Sample Patient

DOB: 1950-01-01
Clinician: T Provider
Order No: AV0999998

PredictScript™ POLY
Pharmacogenomic Test

Phenomics HEALTH™

Sample Analysis: Apr. 13, 2023 12:13 EDT
Sample Collection: Apr. 13, 2023 12:04 EDT

For patients, consult your healthcare provider prior to any medication or dose changes.

This pharmacogenomic report is based on genotypes analyzed by Phenomics Health and the patient's currently available medication list to support clinical treatment decisions.

***Current medications: AMITRIPTYLINE, CARBAMAZEPINE, CLOPIDOGREL, SIMVASTATIN, TRAZODONE, WARFARIN**

PRESCRIBE AS DIRECTED

Cardiovascular, Metabolic & Gastrointestinal Agents

Amiodarone (Pacerone®)
Amlodipine (Norvasc®)
Apixaban (Eliquis®)
Atenolol (Tenormin®)
Bisoprolol (Zebeta®)
Carvedilol (Coreg®)
***Clopidogrel (Plavix®)**
Dexlansoprazole (Dexilant®)
Diltiazem (Cardizem®, Tiazac®)
Esomeprazole (Nexium®)
Flecainide (Tambocor®)
Fluvastatin (Lescol®)
Glimepiride (Amaryl®)
Glipizide (Glucotrol®)
Glyburide (Diabeta®)
Irbesartan (Avapro®)
Labetalol (Trandate®)
Lansoprazole (Prevacid®)
Losartan (Cozaar®)
Meclizine (Antivert®)
Metoclopramide (Reglan®)
Metoprolol (Lopressor®)
Nateglinide (Starlix®)
Nebivolol (Bystolic®)
Nifedipine (Procardia®)
Ondansetron (Zofran®)
Pantoprazole (Protonix®)
Propafenone (Rythmol®)
Propranolol (Inderal®)
Rabeprazole (AcipHex®)
Ranolazine (Ranexa®)
Repaglinide (Prandin®)
Rivaroxaban (Xarelto®)
Ticagrelor (Brilinta®)
Timolol (Betimol®)
Torsemide (Demadex®)

Antidepressants and Anxiolytics

Alprazolam (Xanax®)
***Amitriptyline (Elavil®)**
Amoxapine (Asendin®)
Bupropion (Wellbutrin®)
Buspirone (BuSpar®)
Citalopram (Celexa®)
Clobazam (Onfi®)
Clomipramine (Anafranil®)
Clonazepam (Klonopin®)
Desipramine (Norpramin®)
Desvenlafaxine (Pristiq®)
Diazepam (Valium®)
Doxepin (Sinequan®)
Duloxetine (Cymbalta®)
Escitalopram (Lexapro®)
Eszopiclone (Lunesta®)
Fluoxetine (Prozac®)
Fluvoxamine (Luvox®)
Imipramine (Tofranil®)
Ketamine (Ketalar®)
Lorazepam (Ativan®)
Mirtazapine (Remeron®)
Nortriptyline (Pamelor®)
Oxazepam (Serax®)
Paroxetine (Paxil®)
Protriptyline (Vivactil®)
Sertraline (Zoloft®)
Temazepam (Restoril®)
***Trazodone (Desyrel®)**
Trimipramine (Surmontil®)
Venlafaxine (Effexor®)
Vilazodone (Viibryd®)
Vortioxetine (Trintellix®)
Zolpidem (Ambien®)

Analgesics and Other CNS Agents

Amphetamine (Adderall®)
Atomoxetine (Strattera®)
Celecoxib (Celebrex®)
Clonidine (Catapres®)
Codeine
Dexmethylphenidate (Focalin®)
Dextroamphetamine (Adderall®)
Diclofenac (Voltaren®)
Donepezil (Aricept®)
Fentanyl (Sublimaze®)
Flurbiprofen (Ansaid®)
Galantamine (Razadyne®)
Guanfacine (Intuniv®)
Hydrocodone (Norco®)
Hydromorphone (Exalgo®)
Ibuprofen (Advil®, Motrin®)
Indomethacin (Indocin®)
Lisdexamfetamine (Vyvanse®)
Lithium (Lithobid®, Eskalith®)
Lofexidine (Lucemyra®)
Lornoxicam
Meloxicam (Mobic®)
Methadone (Methadose®)
Methylphenidate (Concerta®)
Morphine (MS Contin®)
Naloxone (Narcan®)
Naltrexone (ReVia®)
Naproxen (Naprosyn®)
Oxycodone (Roxicodone®)
Piroxicam (Feldene®)
Tenoxicam
Tramadol (Ultram®)

Antipsychotics and Anticonvulsants

Aripiprazole (Abilify®)
Brivaracetam (Briviact®)
***Carbamazepine (Epitol®, Tegretol®)**
Cariprazine (Vraylar®)
Chlorpromazine (Thorazine®)
Fluphenazine (Prolixin®)
Fosphenytoin (Cerebyx®)
Haloperidol (Haldol®)
Iloperidone (Fanapt®)
Lamotrigine (Lamictal®)
Lurasidone (Latuda®)
Olanzapine (Zyprexa®)
Oxcarbazepine (Trileptal®)
Paliperidone (Invega®)
Perphenazine (Trilafon®)
Phenytoin (Dilantin®)
Pimozide (Orap®)
Primidone (Mysoline®)
Quetiapine (Seroquel®)
Risperidone (Risperdal®)
Thioridazine (Mellaril®)
Topiramate (Topamax®)
Valproic Acid (Depakene®)

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Cardiovascular, Metabolic & Gastrointestinal Agents	Antidepressants and Anxiolytics	Analgesics and Other CNS Agents	Antipsychotics and Anticonvulsants

PRESCRIBE AS DIRECTED, CONTINUED

Tropisetron			
Valsartan (Diovan®)			
Verapamil (Verelan®)			
***Warfarin (Jantoven®)**			

MAJOR GENE-DRUG INTERACTIONS

Atorvastatin (Lipitor®)			Brexpiprazole (Rexulti®) 1,2
Lovastatin (Mevacor®)			Clozapine (Clozaril®) 1,2
Pravastatin (Pravachol®)			
Rosuvastatin (Crestor®)			
***Simvastatin (Zocor®)**			

MODERATE GENE-DRUG INTERACTIONS

Esketamine (Spravato®) 3	Buprenorphine (Subutex®) 3	Ziprasidone (Geodon®) 3

MTHFR - REDUCED FUNCTION

Decreased MTHFR activity with either the rs1801133 or rs1801131 mutation reduces MTHFR conversion by 25-50%. When either variant is present, consider supplementation with L-methyl-folate or B complex.

CLINICAL IMPACT

1. Medication is contraindicated for this genotype
2. Genotype may result in higher risk for adverse drug reactions
3. Genotype may result in reduced efficacy
4. Higher systemic concentrations may require lower doses
5. Lower systemic concentrations may require higher doses
6. Medication efficacy based on non-genotype clinical values

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MEDICATIONS AFFECTED BY MAJOR INTERACTIONS

Medication	Genes	Recommendations	Source
CURRENT MEDICATIONS			
***Simvastatin**	*SLCO1B1*	Prescribe an alternative statin depending on the desired potency (see source for alternative statins). If simvastatin therapy is warranted, limit dose to d20mg/day.	CPIC
Atorvastatin	*SLCO1B1*	Prescribe d40mg as a starting dose and adjust doses of atorvastatin based on disease-specific guidelines. Prescriber should be aware of possible increased risk for myopathy especially for 40mg dose. If dose >40mg needed for desired efficacy, consider combination therapy (i.e., atorvastatin plus non-statin guideline directed medical therapy)	CPIC
Brexpiprazole	*DRD2*	May cause significant variability in response. Avoid use.	Ref(s) 29
Clozapine	*HTR2C*	May cause an increased risk of drug-induced weight gain. Avoid use.	Ref(s) 16, 56, 57
Clozapine	*MC4R*	May cause an increased risk of drug-induced weight gain. Avoid use.	Ref(s) 16, 56, 57
Lovastatin	*SLCO1B1*	Prescribe an alternative statin depending on the desired potency (see source for alternative statins). If lovastatin therapy is warranted, limit dose to d20mg/day.	CPIC
Pravastatin	*SLCO1B1*	Prescribe desired starting dose and adjust doses of pravastatin based on disease-specific guidelines. Prescriber should be aware of possible increased risk for myopathy with pravastatin especially with doses >40mg per day.	CPIC
Rosuvastatin	*SLCO1B1*	Consider testing for ABCG2 prior to use. Based on SLCO1B1, prescribe desired starting dose and adjust doses of rosuvastatin based on disease-specific and specific population guidelines. Prescriber should be aware of possible increased risk for myopathy especially for doses >20mg.	CPIC

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MEDICATIONS AFFECTED BY MODERATE INTERACTIONS

Medication	Genes	Recommendations	Source
Buprenorphine	*OPRM1*	May cause a decrease in drug efficacy.	Ref(s) 30, 31, 32, 33, 34
Esketamine	*BDNF*	May cause a decrease in drug efficacy.	Ref(s) 79
Ziprasidone	*DRD2*	May cause a decrease in drug efficacy.	Ref(s) 45, 47, 48, 49, 50, 51, 165, 166, 167

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PATIENT GENETICS

Gene	Genotype		Phenotype
ABCB1	rs2032582, rs1045642, rs1128503	C/C, G/G, G/G	Decreased Function, Decreased Function, Decreased Function
ADRA2A	rs1800544	C/C	Decreased Function
BDNF	rs6265	C/C	Normal Function
CACNA1C	rs3819536, rs2007004	A/A, A/G	Decreased Response, Decreased Response
COMT	rs4680	A/G	Decreased Function
CPS1	rs715	C/C	Increased Risk
CYP1A2	rs11631198, rs2134688	No Call, No Call, No Call	Inconclusive, Inconclusive, Inconclusive
CYP2B6		*1/*1	Normal Metabolizer
CYP2C19	rs61886222, rs77957608	*1/*17, A/A, G/G	Rapid Metabolizer, Normal Function, Normal Function
CYP2C9		*1/*1	Normal Metabolizer
CYP2D6		2N *2/*4	Intermediate Metabolizer
CYP3A4	rs17161937, rs2740574	*1/*1, A/A, T/T	Normal Metabolizer, Unknown Function, Unknown Function
CYP3A5		No Call	Inconclusive
CYP4F2		No Call	Inconclusive
DRD2	rs1799978	T/T	Normal Function
GRIK1	rs2832407	A/C	Increased Response
GRIK4	rs12800734, rs1954787	G/G, No Call	Normal Function, Inconclusive
*HLA-A*31:01*			Negative/Negative
*HLA-B*15:02*			Negative/Negative
HTR2A	rs6313, rs6314, rs9316233, rs6305, rs6311, rs2770296	A/A, A/G, C/G, No Call, T/T, T/T	Altered Function, Increased Response, Decreased Response, Inconclusive, Altered Function, Decreased Response
HTR2C	rs3813929, rs518147	C/C, No Call	Normal Function, Inconclusive
MC4R	rs489693	C/C	Normal Function

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PATIENT GENETICS

Gene	Genotype		Phenotype
OPRM1	rs1799971	A/A	Normal Function
SLCO1B1		*1/*5	Decreased Function
UGT1A1		No Call	Inconclusive
UGT2B15		No Call	Inconclusive
VKORC1		*1/*1	Normal Metabolizer

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TEST PANEL INFORMATION

The PredictScript clinical decision support tool is based on evidence from clinical trials and scientific literature. Detailed information is available upon request, and from www.phenomicshealth.com/references. Results from studies of the genetic basis of drug response variation and adverse drug events have been examined in hundreds of thousands of curated patient samples and updated based on measures of scientific and clinical validity. In parallel, ongoing pharmacometabolomic analyses from Phenomics Health Inc.'s proprietary PrecisMed® diagnostic platform can help power improvements in accuracy and inform the validation of PredictScript.

Primary information on single nucleotide polymorphisms (SNPs), copy number variants (CNVs), and other genome variants were referenced from clinical significance Reference SNP reports of the National Center for Biotechnology Information (NCBI), National Library of Medicine (NLM), and National Institutes of Health (NIH)[9]. These include results from the Human Genome Variation Society[10], the reference genome browser of the University of California Santa Cruz[11], and the Clinical Genome consortium[5].

Genotypes specified by rsID numbers are informed by the NCBI of the NIH and, where applicable, star (*) alleles as described on Phenomics Health Inc. web portal. All genotype data are translated from star allele nomenclature into rsID numbers, based on standards used in clinical genetics[6,7]. Star alleles are also provided to increase usability; however, star allele haplotypes and diplotypes were derived based on patients of European ancestry and may not be applicable to all patients. Assignment of variants to specific genes is provided for reference only, as polymorphisms located in a specified gene may not always be indicative of the function of the gene in which it is located.

The following genetic variants are evaluated in this test: *CYP1A2* (rs11631198, rs12720461, rs2069514, rs2069526, rs2134688, rs2470890, rs35694136, rs3818740, rs72547511, rs72547513, rs762551); *CYP2B6* (rs11083595, rs2054675, rs2279343, rs28399499, rs3745274, rs8109525); *CYP2C9* (rs1057910, rs1799853, rs28371685, rs28371686, rs56165452, rs7900194, rs9332131, rs9332239); *CYP2C19* (rs12248560, rs2093434, rs28399504, rs4244285, rs4986893, rs56337013, rs61886222, rs77957608); *CYP2D6* (rs1065852, rs1080985, rs1135840, rs16947, rs201377835, rs28371706, rs28371725, rs35742686, rs3892097, rs5030655, rs5030656, rs5030862, rs5030867, rs59421388, rs72549353, rs765776661, rs769258, rs774671100); *CYP3A4/CYP3A5* (rs17161937, rs2740574, rs35599367, rs10264272, rs41303343, rs776746); *CYP4F2* (rs2108622); *ABCB1* (rs1128503, rs2032582, rs1045642); *ADRA2A* (rs1800544); *BDNF* (rs6265); *CACNA1C* (rs3819536, rs2007004); *COMT* (rs4680); *CPS1* (rs715); *DRD2* (rs1799978); *GRIK1* (rs2832407); *GRIK4* (rs1954787, rs12800734); *HLA-A* (rs1116221, rs2523979, rs1061235); *HLA-B* (rs10484555, rs144012689); *HTR2A* (rs6311, rs6305, rs9316233, rs2770296, rs6313, rs6314); *HTR2C* (rs3813929, rs518147); *MC4R* (rs489693); *OPRM1* (rs1799971); *SLCO1B1* (rs4149056); *UGT1A1* (rs4148323, rs35350960, rs887829); *UGT2B15* (rs1902023); and *VKORC1* (rs9923231).

This test does not provide medical advice and is not approved by the U.S. Food & Drug Administration (FDA). Information on pharmacogene variants specified by the FDA[1,2], Clinical Pharmacogenetics Implementation Consortium (CPIC)[3], and Dutch Pharmacogenetics Working Group (DPWG) of the European Medicines Agency[4], including genes involved in absorption, distribution, metabolism, and excretion (ADME), are sourced from Sequence2Script[12]. Further information provided by this test may be based on Phenomics Health's interpretation of scientific literature and the pharmacokinetic and pharmacodynamic properties of drugs sourced outside of Sequence2Script. The information provided in this report is believed to be current, accurate, and consistent with available scientific literature and the described research. This information may not necessarily be clinically validated for any specific patient population. The pharmacogenomic technology and report is used to support clinical decisions. The healthcare professional directly managing the patient's care is responsible for all decisions made regarding said patient's care, including prescribing decisions made with consideration for the patient's genetic information.

This test was performed by a lab with CLIA #23D2194915 and approved by the Laboratory Director, Dr. Wenbing Chen.

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PATIENT PHARMACOGENE CARD

This test was developed and its performance characteristics determined by Phenomics Health Inc. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing. This test is used for clinical purposes, though results should not be intended for use as a sole means for a clinical diagnosis or patient management decisions. It should not be regarded as investigational or for research.