	g.60215554C>A C/A	Heterozygous for A Allele (rs489693)
MTHFR	c.1286A>C TT	Normal MTHFR Activity
MTHFR	c.665C>T GA	Reduced MTHFR Activity
OPRM1	A118G A/A	Normal OPRM1 Function
SLCO1B1	521T>C T/C	Decreased Function
UGT2B15	*1/*2	Intermediate Metabolizer
VKORC1	-1639G>A G/G	Low Warfarin Sensitivity

For a complete report contact DNAlysis Biotechnology
www.dnalysis.co.za