



ORDERING PRACTICE

Practice Code: 100
Sample Cardiology Clinic
374 Broadway
New York, NY 10001
Physician: Dr. Sample

JANE DOE

DOB: 1973-02-19
Gender: Female
Ethnicity: European
Procedure ID: 87000
Kit Barcode: 201612092248585
Specimen: Blood, #10000
Specimen Collected: 2016-01-12
Specimen Received: 2016-01-13
Specimen Analyzed: 2016-01-21
Report Generated: 2016-02-03

TEST INFORMATION

Panel: Drug Response Panel

SUMMARY OF RESULTS

Consider Alternatives/Use with Extreme Caution

The drugs below are expected to have serious adverse effects or are contraindicated based on the patient's genotype.

CARDIOVASCULAR

Drug	Drug Type	Gene	Variant / Haplotype	Interpretation	Reference Type	Reference (PMID)
Clopidogrel	Antiplatelets	CYP2C19	rs4244285 G/A (*1/*2)	1) May have poor metabolism of clopidogrel and decreased formation of active drug metabolite, resulting in decreased response 2) May have an increased risk for secondary cardiovascular events	CPIC Guideline	21716271;23698643
Simvastatin	Statins	SLOC1B	rs4149056 T/C	Increased risk of simvastatin-related myopathy, as compared to patients with the TT genotype.	CPIC Guideline	22617227;24918167

Use with Caution

The drugs below may be less effective or result in adverse effects based on the patient's genotype.

PSYCHIATRY

Drug	Drug Type	Gene	Variant / Haplotype	Interpretation	Reference Type	Reference (PMID)
Citalopram	SSRI	CYP2C19	rs4244285 G/A (*1/*2)	Decreased drug clearance/metabolism and decreased tolerance, especially in combination with another no function allele (*2, *3, *4, *6, *8) (poor metabolizer phenotype) as compared to patients with the CYP2C19 *1/*1 genotype	CPIC Guideline	25974703
Escitalopram	SSRI				CPIC Guideline	25974703
Sertraline	SSRI	CYP2C19	rs4244285 G/A (*1/*2)	Increased clearance as compared to patients with the *2/*2 or *2/*3 diplotype and a decreased clearance as compared to patients with the *1/*1 diplotype	CPIC Guideline	25974703
Amitriptyline	Tricyclic Antidepressant	CYP2C19	rs4244285 G/A (*1/*2)	Decreased metabolism, CYP2C19 alleles *17 rs12248560 and *3 rs4986893, along with clinical factors, may also influence a patient's required dose	CPIC Guideline	2323254; 26094938



Use with Caution (continued)

The drugs below may be less effective or result in adverse effects based on the patient's genotype.

INFECTIOUS DISEASE

Drug	Drug Type	Gene	Variant / Haplotype	Interpretation	Reference Type	Reference (PMID)
Voriconazole	Antifungal	CYP2C19	rs4244285 G/A (*1/*2)	Decreased metabolism of voriconazole as compared to patients with the CYP2C19 *1/*1 diplotype (normal metabolizers) or the CYP2C19 *1/*17 or *17/*17 diplotypes (rapid and ultrarapid metabolizers), or may have increased metabolism as compared to patients with the CYP2C19 *2/*2, *3/*3 or *2/*3 diplotypes (poor metabolizers).	CPIC Guideline	27981572

Normal Response Expected

The drugs below are expected to have a normal response based on the patient's genotype.

Drug Type	Drug	Reference (PMID)	Drug Type	Drug	Reference (PMID)
CARDIOVASCULAR			GASTROENTEROLOGY		
ACE Inhibitors	Captopril	22992668	Proton Pump Inhibitors (PPIs)	Dexlansoprazole	*See drug label
Antiarrhythmic	Digoxin	22992668		Esomeprazole	*See drug label
	Flecainide	22992668		Lansoprazole	*See drug label
	Propafenone	*See drug label		Omeprazole	*See drug label
	Quinidine	*See drug label		Pantoprazole	*See drug label
Anticoagulant	Acenocoumarol	22992668		Rabeprazole	*See drug label
	Phenprocoumon	22992668	Laxatives	Moviprep	*See drug label
	Warfarin	21900891;28198005	PAIN MANAGEMENT		
Beta Blockers	Carvedilol	*See drug label	Nonsteroidal Anti-Inflammatory Drugs (NSAIDS)	Aspirin	22992668
	Timolol	22992668		Celecoxib	*See drug label
	Metoprolol	*See drug label		Diclofenac	22992668
Diuretics	Furosemide	22992668		Flurbiprofen	*See drug label
	Spirolactone	22992668		Piroxicam	*See drug label
Statins	Atorvastatin	22992668	Opioids	Alfentanil	22992668
	Cerivastatin	22992668		Fentanyl	22992668
	Pravastatin	22992668		Heroin	22992668
	Rosuvastatin	*See drug label		Codeine	22205192;24458010
ENDOCRINOLOGY				Methadone	22992668
Antithyroid	Carbimazole	22992668		Morphine	22992668
	Methimazole	22992668		Naloxone	22992668
	Propylthiouracil	22992668		Naltrexone	22992668



Normal Response Expected (continued)

The drugs below are expected to have a normal response based on the patient's genotype.

Drug Type	Drug	Reference (PMID)
ENDOCRINOLOGY (CONT'D.)		
Sulfonylureas (cont'd.)	Chlorpropamide	*See drug label
	Glibenclamide	*See drug label
	Glipizide	*See drug label
Thiazolidinediones	Rosiglitazone	22992668
IMMUNOLOGY		
	Adalimumab	22992668
	Allopurinol	23232549;26094938
	Azathioprine	21270794;23422873
	Cyclosporine	22992668
	Etanercept	22992668
	Infliximab	22992668
	Lesinurad	*See drug label
	Pegloticase	*See drug label
	Probenecid	*See drug label
	Sirolimus	22992668
	Sulfasalazine	*See drug label
	Tacrolimus	25801146
PSYCHIATRY		
Antipsychotics	Amisulpride	22992668
	Aripiprazole	*See drug label
	Brexipiprazole	*See drug label
	Clozapine	*See drug label
	Haloperidol	22992668
	Iloperidone	*See drug label
	Olanzapine	22992668
	Paliperidone	22992668
	Perphenazine	*See drug label
	Pimozide	*See drug label
	Quetiapine	22992668
	Risperidone	22992668
	Thioridazine	*See drug label
	Ziprasidone	22992668
Benzodiazepines	Clobazam	*See drug label

Drug Type	Drug	Reference (PMID)
PAIN MANAGEMENT (CONT'D.)		
Opioids (cont'd.)	Oxycodone	22992668
	Tramadol	*See drug label
Others	Carisoprodol	*See drug label
	Lidocaine	*See drug label
	Prilocaine	*See drug label
NEUROLOGY		
Anticonvulsant	Brivaracetam	*See drug label
	Carbamazepine	23695185
	Lamotrigine	22992668
	Oxcarbazepine	*See drug label
	Phenytoin	25099164
Central ACH Inhibitors	Donepezil	*See drug label
Central Monoamine-Depleting Agents	Tetrabenazine	*See drug label
INFECTIOUS DISEASE		
Antibiotics	Dapsone	*See drug label
	Erythromycin Ethylsuccinate and Sulfisoxazole Acetyl	*See drug label
	Ethambutol	22992668
	Isoniazid	*See drug label
	Mafenide	*See drug label
	Nalidixic acid	*See drug label
	Nitrofurantoin	*See drug label
	Norfloxacin	*See drug label
	Pyrazinamide	22992668
	Rifampin	22992668
	Sulfadiazine	*See drug label
	Sulfamethoxazole	*See drug label
	Sulfisoxazole	*See drug label
	Trimethoprim	*See drug label
Antimalarials	Chloroquine	*See drug label
	Chlorproguanil	22992668
	Primaquine	*See drug label
	Quinine	*See drug label



Normal Response Expected (continued)

The drugs below are expected to have a normal response based on the patient's genotype.

Drug Type	Drug	Reference (PMID)
PSYCHIATRY (CONT'D.)		
Benzodiazepines	Diazepam	*See drug label
	Lorazepam	22992668
	Midazolam	22992668
	Oxazepam	22992668
Selective Serotonin Reuptake Inhibitors	Fluoxetine	*See drug label
	Fluvoxamine	25974703
	Paroxetine	25974703
Serotonin-Norepinephrine Reuptake Inhibitors	Atomoxetine	*See drug label
	Duloxetine	*See drug label
	Venlafaxine	22992668
Tricyclic Antidepressants	Amitriptyline	23486447;27997040
	Clomipramine	23486447;27997040
	Desipramine	23486447;27997040
	Doxepin	23486447;27997040
	Imipramine	23486447;27997040
	Nortriptyline	23486447;27997040
	Protriptyline	*See drug label
	Trimipramine	23486447;27997040
Others	Bupropion	22992668
	Flibanserin	*See drug label
	Mirtazapine	22992668
	Modafinil	*See drug label

Drug Type	Drug	Reference (PMID)
INFECTIOUS DISEASE (CONT'D.)		
Antivirals	Boceprevir	*See drug label
	Peginterferon Alfa-2A	24096968
	Peginterferon Alfa-2B	24096968
	Ribavirin	24096968
	Abacavir	22378157;24561393
	Atazanavir	26417955
	Dolutegravir	*See drug label
	Efavirenz	*See drug label
	Epclusa	*See drug label
	Ledipasvir/Sofosbuvir	*See drug label
	Nevirapine	22992668
	Simeprevir	*See drug label
	Sofosbuvir	*See drug label
	Technivie	*See drug label
	Telaprevir	*See drug label
Zepatier	22992668	

GENOTYPING RESULTS

Gene	Genotype	Phenotype	Variants/ Haplotypes Assayed	Gene	Genotype	Phenotype	Variants/ Haplotypes Assayed
ABCB1	*1/*1	Wildtype	rs2032582, rs1045642, *1/*1, *1/*2, *2/*2	HLA-C	WT/WT	Wildtype	*03:02, *01:02:01
ABCG2	WT/WT	Wildtype	rs2231142	HLA-DPB1	WT/WT	Wildtype	*03:01:01
ACE	WT/WT	Wildtype	rs1799752	HLA-DQA1	WT/WT	Wildtype	*02:01
ADD1	WT/WT	Wildtype	rs4961	HLA-DRB1	WT/WT	Wildtype	*01:01:01
ADORA2A	WT/WT	Wildtype	rs2298383	HMGCR	WT/WT	Wildtype	rs17244841
ANKK1	WT/WT	Wildtype	rs1800497	HTR1A	WT/WT	Wildtype	rs6295
APOE	WT/WT	Wildtype	rs7412	HTR2A	WT/WT	Wildtype	rs7997012



GENOTYPING RESULTS (CONT'D.)

Gene	Genotype	Phenotype	Variants/ Haplotypes Assayed	Gene	Genotype	Phenotype	Variants/ Haplotypes Assayed
ATIC	WT/WT	Wildtype	rs4673993	HTR2C	WT/WT	Wildtype	rs1414334, rs3813929
CBR3	WT/WT	Wildtype	rs1056892	IFNL3	WT/WT	Favorable Response Genotype	rs12979860, rs8099917, rs11881222
CCHCR1	WT/WT	Wildtype	rs746647	ITPA	WT/WT	Wildtype	rs1127354, rs7270101
CES1	WT/WT	Wildtype	rs71647871	KCNIP4	WT/WT	Wildtype	rs145489027
CETP	WT/WT	Wildtype	rs1532624	KIF6	WT/WT	Wildtype	rs20455
CFTR	WT/WT	Wildtype	rs78655421, rs80282562, rs121908757, rs121908755, rs121909005, rs121909013, rs75527207, rs267606723, rs74503330, rs121909041, rs193922525, rs113993960, rs113993959, rs75039782, rs77010898	LPA	WT/WT	Wildtype	rs10455872
COMT	WT/WT	Wildtype	rs4680, rs13306278	LTC4S	WT/WT	Wildtype	rs730012
COQ2	WT/WT	Wildtype	rs4693075	MC4R	WT/WT	Wildtype	rs17782313, rs489693
CRHR1	WT/WT	Wildtype	rs1876828	MTHFR	WT/WT	Wildtype	rs1801133
CRHR2	WT/WT	Wildtype	rs7793837	NAT2	WT/WT	Wildtype	rs1041983, rs1799930, *12, *13, *14, *4, *5, *6, *7
CYP2B6	WT/WT	Wildtype	*1, *6, *18, rs4803419	NQO1	WT/WT	Wildtype	rs1800566
CYP2C19	*1/*1	Wildtype	*1, *2, *3, *4, *5, *6, *7, *8, *12, *9, *10, *17	NT5C2	WT/WT	Wildtype	rs11598702
CYP2C8	WT/WT	Wildtype	rs10509681	NUDT15	WT/WT	Wildtype	rs116855232
CYP2C9	*1/*1	Normal Metabolizer	*1, *2, *3, *5, *6, *8, *11, *4, rs4917639	OPRM1	WT/WT	Wildtype	rs1799971
CYP2D6	*1/*1	Normal Metabolizer	*1, *2, *35, *9, *10, *5, *17, *36, *41, *29, *3, *4, *6, *14, *21, *31, *40, *1XN, *2XN	PTGS1	WT/WT	Wildtype	rs10306114
CYP3A4	*1/*1	Wildtype	*1, *1B, *1G	PTPGR	WT/WT	Wildtype	rs3753380
CYP3A5	*1/*1	Normal Metabolizer	*1, *3, *3A, *1A, *6, *7	SCN1A	WT/WT	Wildtype	rs3812718
CYP4F2	*1/*1	Normal Metabolizer	*1, *3	SEMA3C	WT/WT	Wildtype	rs7779029



GENOTYPING RESULTS (CONT'D.)

Gene	Genotype	Phenotype	Variants/ Haplotypes Assayed	Gene	Genotype	Phenotype	Variants/ Haplotypes Assayed
DPYD	WT/WT	Wildtype	*1, *2A, *13, rs67376798	SLC28A3	WT/WT	Wildtype	rs7853758, rs885004
DRD2	WT/WT	Wildtype	rs1799978, rs1800497, rs1076560	SLC6A4	WT/WT	Wildtype	5-HTTLPR Long allele/long allele
DYNC2H1	WT/WT	Wildtype	rs716274	SLCO1B1	RS4149056 T/C	Decreased activity	rs4149056, rs4149015, rs11045879, *1, *5, *15, *1A, *1B
EPHX1	WT/WT	Wildtype	rs1051740, rs2234922	TANC1	WT/WT	Wildtype	rs264651, rs264631, rs10497203, rs7582141, rs6432512, rs264588
ERCC1	WT/WT	Wildtype	rs3212986, rs11615	TCF7L2	WT/WT	Wildtype	rs7903146
F2	WT/WT	Wildtype	G20210A	TNF	WT/WT	Wildtype	rs1800629
F5	WT/WT	Wildtype	rs6025	TP53	WT/WT	Wildtype	rs1042522
FASTKD3,MTRR	WT/WT	Wildtype	rs1801394	TPMT	*1/*1	Wildtype	*1, *2, *3A, *3B, *3C, *4
FDPS	WT/WT	Wildtype	rs2297480	TYMS	WT/WT	Wildtype	rs151264360
G6PD	WT/WT	Wildtype	Null alleles	UGT1A1	WT/WT	Wildtype	rs887829, rs8175347, rs4148323
GRIK4	WT/WT	Wildtype	rs1954787	UGT1A4	WT/WT	Wildtype	rs2011425
GSTM1	WT/WT	Wildtype	Null alleles	UGT2B15	WT/WT	Wildtype	rs1902023
GSTP1	WT/WT	Wildtype	rs1695	UMPS	WT/WT	Wildtype	rs1801019
HAS3	WT/WT	Wildtype	rs2232228	VDR	WT/WT	Wildtype	rs2228570
HLA-A	WT/WT	Wildtype	*33:03, *31:01:02	VKORC1	WT/WT	Wildtype	rs9923231, rs7294, rs9934438, rs9923231, rs7294, rs2359612, rs8050894, rs17708472, rs2884737, rs61742245, rs7196161
HLA-B	WT/WT	Wildtype	*15:02:01, *57:01:01, *58:01, *13:01:01, *15:11:01, *40:01:01, *35:01:01:01, *38:02:01, *59:01:01:01	XPC	WT/WT	Wildtype	rs2228001
				XRCC1	WT/WT	Wildtype	rs25487

WT = Wildtype, HT = Heterogeneous



METHODS

SEQUENCING

Genomic DNA obtained from the submitted sample is enriched for targeted regions using a hybridization-based protocol and sequenced using Illumina technology. Reads are aligned to the reference sequence (Grch37, standard genome build hg19), and sequence changes are identified and interpreted in the context of a single clinically relevant transcript. Exonic deletions and duplications are called using a copy number variation (CNV) algorithm. The CNV algorithm calculates a statistical likelihood of each copy number state by comparing the depth of sequencing coverage at targeted exons to a baseline depth measure in control samples. A confidence threshold is used for each assertion of copy number state for each exon where the sequence data met a minimum quality standard of >20x depth of unique properly paired reads. This algorithm detects most intragenic deletions and duplications, although rare single-exon events may be missed.

The analytical sensitivity and specificity of this assay is >99% and >99%, respectively. All reportable variants are confirmed by orthogonal technologies as part of our ongoing quality management process. Unless otherwise indicated, all targeted regions were sequenced with >20x depth of coverage. Regions with a read depth below this are supplemented with orthogonal testing, if they contain previously reported pathogenic variants. The assay targets all coding regions of the indicated transcript, 10 base pairs of flanking intronic sequence, and specific intronic and intragenic genomic regions demonstrated to be causative of disease. However, for some genes, only targeted loci are analyzed.

All data is processed and analyzed using Elements Software Version 1.

Phosphorus can be contacted via phone at 1-855-746-7423 or by email at support@phosphorus.com.

LIMITATIONS

Although this test is highly accurate, no genetic test is 100% sensitive. This analysis is designed to detect variants with pharmacogenomics association within the genes included in this assay. Hence this analysis will not detect novel sequence variants in the promoter region and other non-coding regions, as well as it does not assay untranslated exons. Also, the sensitivity to detect insertions and deletions larger than 15 base pairs but smaller than a full exon may be reduced. Some exons of a few individual genes have inherent sequence properties that yield suboptimal data, and pathogenic variants in those regions may not be reliably identified. The low-level mosaicism will not be detected. Moreover, this analysis does not detect every pathogenic variant associated with this disease because of genes not included in the current panel or unknown to be associated with the disease at this time. It also does not test for all known genetic diseases. Errors in testing (both false positives and false negatives) may also occur for reasons that include, but are not limited to specimen issues (e.g. inaccurately marked samples causing sample mix-up, DNA quality and quantity not meeting minimum requirements), rare genetic variants interfering with analysis, assay technical limitations, biological factors (e.g. recent blood transfusions, circulating hematolymphoid neoplasm, or history of bone marrow transplantation), and other technical issues. If a pathogenic variant is detected, the patient may be a carrier of, affected with, predisposed to, or at risk for certain disease(s) or condition(s) associated with that variant. If no pathogenic variant is found, the patient may be at reduced risk of being carrier of, affected with, predisposed to, or at risk for the disease(s) or condition(s) tested for in the current panel. However, further testing may be necessary, since negative test results may reduce, but do not eliminate, the chance that the patient is a carrier of, affected with, predisposed to, or at risk of having said disease(s) or condition(s). In addition, other pathogenic variant(s) or factors that are not included in our services may impact an individual's risk of, or predisposition to certain disease(s) or condition(s). Thus, this report does not provide definitive conclusions regarding risk of, predisposition to, or diagnosis of certain disease(s) or condition(s).

DISCLAIMER

This report reflects the analysis of an extracted DNA sample; and it does not constitute medical advice. Any questions or concerns regarding the contents of this report or any prevention, cure, mitigation, or treatment of a medical condition or disease should be directed to a qualified medical professional.

This test was developed and its performance characteristics determined by Phosphorus Diagnostics, LLC. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing. These test results are to be used for clinical purposes and should not be regarded as investigational or for research.

This assay only detects and reports variants with known pharmacogenomic associations, as listed in the Genotyping Results section, and does not report all variants in the genes assayed.

VARIANT CLASSIFICATION

This test includes analysis of variants with strong evidence of pharmacogenomic association. The variants included in this test are either classified as evidence level A and B by the Clinical Pharmacogenetics Implementation Consortium (CPIC), evidence level 1 and 2 by PharmGKB, or referenced in an FDA drug label.

SIGNED BY

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