natural molecular
TESTING CORPORATION

Analysis Report

Patient / Procedure Information

Patient: Test Patient
Patient ID #
Tracking #: 200101
Location: Natural Molecular Testing Corp.

Sample Date: 2/13/2013
Sample Type: Buccal Swab
Administered B Sample Staff

Pharmacogenetic Analysis

The following are medications used by this patient and their pharmacogenetic identifiers:

POTENTIAL ISSUES

Drug	Dose	Assay / Pathway	Phenotype
Carvedilol (Active)	25 mg BID	2D6	Intermediate Metabolizer

Analysis: Patient may have increased levels of carvedilol compared to a normal metabolizer. Dose adjustments to be made based on tolerance.

POTENTIAL ISSUES

Drug	Dose	Assay / Pathway	Phenotype
Losartan (Active)	50-12.5 mg Every_Day	2C9	Intermediate Metabolizer

Analysis: Less conversion of losartan to its more active metabolite. Dose adjustments should be based on patient response.

POTENTIAL ISSUES

Drug	Dose	Assay / Pathway	Phenotype
Tamsulosin (Active)	.4 mg Every_Day	3A4 2D6	Normal Metabolizer Intermediate Metabolizer

Analysis:

Interactions / Considerations for Alternative Pharmacology:
Patient is on two alpha blockers (tamsulosin and silodosin). Consider discontinuing one to avoid duplicate therapy.

Current Medications Without Issues

Drug	Dose	Assay / Pathway	Phenotype
Silodosin (Active)	8 mg Every_Day	3A4	Normal Metabolizer

The following are medications and/or supplements that are metabolized via pathways outside this analysis:

Other Medications And/Or Supplements

Drug	Dose	Assay / Pathway	Phenotype
Adalimumab (Active)	40 unit Every_Other_Week	NA	NA
Aspirin (Active)	325 mg Every_Day	NA	NA
Psyllium (Active)	- mg Every_Day	NA	NA
Multiple Vitamins (Active)	- mg Every_Day	NA	NA

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Lab Report

Patient / Procedure Information

Patient:	Test Patient	**Date Of Birth:**	4/18/1945	**Sample Type:**	Buccal Swab
Location:	Natural Molecular Testing Corp.	**Patient MRN:**		**Collection Date:**	2/13/2013
Administered By:	Sample Staff	**Tracking #:**	200101	**Received Date:**	2/13/2013

Assay	Genotype	Phenotype	Date
CYP450_VKORC1	A/A	High Warfarin Sensitivity	2/13/2013

VKORC1 - Based on VKORC1 genotyping, high warfarin sensitivity is anticipated. Low Dose VKORC1 Haplotypes consist of two mutated alleles in the VKORC1 gene. A lower dose is recommended for low dose group A VKORC1 haplotypes.

Variants: -1639G>A-LOW DOSE (High Sensitivity) HAPLOTYPE A (A/A)

CYP450_3A5	*1D/*3/*6	Poor Metabolizer	2/13/2013

The patient is a CYP450 3A5 poor metabolizer (PM). This phenotype consists of two inactive CYP450 3A5 alleles. CYP450 3A5 poor metabolizers have significantly lower levels of enzyme activity. For drugs metabolized by CYP450 3A5, PMs may require alternative treatments or less than standard dosage to avoid possible adverse effects. In addition, please consult drug labeling for further dosing guidance.

Variants: ***1D-Heterozygote** | *2-Normal | ***3-Heterozygote** | *3B-Normal | ***6-Heterozygote** | *7-Normal | *8-Normal | *9-Normal

CYP450_2C9	*1/*2	Intermediate Metabolizer	2/13/2013

CYP2C9 - The patient is an intermediate metabolizer (IM). Intermediate (lower than normal) CYP2C9 metabolism is anticipated. This phenotype consists of one inactive CYP2C9 allele and one active CYP2C9 allele. It is suggested that IMs be administered CYP2C9 metabolized drugs at a reduced dosage. In addition, please consult drug labeling for further dosing guidance.

Variants: ***2-Heterozygote** | *3-Normal

CYP450_2D6I	*1/*41	Intermediate Metabolizer	2/13/2013

The patient is an intermediate metabolizer (IM). This phenotype consist of one active CYP2D6 allele and one inactive CYP2D6 allele. CYP2D6 IMs have lower levels of enzyme activity and for prodrugs requiring activation by CYP2D6, IMs may require alternative treatment or increased dosage of prodrug. For parent (active) drugs that don't require activation, it is suggested that IMs be administered CYP2D6 metabolized drugs at a reduced dosage. In addition, please consult drug labeling for further dosing guidance.

Variants: CNV (*XN)-Normal | CNV (*5)-Normal | -1584C>G-Normal | *10-Normal | *12-Normal | *15-Normal | *11-Normal | *17-Normal | *6-Normal | *8/*14-Normal | *4-Normal | *3-Normal | *9-Normal | ***2-Heterozygote** | *7-Normal | ***41-Heterozygote**

Thrombosis_Mthfr	667:C/T, 1298:A/C	Moderate Thrombosis and Cardiovascular Disease Risk	2/13/2013

The patient is a heterozygote for both the 677C>T and 1298A>C MTHFR mutations. Compound heterozygosity (677C/T and 1298A/C) is associated with increased plasma homocysteine levels and may be associated with increased risk of premature cardiovascular disease.

Variants: 677 C>T-C/T | 1298 A>C-A/C

CYP450_2C19	*1/*1	Normal Metabolizer	2/13/2013

The patient is a normal metabolizer (NM), and changes in metabolism are not generally expected.

Variants: *2-Normal | *3-Normal | *4-Normal | *5-Normal | *6-Normal | *7-Normal | *8-Normal | *9-Normal | *10-Normal | *13-Normal | *17-Normal

CYP450_3A4	*1/*1B	Normal Metabolizer	2/13/2013

The patient is a normal metabolizer (NM), and changes in metabolism are not generally expected.

Variants: ***1B-Heterozygote** | *2-Normal | *3-Normal | *12-Normal | *17-Normal

Thrombosis_FactorII	G/G	Normal Thrombosis Risk	2/13/2013

The patient is wildtype for Factor II Prothrombin. Wildtype genotypes consist of two G residues at the 20210 position of the Factor II gene. Wildtype genotypes are associated with a normal risk of developing an abnormal blood clot.

Variants: 20210 G>A-G/G

Thrombosis_FactorV	G/G	Normal Thrombosis Risk	2/13/2013

The patient is wildtype for Factor V Leiden. Wildtype genotypes consist of two G residues at the 1691 position of the Factor V gene. Wildtype genotypes are associated with a normal risk of developing an abnormal blood clot.

Variants: 1691 G>A-G/G

Illustrative Guide to Cytochrome P450 Genes: Notable Examples and Prevalence

	Medicines Affected	Patients w/ Variants
CYP2CI9	Some examples include clopidogrel some antidepressants (amitriptyline, citalopram, escitalopram, imipramine, sertraline), phenytoin, diazepam, PPIs (lansoprazole, omeprazole), carisoprodol, propranolol and methadone.	~40% typical U.S., higher in Asians and Africans
CYP2D6	Some examples include SSRIs/SNRIs (fluoxetine, paroxetine, duloxetine) TCAs (amitriptyline, imipramine, desipramine), most beta blockers, opioids (tramadol, meperidine, hydrocodone, oxycodone, codeine), antipsychotics (haloperidol, risperidone, aripiprazole), some antiarrhythmics and tamoxifen.	~40%, increased prevalence in Africans
CYP2C9	Some examples include some angiotensin II blockers (losartan, irbesartan), NSAIDs (ibuprofen, naproxen, diclofenac), some oral hypoglycemics (rosiglitazone) warfarin,, phenytoin and one notable statin (rosuvastatin).	~70%
CYP450 3A4 & 3A5	Some examples include tamoxifen, many statins (atorvastatin, lovastatin, simvastatin), many benzodiazepines (alprazolam, triazolam, midazolam), many calcium channel blockers (amlodipine, diltiazem, nifedipine, verapamil), macrolide antibiotics (clarithromycin, erythromycin, azithromycin), and some opioids (fentanyl, methadone, hydrocodone, buprenorphine).	~5-10% Caucasians, 5-8% African Americans, 1-3% Asians 3A4 99% and 3A5 10%

These principles guide the following recommendations based on your patient's genotype and phenotype. As always, these are guidelines and recommendations only and are provided as such. The predictive capacity of these tests are significantly altered in the presence of altered absorption, hepatic dysfunction, and for drugs eliminated by renal excretion . Pharmacogenetic testing does not exclude the need for therapeutic drug monitoring and other relevant clinical variables needed to individualize drug therapy.

The treating physician or other healthcare professional should individualize decision making and assume ultimate responsibility for treatment decisions based on this genotype analysis report.

Methodologies: PCR based assays detect listed alleles, including all common and most rare variants with known clinical significance at analytical sensitivity and specificity > 99%. CYP2C19: 10 variants (active *1; inactive *2, *3, *4, *6, *7, *8, *9, *10; rapid *17). CYP2D6: 15 variants (active *1, *2; inactive *3, *4, *5, *6, *7, *8, *12, *14; partially active *9, *10, *17, *29, *41; gene duplications XN; gene deletion XN). CYP2C9: 3 variants (active *1, inactive *2, *3). VKORC1: 1 variant (□1639G>A). Rare variants of CYP2D6 (*7, *8, *12, *14) may not have been observed at NMTC. These assays have been developed and performance characteristics determined by NMTC. Rare false negative or false positive results may occur . CYP2C19 and CYP2D6 have not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance is not necessary. These tests are used for clinical purposes and should not be considered as investigational. CYP450□3A4: 6 variants (active *1, *1B, *3; inactive *2, *12, *17). CYP450-3A5: 8 variants (active *1, *1D, *2, *7; inactive *3, *3B, *6, *8, *9). variants of CYP450□3A4 and 3A5 may not have been observed at NMTC. These assays have been developed and performance characteristics determined by NMTC. Rare false negative or false positive results may occur. CYP2C19 and CYP2D6 have not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance is not necessary. These tests are used for clinical purposes and should not be considered as investigational. Factor V Leiden: 1 variant (1691G>A). Factor II Prothrombin: 1 variant (20210G>A). MTHFR: 2 variants (677C>T and 1298A>C). false negative or false positive results may occur. Each test in this assay has been cleared by the FDA for in vitro diagnostic use.

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CLIA Certified DNA Testing Lab Since 2009 Credential Number MTSC.FS.60063043, CLIA #50D1092274

Digitally signed by Michael H. Kalnoski, M.D., FCAP
Location: Washington

**Per CMS regulations, the electronic signature indicates that this case has been reviewed and the results confirmed by the named pathologist.*