PredictScript™ CNS
Pharmacogenomic Test

Phenomics HEALTH™

Jane Doe

DOB: 01/01/1955 Clinician: John Smith

Sample Analysis: Jan. 28, 2022 11:25 EST
Sample Collection: Jan. 01, 2022 22:13 EST
Order No: SA0000001.2-TH

*Current medications: ARIPIPRAZOLE, ATORVASTATIN, CLOPIDOGREL, ESCITALOPRAM, GLIPIZIDE, METOPROLOL, TRAMADOL

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

Antidepressants and Anxiolytics	Analgesics and Other CNS Agents	Antipsychotics and Anticonvulsants

PRESCRIBE AS DIRECTED

Antidepressants and Anxiolytics	Analgesics and Other CNS Agents	Antipsychotics and Anticonvulsants
Alprazolam (Xanax®)	Buprenorphine (Subutex®)	Carbamazepine (Epitol®, Tegretol®)
Amoxapine (Asendin®)	Celecoxib (Celebrex®)	Cariprazine (Vraylar®)
Bupropion (Wellbutrin SR®)	Clonidine (Catapres®)	Chlorpromazine (Thorazine®)
Buspirone (BuSpar®)	Dexmethylphenidate (Focalin®)	Clozapine (Clozaril®, FazaClo®)
Citalopram (Celexa®)	Dextroamphetamine(Adderall®)	Fluphenazine (Prolixin®)
Clobazam (Onfi®)	Diclofenac (Voltaren®)	Lurasidone (Latuda®)
Clonazepam (Klonopin®)	Fentanyl (Sublimaze®)	Olanzapine (Zyprexa®)
Desvenlafaxine (Pristiq®)	Flurbiprofen (Ansaid®)	Paliperidone (Invega®)
Diazepam (Valium®)	Guanfacine (Intuniv®)	Phenytoin (Dilantin®)
Duloxetine (Cymbalta®)	Hydromorphone (Exalgo®)	Pimozide (Orap®)
***Escitalopram (Lexapro®)**	Ibuprofen (IBU, Motrin®)	Primidone (Mysoline®)
Esketamine (Spravato®)	Indomethacin (Indocin SR)	Quetiapine (Seroquel®)
Eszopiclone (Lunesta®)	Lisdexamfetamine (Vyvanse®)	Risperidone (Risperdal®)
Ketamine (Ketalar®)	Lofexidine (Lucemyra®)	Thioridazine (Mellaril®)
Lorazepam (Ativan®)	Lornoxicam (Xefocam®)	Topiramate (Topamax®, Topiragen®)
Fluoxetine (Prozac®)	Meloxicam (Mobic®)	
Fluvoxamine (Luvox®)	Methadone (Dolophine®, Methadose®)	
Imipramine (Tofranil®)	Methylphenidate (Concerta®)	
Mirtazapine (Remeron®)	Morphine (MS Contin®)	
Oxazepam (Serax®)	Naloxone (Narcan®)	
Paroxetine (Paxil®)	Naltrexone (ReVia®)	
Protriptyline (Vivactil®)	Naproxen (Naprosyn®)	
Temazepam (Restoril®)	Oxycodone (Roxicodone®)	
Trazodone (Desyrel®)	Piroxicam (Feldene®)	
Trimipramine (Surmontil®)	Tenoxicam (Mobiflex®)	
Zolpidem (Ambien®)		

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Antidepressants and Anxiolytics	Analgesics and Other CNS Agents	Antipsychotics and Anticonvulsants

MAJOR GENE-DRUG INTERACTIONS

Antidepressants and Anxiolytics		Analgesics and Other CNS Agents		Antipsychotics and Anticonvulsants	
Amitriptyline (Elavil®)	5	Donepezil (Aricept®)	4	Brexpiprazole (Rexulti®)	4
Clomipramine (Anafranil®)	5	Codeine (Fioricet®)	4	Brivaracetam (Briviact®)	4
Desipramine (Norpramin®)	2, 5	***Tramadol (Ultram®)**	3	Fosphenytoin (Cerebyx®)	1,2,4
Vilazodone (Viibryd®)	3			Haloperidol (Haldol®)	4
				Iloperidone (Fanapt®)	2,4
				Lamotrigine (Lamictal®)	3
				Ziprasidone (Geodon®)	3

MODERATE GENE-DRUG INTERACTIONS

Antidepressants and Anxiolytics		Analgesics and Other CNS Agents		Antipsychotics and Anticonvulsants	
Doxepin (Sinequan®)	1,4	Amphetamine(Adderall®)	2,4	***Aripiprazole (Abilify®)**	2,4
Nortriptyline (Pamelor®)	5	Atomoxetine (Strattera®)	2,4	Oxcarbazepine (Trileptal®)	1,2
Sertraline (Zoloft®)	4	Hydrocodone (Lorcet HD®, Lortab®, Norco®)	3	Perphenazine (Trilafon®)	2,4
Venlafaxine (Effexor XR®)	4	Galantamine	4	Valproic Acid (Depakene®)	2
Vortioxetine (Trintellix®)	4	Lithium (Eskalith®, Lithobid®)	2		

CLINICAL IMPACT

1. Medication is contraindicated by the FDA 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 is based on clinical values other than genotype.

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MEDICATIONS AFFECTED BY MAJOR INTERACTIONS

Medication	Genes	Recommendations	Source
Amitriptyline	*CYP2C19, CYP2D6*	Avoid use. If warranted, consider a 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.	CPIC
Brexpiprazole	*CYP2D6*	Use half the standard dose.	DPWG
	DRD2	May cause significant variability in response. Avoid use.	Ref 29
Brivaracetam	*CYP2C19*	May have higher systemic concentrations and higher adverse reaction risk.	FDA
Clomipramine	*CYP2C19, CYP2D6*	Avoid use. If warranted, consider a 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.	CPIC
Codeine	*CYP2D6*	Avoid codeine use because of possibility of diminished analgesia. If opioid use is warranted, consider a non-tramadol opioid.	CPIC
	OPRM1	May cause a decrease in drug efficacy	Ref 58, 59, 61, 62, 63, 64
Desipramine	*CYP2D6*	Avoid use. If warranted, consider a 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.	CPIC
Donepezil	*CYP2D6*	Alters systemic concentration	FDA
Fosphenytoin	*CYP2C9, HLA-B*	If patient is phenytoin-naïve, do not use phenytoin/ fosphenytoin. Avoid carbamazepine and oxcarbazepine.	CPIC
Haloperidol	*CYP2D6*	Reduce dose by 50% or select alternative drug (e.g., flupenthixol, fluphenazine, quetiapine, olanzapine, clozapine).	DPWG
Iloperidone	*CYP2D6*	Greater risk for higher systemic concentrations and higher adverse reaction risk (QT prolongation). Reduce dose by 50%.	FDA
Lamotrigine	*ABCB1*	May cause a variable drug response. Consider an alternative	Ref 96
***Tramadol**	*CYP2D6*	Avoid use because of possibility of diminished analgesia. If opioid use is warranted, consider a non-codeine opioid.	CPIC
Vilazodone	*ABCB1*	May require a lower dose due to an increase in drug exposure	Ref 97, 160, 161, 162, 163, 164
Ziprasidone	*DRD2*	May cause a decrease in drug efficacy	Ref 45, 47, 48, 49, 50, 51, 165, 166, 167

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MEDICATIONS AFFECTED BY MODERATE INTERACTIONS

Medication	Genes	Recommendations	Source
Amphetamine	*CYP2D6*	May affect systemic concentrations and adverse reaction risk. Consider lower starting dosage or use alternative agent.	FDA
***Aripiprazole**	*CYP2D6*	Reduce maximum dose to 10 mg/day or 300mg/month (67% of the maximum recommended dose).	DPWG
Atomoxetine	*CYP2D6*	CHILD: Initiate with a dose of 0.5 mg/kg/day and if no clinical response and in the absence of adverse events after 2 weeks, consider a proportional dose increase. If unacceptable side effects are present at any time, consider a reduction in dose. ADULT: Initiate with a dose of 40 mg/day and if no clinical response and in the absence of adverse events after 2 weeks increase dose to 80 mg/day. If response is inadequate after 2 weeks consider a proportional dose increase. If unacceptable side effects are present at any time, consider a reduction in dose.	CPIC
Doxepin	*CYP2C19, CYP2D6*	Avoid use. If warranted, consider a 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.	CPIC
Galantamine	*CYP2D6*	Results in higher systemic concentrations. Titrate dosage based on tolerability.	FDA
Hydrocodone	*CYP2D6*	Use label recommended age- or weight-specific dosing. If no response and opioid use is warranted, consider non-codeine and non-tramadol opioid.	CPIC
Amphetamine	*DRD2*	May affect systemic concentrations and adverse reaction risk. Consider lower starting dosage or use alternative agent.	FDA
Lithium	*CACNA1C*	May cause an increased risk of adverse drug reaction. Avoid use	Ref 17, 22, 24, 28
Nortriptyline	*CYP2D6*	Avoid use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6 (e.g., escitalopram). If a nortriptyline is warranted, consider a 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.	CPIC
Oxcarbazepine	*HLA-B*	If patient is oxcarbazepine naïve, do not use oxcarbazepine.	CPIC
Perphenazine	*CYP2D6*	Greater risk of side effects due to higher drug concentrations	FDA

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MEDICATIONS AFFECTED BY MODERATE INTERACTIONS

Medication	Genes	Recommendations	Source
Sertraline	*CYP2C19* *HTR2A*	Initiate therapy with recommended starting dose (25mg/d or 50mg/d, depending on age and indication). May cause an increased risk of adverse drug reaction. Consider an alternative	CPIC Ref 6, 8, 9
Valproic Acid	*CPS1*	May cause an increased risk of severe adverse drug reaction. Avoid use	Ref 20
Venlafaxine	*CYP2D6*	Select alternative drug not predominantly metabolized by CYP2D6 (e.g., escitalopram) or reduce the dose and monitor patient's plasma metabolite level.	DPWG
Vortioxetine	*CYP2D6*	Greater risk of higher systemic concentrations. The maximum recommended dose is 10 mg/d.	FDA

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PATIENT GENETICS

Gene	Genotype		Phenotype
ABCB1		A/A, A/A, A/A	Normal Function
ADRA2A	rs1800544	C/C	Decreased Function
BDNF		C/C	Normal Function
CACNA1C		G/G, G/G	Normal Function
COMT	rs4680	A/A	Decreased Function
CPS1		T/T	Normal Function
CYP1A2		*1/*1	Normal Function
CYP2B6		*1/*1	Normal Function
CYP2C9		*1/*1	Normal Function
CYP2C19		*1/*1	Normal Function
CYP2D6	rs1135840, rs16947	2N *1/*2	Increased Function
CYP3A4		*1/*1	Normal Function
CYP3A5		*1/*1	Normal Function
DRD2		T/T	Normal Function
GRIK1		C/C	Normal Function
GRIK4	rs1954787	C/C	Increased Function
HLA-A	rs1061235	*31:01	Increased Risk
HLA-B	rs10484555, rs144012689	*15:02	Increased Risk
HTR2A		C/C, G/G, C/C, C/C, G/G, G/G	Normal Function
HTR2C		C/C, C/C	Normal Function
MC4R		C/C	Normal Function
OPRM1	rs1799971	G/G	Decreased Function
UGT1A1	rs35350960	*27/*27	Decreased Function
UGT2B15		*1/*1	Normal Function

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TEST PANEL INFORMATION

The PredictScript™ diagnostic assay is based on evidence from clinical trials and scientific literature. Detailed information about references 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 the Company's proprietary PrecīsMed® diagnostic platform can help power improvements in accuracy and inform the validation of the PredictScript™ assay.

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 (rs762551, rs2069514, rs12720461, rs35694136, rs2069526, rs72547511, rs72547513, rs11631198, rs2093434, rs2470890, rs2134688. rs3818740); CYP2B6 (rs2279343, rs3745274, rs28399499, rs11083595, rs8109525, rs2054675); CYP2C9 (rs1799853, rs1057910, rs56165452, rs28371686, rs9332131, rs7900194, rs28371685, rs9332239); CYP2C19 (rs4244285, rs4986893, rs28399504, rs56337013, rs12248560, rs77957608, rs61886222); CYP2D6 (rs28371706, rs1065852, rs1135840, rs16947, rs3892097, rs769258, rs5030862, rs201377835, rs5030867, rs765776661, rs5030656, rs35742686, rs72549353, rs5030655, rs774671100, rs1080985, rs59421388, rs28371725); CYP3A4/CYP3A5 (rs2740574, rs35599367, rs776746, rs10264272, rs17161937, rs41303343); 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); UGT1A1 (rs4148323, rs35350960 rs887829); and UGT2B15 (rs1902023).

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 Srinivas Narayan, Ph.D.

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PATIENT PHARMACOGENE CARD

Patient Pharmacogenomic Gene-Drug Interaction Card

Jane Doe

FOR USE BY YOUR HEALTHCARE PROFESSIONALS ONLY

This card contains information about medications that should be avoided based on your genetics. This may help your healthcare provider make clinical decisions for your medication therapy to avoid certain gene-drug interactions.

Do NOT stop or change your medication or dosage without discussing with your healthcare provider

MAJOR GENE-DRUG INTERACTIONS

Antidepressants and Anxiolytics
Amitriptyline
Clomipramine
Desipramine
Vilazodone

Analgesics and Other CNS Agents
Donepezil
Codeine
Tramadol

Antipsychotics and Anticonvulsants
Fosphenytoin
Haloperidol
Iloperidone
Lamotrigine
Ziprasidone