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PATIENT INFORMATION	
NAME:	Sample Report
DOB:	5/9/2016
SEX:	Female
ACC #:	DNA123

SPECIMEN DETAILS	
SPECIMEN TYPE:	Buccal Swab
ORDERED BY:	Private
REPORT DATE:	9/12/2017

medcheck™

Current Patient Medications

Sertraline, Levothyroxine, Simvastatin, Amitriptyline

Amitriptyline

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.

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 521C>T 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 521C>T variant.

Sertraline

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.

Medications outside the scope of the report: Levothyroxine

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

Increased Risk of Antipsychotic-Induced Tardive Dyskinesia

The patient does not carry the Taq1A variant (homozygous for the A2 allele).

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

Closely monitor the patient for signs of tardive dyskinesia.

✓ Antipsychotic-Induced Hyperprolactinemia

Normal Risk of Antipsychotic-Induced Hyperprolactinemia

The patient does not carry the Taq1A variant (homozygous for the A2 allele).

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

Monitor the patients closely for any signs of hyperprolactinemia.

✓ Antipsychotic-Induced Weight Gain

Low Risk of Antipsychotic-Induced Weight Gain

The patient does not carry the Taq1A variant (homozygous for the A2 allele).

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

Monitor the patient closely for signs weight gain.

⚠ Hyperhomocysteinemia - Depression

Increased Risk of Hyperhomocysteinemia

The patient carries two MTHFR C677T mutations (homozygous). MTHFR enzyme activity is severely reduced (30% 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. This patient exhibits significantly reduced MTHFR activity, which is a risk factor for hyperhomocysteinemia. Low MTHFR activity may further exacerbate folate deficiency in patients with depression and may increase the risk of depressive relapse or delay the response to antidepressants.

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, this patient is likely to benefit from methylfolate as an antidepressant-augmenting agent. Testing for homocysteine levels and serum folate levels may be informative for this patient. Although methylfolate may substantially benefit this patient, it should not replace the antidepressant therapy and methylfolate should always be used as an adjuvant to antidepressant medication.

✓ 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

Increased Risk of Hyperhomocysteinemia

The patient carries two MTHFR C677T mutations (homozygous) and no MTHFR A1298C mutation. MTHFR enzyme activity is severely reduced (30% of normal activity).

The patient's significantly reduced MTHFR activity is a risk factor for hyperhomocysteinemia, especially in the presence of low serum folate levels. Mild to moderate hyperhomocysteinemia appears to be associated with an increased risk for venous thromboembolism (VTE).

Testing total plasma homocysteine level may be beneficial. Hyperhomocysteinemia can be treated with nutritional supplementation.

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Potentially Impacted Medications

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Anticancer Agents	Antifolates		Methotrexate	
Cardiovascular	**Angiotensin II Receptor Antagonists**	Azilsartan Candesartan Eprosartan Irbesartan Losartan Olmesartan Telmisartan Valsartan		
	Antianginal Agents	Ranolazine		
	Antiarrhythmics	Flecainide Mexiletine Propafenone		
	Anticoagulants	Apixaban Dabigatran Etexilate Edoxaban Fondaparinux Rivaroxaban	Warfarin	
	Antiplatelets	Prasugrel Ticagrelor Vorapaxar	Clopidogrel	
	Beta Blockers	Atenolol Bisoprolol Carvedilol Labetalol Metoprolol Nebivolol Propranolol Timolol		
	Diuretics	Torsemide		
	Statins	Fluvastatin	Atorvastatin Lovastatin Pitavastatin Pravastatin Rosuvastatin	Simvastatin
Diabetes	**Meglitinides**	Nateglinide Repaglinide		
	Sulfonylureas	Chlorpropamide Glimepiride Glipizide Glyburide Tolbutamide		

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Gastrointestinal	Antiemetics	Aprepitant Dolasetron Dronabinol Fosaprepitant Granisetron Metoclopramide Netupitant-Palonosetron Ondansetron Palonosetron Rolapitant		
	Proton Pump Inhibitors	Rabeprazole	Dexlansoprazole Esomeprazole Lansoprazole Omeprazole Pantoprazole	
Infections	Antifungals	Amphotericin B Anidulafungin Caspofungin Fluconazole Isavuconazonium Itraconazole Micafungin Posaconazole		Voriconazole
	Anti-HIV Agents	Dolutegravir Raltegravir		
	Antimalarials	Proguanil		

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Pain	Fibromyalgia Agents	Milnacipran		
	Muscle Relaxants	Cyclobenzaprine Metaxalone Methocarbamol	Carisoprodol Tizanidine	
	NSAIDs	Celecoxib Diclofenac Flurbiprofen Ibuprofen Indomethacin Ketoprofen Ketorolac Meloxicam Nabumetone Naproxen Piroxicam Sulindac		
	Opioids	Alfentanil Buprenorphine Codeine Dihydrocodeine Fentanyl Hydrocodone Hydromorphone Levorphanol Meperidine Methadone Morphine Oxycodone Oxymorphone Sufentanil Tapentadol Tramadol		
	Antiaddictives	Bupropion	Naltrexone	
	Anti-ADHD Agents	Amphetamine Atomoxetine Clonidine Dextroamphetamine Guanfacine Lisdexamfetamine	Dexmethylphenidate Methylphenidate	

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Psychotropic	Anticonvulsants	Brivaracetam Carbamazepine Eslicarbazepine Ethosuximide Ezogabine Felbamate Fosphenytoin Gabapentin Lacosamide Lamotrigine Levetiracetam Oxcarbazepine Perampanel Phenobarbital Phenytoin Pregabalin Primidone Rufinamide Tiagabine Topiramate Valproic Acid Vigabatrin Zonisamide		
	Antidementia Agents	Donepezil Galantamine Memantine		
	Antidepressants	Amoxapine Desipramine Desvenlafaxine Duloxetine Fluoxetine Fluvoxamine Levomilnacipran Maprotiline Mirtazapine Nefazodone Nortriptyline Paroxetine Protriptyline Trazodone Venlafaxine Vilazodone Vortioxetine	Sertraline	Amitriptyline Citalopram Clomipramine Doxepin Escitalopram Imipramine Trimipramine

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	Antipsychotics	Aripiprazole Asenapine Brexpiprazole Cariprazine Chlorpromazine Fluphenazine Haloperidol Iloperidone Loxapine Lurasidone Paliperidone Perphenazine Pimavanserin Pimozide Quetiapine Risperidone Thioridazine Thiothixene Trifluoperazine Ziprasidone	Clozapine Olanzapine	
	Benzodiazepines	Alprazolam Clobazam Clonazepam	Diazepam Lorazepam Oxazepam	
	Mood Stabilizers		Lithium	
	Other Neurological Agents	Deutetrabenazine Dextromethorphan / Quinidine Flibanserin Valbenazine	Tetrabenazine	
Rheumatology	Anti-Hyperuricemics and Anti-Gout Agents	Allopurinol Colchicine Febuxostat Lesinurad		
	Immunomodulators	Apremilast Leflunomide Tofacitinib		
	Other Antirheumatic Agents		Sulfasalazine	
Transplantation	Immunosupressants	Tacrolimus		

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Urologicals	5-Alpha Reductase Inhibitors for Benign Prostatic Hyperplasia	Dutasteride Finasteride		
	Alpha-Blockers for Benign Prostatic Hyperplasia	Alfuzosin Doxazosin Silodosin Tamsulosin Terazosin		
	Antispasmodics for Overactive Bladder	Darifenacin Fesoterodine Mirabegron Oxybutynin Solifenacin Tolterodine Trospium		
	Phosphodiesterase Inhibitors for Erectile Dysfunction	Avanafil Sildenafil Tadalafil Vardenafil		

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Dosing Guidance

Amitriptyline

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

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

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

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

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

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.

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 521C>T 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 521C>T variant.

Trimipramine

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.

Voriconazole

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

Voriconazole plasma concentrations are expected to be low if a standard dose is used, increasing the risk of loss of response and effectiveness and subsequent disease progression. Consider an alternative medication that is not dependent on CYP2C19 metabolism, such as isavuconazole, liposomal amphotericin B or posaconazole.

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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.

Carisoprodol

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.

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.

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.

Dexlansoprazole

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

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

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.

Esomeprazole

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%.

Lansoprazole

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%.

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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.

Methotrexate

Increased risk for methotrexate toxicity (MTHFR: Reduced MTHFR Activity) — INFORMATIVE

The patient carries two MTHFR 677 T alleles, resulting in a significantly reduced MTHFR activity. **Malignancy:** Leukemia or lymphoma patients who are treated with methotrexate standard regimens may have an increased risk of overall toxicity (including mucositis, thrombocytopenia, and hepatic toxicity), and an increased severity of mucositis. Consider at least a 50% reduction in methotrexate starting dose, followed by titration based on toxicity. Other genetic and clinical factors may also influence the patient's risk for toxicity and response to methotrexate treatment. **Nonmalignant conditions:** a limited number of studies found an association between the MTHFR 677 T allele and methotrexate-induced toxicity in rheumatoid arthritis patients. However, there is insufficient data to calculate dose adjustment. Monitor patient closely for increased side effects and adjust the dose accordingly. Other genetic and clinical factors may also influence the patient's risk for toxicity and response to methotrexate treatment.

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.

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.

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.

Omeprazole

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%.

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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.

Pantoprazole

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%.

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.

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.

Sertraline

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.

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

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

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

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⚠ 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.

⚠ Warfarin

Normal Sensitivity to Warfarin (CYP2C9 *1/*1 VKORC1 -1639G>A G/A) — **ACTIONABLE**

Initiation Therapy: consider using the following standard warfarin dose range as provided in the FDA-approved label: **5-7 mg/day**. OR consider using a personalized dose calculated by a pharmacogenetic algorithm. The estimated time to reach steady state is 4-5 days.

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Test Details

Gene	Genotype	Phenotype	Clinical Consequences
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.
CYP2C19	*1/*17	Rapid Metabolizer	Consistent with a significant increase in CYP2C19 activity. Potential risk for side effects or loss of efficacy with drug substrates.
CYP2D6	*1/*4	Normal Metabolizer	Consistent with a typical CYP2D6 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
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.
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.
VKORC1	-1639G>A G/A	Intermediate Warfarin Sensitivity	VKORC1 is the site of action of warfarin. The patient may require a decrease in warfarin dosage.
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.
CYP1A2	*1F/*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.
SLCO1B1	521T>C T/C	Decreased Function	Consistent with a decreased SLCO1B1 transporter function. The patient's risk for statin-induced myopathy is intermediate.
COMT	Val158Met A/G	Intermediate COMT Activity	Consistent with a reduced catechol O-methyltransferase (COMT) function.
ANKK1/DRD2	DRD2:Taq1A G/G	Unaltered DRD2 function	Consistent with a normal dopamine receptor D2 function.
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.
UGT2B15	*1/*2	Intermediate Metabolizer	Consistent with a moderately decreased UGT2B15 glucuronidation function. Potential risk for side effects with drug substrates.
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.
BDNF	434C>T C/C	Homozygous for rs6265 C Allele	Consistent with normal activity-dependent secretion of BDNF from neurons and normal BDNF signaling.
MTHFR	1298A>C AA 677C>T TT	Increased Risk of Hyperhomocysteinemia	The patient's significantly reduced MTHFR activity is a risk factor for hyperhomocysteinemia, especially in the presence of low serum folate levels. Mild to moderate hyperhomocysteinemia appears to be associated with an increased risk for venous thromboembolism (VTE).
MTHFR	677C>T TT	Reduced MTHFR Activity	The patient carries two MTHFR C677T mutations (homozygous). MTHFR enzyme activity is severely reduced (30% of normal activity) and the risk of hyperhomocysteinemia is severely increased.

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PATIENT INFORMATION	
NAME:	Sample Report
DOB:	5/9/2016
SEX:	Female
ACC #:	DNA123

SPECIMEN DETAILS	
SPECIMEN TYPE:	Buccal Swab
ORDERED BY:	Private
REPORT DATE:	9/12/2017

Factor II	20210G>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.
Factor V Leiden	1691G>A GG		

Alleles Tested: **ABCG2** 421C>A; **ADRA2A** C-1291G; **ANKK1/DRD2** DRD2:Taq1A; **BDNF** 434C>T; **COMT** Val158Met; **CYP1A2** *1F, *1K; **CYP2B6** *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; **Factor II** 20210G>A; **Factor V Leiden** 1691G>A; **MTHFR** 1298A>C, 677C>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	Quality Manager Thabisile Xaba MT 0095451

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PATIENT INFORMATION

NAME: Sample Report
DOB: 5/9/2016
SEX: Female
ACC #: DNA123

SPECIMEN DETAILS

SPECIMEN TYPE: Buccal Swab
ORDERED BY: Private
REPORT DATE: 9/12/2017

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.

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REPORT DETAILS

Name: Sample Report
DOB: 5/9/2016
ACC #: DNA123

Pharmacogenetic Test Summary

ABCG2	421C>A C/C	Normal Function
ADRA2A	C-1291G C/G	Heterozygous for the G Allele
ANKK1/DRD2	DRD2:Taq1A G/G	Unaltered DRD2 function
BDNF	434C>T C/C	Homozygous for rs6265 C Allele
COMT	Val158Met A/G	Intermediate COMT Activity
CYP1A2	*1F/*1F	Normal Metabolizer - Higher Inducibility
CYP2B6	*1/*1	Normal Metabolizer
CYP2C19	*1/*17	Rapid Metabolizer
CYP2C9	*1/*1	Normal Metabolizer
CYP2D6	*1/*4	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
MTHFR	1298A>C AA	Normal MTHFR Activity
MTHFR	677C>T TT	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/A	Intermediate Warfarin Sensitivity

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

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