CNS Test 001

DOB: 2001-03-02
Clinician: Phenomics
Order No: SA0011403-B03

PredictScript™ CNS
Pharmacogenomic Test

Phenomics HEALTH™

Sample Analysis: Feb. 10, 2023 09:14 EST
Sample Collection: Feb. 08, 2023 16:00 EST

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: ARIPIPRAZOLE, BENZTROPINE, HALOPERIDOL, PROPRANOLOL, TRAZODONE**

PRESCRIBE AS DIRECTED

Antidepressants and Anxiolytics

Alprazolam (Xanax®)
Amitriptyline (Elavil®)
Amoxapine (Asendin®)
Buspirone (BuSpar®)
Clobazam (Onfi®)
Clomipramine (Anafranil®)
Clonazepam (Klonopin®)
Desipramine (Norpramin®)
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®)
Temazepam (Restoril®)
Trimipramine (Surmontil®)
Venlafaxine (Effexor®)
Vilazodone (Viibryd®)
Vortioxetine (Trintellix®)
Zolpidem (Ambien®)

Analgesics and Other CNS Agents

Amphetamine (Adderall®)
Atomoxetine (Strattera®)
Clonidine (Catapres®)
Codeine
Dexmethylphenidate (Focalin®)
Diclofenac (Voltaren®)
Donepezil (Aricept®)
Fentanyl (Sublimaze®)
Galantamine (Razadyne®)
Guanfacine (Intuniv®)
Hydrocodone (Norco®)
Hydromorphone (Exalgo®)
Indomethacin (Indocin®)
Lisdexamfetamine (Vyvanse®)
Lithium (Lithobid®, Eskalith®)
Methadone (Methadose®)
Methylphenidate (Concerta®)
Morphine (MS Contin®)
Naloxone (Narcan®)
Naltrexone (ReVia®)
Naproxen (Naprosyn®)
Oxycodone (Roxicodone®)
Tramadol (Ultram®)

Antipsychotics and Anticonvulsants

***Aripiprazole (Abilify®)**
Brivaracetam (Briviact®)
Carbamazepine (Epitol®, Tegretol®)
Cariprazine (Vraylar®)
Chlorpromazine (Thorazine®)
Fluphenazine (Prolixin®)
***Haloperidol (Haldol®)**
Iloperidone (Fanapt®)
Lurasidone (Latuda®)
Olanzapine (Zyprexa®)
Oxcarbazepine (Trileptal®)
Paliperidone (Invega®)
Perphenazine (Trilafon®)
Pimozide (Orap®)
Primidone (Mysoline®)
Quetiapine (Seroquel®)
Risperidone (Risperdal®)
Thioridazine (Mellaril®)

CNS Test 001

DOB: 2001-03-02
Clinician: Phenomics
Order No: SA0011403-B03

PredictScript™ CNS
Pharmacogenomic Test

Phenomics HEALTH™

Sample Analysis: Feb. 10, 2023 09:14 EST
Sample Collection: Feb. 08, 2023 16:00 EST

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: ARIPIPRAZOLE, BENZTROPINE, HALOPERIDOL, PROPRANOLOL, TRAZODONE**

MAJOR GENE-DRUG INTERACTIONS

Antidepressants and Anxiolytics		Analgesics and Other CNS Agents		Antipsychotics and Anticonvulsants	
Sertraline (Zoloft®)	2	Dextroamphetamine (Adderall®)	2	Brexpiprazole (Rexulti®)	1,2
***Trazodone (Desyrel®)**	**2**	Meloxicam (Mobic®)		Clozapine (Clozaril®)	1,2
		Piroxicam (Feldene®)	1,2	Fosphenytoin (Cerebyx®)	
		Tenoxicam	1,2	Lamotrigine (Lamictal®)	2
				Phenytoin (Dilantin®)	
				Valproic Acid (Depakene®)	1,2

MODERATE GENE-DRUG INTERACTIONS

Bupropion (Wellbutrin®)	5	Buprenorphine (Subutex®)	5	Topiramate (Topamax®)	3
Citalopram (Celexa®)	3	Celecoxib (Celebrex®)	2,4	Ziprasidone (Geodon®)	3
Desvenlafaxine (Pristiq®)	3	Flurbiprofen (Ansaid®)	2,4		
Esketamine (Spravato®)	3	Ibuprofen (Advil®, Motrin®)	2,4		
		Lofexidine (Lucemyra®)	3		
		Lornoxicam	2,4		

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

CNS Test 001

DOB: 2001-03-02
Clinician: Phenomics
Order No: SA0011403-B03

Sample Analysis: Feb. 10, 2023 09:14 EST
Sample Collection: Feb. 08, 2023 16:00 EST

MEDICATIONS AFFECTED BY MAJOR INTERACTIONS

Medication	Genes	Recommendations	Source
CURRENT MEDICATIONS			
***Trazodone**	*ABCB1*	May cause decreased drug clearance and increased risk of adverse drug reaction. Consider an alternative.	Ref(s) 66, 67, 68, 150, 151, 152, 153
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
Dextroamphetamine	*COMT*	May cause an increased risk of adverse drug reaction. Consider an alternative.	Ref(s) 70, 71, 72, 73, 74
Fosphenytoin	*CYP2C9*	For first dose, use typical initial or loading dose. For subsequent doses, use approximately 25% less than typical maintenance dose. Subsequent doses should be adjusted according to therapeutic drug monitoring, response and side effects.	CPIC
Fosphenytoin	*HLA-B*15:02*	For first dose, use typical initial or loading dose. For subsequent doses, use approximately 25% less than typical maintenance dose. Subsequent doses should be adjusted according to therapeutic drug monitoring, response and side effects.	CPIC
Lamotrigine	*ABCB1*	May cause a variable response to drug. Consider an alternative.	Ref(s) 96
Meloxicam	*CYP2C9*	Initiate therapy with 50% of the lowest recommended starting dose. Use the lowest effective dosage for shortest duration consistent with individual patient treatment goals.	CPIC
Phenytoin	*CYP2C9*	For first dose, use typical initial or loading dose. For subsequent doses, use approximately 25% less than typical maintenance dose. Subsequent doses should be adjusted according to therapeutic drug monitoring, response and side effects.	CPIC
Phenytoin	*HLA-B*15:02*	For first dose, use typical initial or loading dose. For subsequent doses, use approximately 25% less than typical maintenance dose. Subsequent doses should be adjusted according to therapeutic drug monitoring, response and side effects.	CPIC

CNS Test 001

DOB: 2001-03-02
Clinician: Phenomics
Order No: SA0011403-B03

Sample Analysis: Feb. 10, 2023 09:14 EST
Sample Collection: Feb. 08, 2023 16:00 EST

MEDICATIONS AFFECTED BY MAJOR INTERACTIONS

Medication	Genes	Recommendations	Source
Piroxicam	*CYP2C9*	Consider an alternate therapy not metabolized by CYP2C9 (e.g., aspirin, ketorolac, naproxen and sulindac).	CPIC
Sertraline	*HTR2A*	May cause an increased risk of adverse drug reaction. Consider an alternative.	Ref(s) 138
Tenoxicam	*CYP2C9*	Consider an alternate therapy not metabolized by CYP2C9 (e.g., aspirin, ketorolac, naproxen and sulindac).	CPIC
Valproic Acid	*CPS1*	May cause an increased risk of severe adverse drug reaction. Avoid use.	Ref(s) 154, 155, 156

CNS Test 001

DOB: 2001-03-02
Clinician: Phenomics
Order No: SA0011403-B03

Sample Analysis: Feb. 10, 2023 09:14 EST
Sample Collection: Feb. 08, 2023 16:00 EST

MEDICATIONS AFFECTED BY MODERATE INTERACTIONS

Medication	Genes	Recommendations	Source
Buprenorphine	*CYP3A4*	May cause a decrease in drug efficacy due to increased drug metabolism.	Ref(s) 30, 31, 32, 33, 34
Buprenorphine	*OPRM1*	May cause a decrease in drug efficacy.	Ref(s) 30, 31, 32, 33, 34
Bupropion	*COMT*	May require a higher dose due to a decrease in the primary metabolite.	Ref(s) 35, 36, 37
Celecoxib	*CYP2C9*	Use the lowest effective dosage for shortest duration consistent with individual patient treatment goals.	CPIC
Citalopram	*GRIK4*	May require a higher dose due to a decrease in drug efficacy.	Ref(s) 52
Desvenlafaxine	*ABCB1*	May require a higher dose due to a decrease in drug efficacy.	Ref(s) 65, 66, 67, 68
Esketamine	*BDNF*	May cause a decrease in drug efficacy.	Ref(s) 79
Flurbiprofen	*CYP2C9*	Use the lowest effective dosage for shortest duration consistent with individual patient treatment goals.	CPIC
Ibuprofen	*CYP2C9*	Use the lowest effective dosage for shortest duration consistent with individual patient treatment goals.	CPIC
Lofexidine	*ADRA2A*	May cause a decrease in drug efficacy.	Ref(s) 104, 105, 106, 107
Lornoxicam	*CYP2C9*	Use the lowest effective dosage for shortest duration consistent with individual patient treatment goals.	CPIC
Topiramate	*GRIK1*	May cause a decrease in drug efficacy.	Ref(s) 144, 145, 146, 147
Ziprasidone	*DRD2*	May cause a decrease in drug efficacy.	Ref(s) 45, 47, 48, 49, 50, 51, 165, 166, 167

CNS Test 001

DOB: 2001-03-02
Clinician: Phenomics
Order No: SA0011403-B03

PredictScript™ CNS
Pharmacogenomic Test

Phenomics HEALTH™

Sample Analysis: Feb. 10, 2023 09:14 EST
Sample Collection: Feb. 08, 2023 16:00 EST

PATIENT GENETICS

Gene	Genotype		Phenotype
ABCB1	rs2032582, rs1128503, rs1045642	A/C, A/G, A/G	Decreased Function, Decreased Function, Decreased Function
ADRA2A	rs1800544	G/G	Normal Function
BDNF	rs6265	C/C	Normal Function
CACNA1C	rs3819536, rs2007004	A/A, A/G	Decreased Response, Decreased Response
COMT	rs4680	G/G	Normal Function
CPS1	rs715	T/T	Normal Function
CYP1A2			
CYP2B6		*4/*9	Intermediate Metabolizer
CYP2C19	rs61886222, rs77957608	*1/*1, A/A, A/G	Normal Metabolizer, Normal Function, Unknown Function
CYP2C9		*1/*3	Intermediate Metabolizer
CYP2D6			
CYP3A4	rs17161937, rs2740574	*1/*1, A/G, C/T	Normal Metabolizer, Unknown Function, Unknown Function
CYP3A5		*3/*7	Poor Metabolizer
DRD2	rs1799978	T/T	Normal Function
GRIK1	rs2832407	C/C	Normal Function
GRIK4	rs12800734, rs1954787	A/G, T/T	Increased Response, Normal Function
*HLA-A*31:01*			Negative/Negative
*HLA-B*15:02*			Negative/Negative
HTR2A	rs6313, rs9316233, rs6311, rs6305, rs6314, rs2770296	A/G, C/G, C/T, G/G, G/G, T/T	Altered Function, Decreased Response, Altered Function, Normal Function, Normal Function, Decreased Response
HTR2C	rs3813929, rs518147	C/C, C/C	Normal Function, Normal Function
MC4R	rs489693	A/C	Increased Risk

CNS Test 001

DOB: 2001-03-02
Clinician: Phenomics
Order No: SA0011403-B03

PredictScript™ CNS
Pharmacogenomic Test

Phenomics HEALTH™

Sample Analysis: Feb. 10, 2023 09:14 EST
Sample Collection: Feb. 08, 2023 16:00 EST

PATIENT GENETICS

Gene	Genotype		Phenotype
OPRM1	rs1799971	A/A	Normal Function
UGT1A1		*1/*1	Normal Metabolizer
UGT2B15		*1/*2	Decreased Function

CNS Test 001

DOB: 2001-03-02
Clinician: Phenomics
Order No: SA0011403-B03

Sample Analysis: Feb. 10, 2023 09:14 EST
Sample Collection: Feb. 08, 2023 16:00 EST

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); *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, Dr. Manoj Tyagi, Ph.D.

CNS Test 001

DOB: 2001-03-02
Clinician: Phenomics
Order No: SA0011403-B03

PredictScript™ CNS
Pharmacogenomic Test

Phenomics HEALTH™

Sample Analysis: Feb. 10, 2023 09:14 EST
Sample Collection: Feb. 08, 2023 16:00 EST

PATIENT PHARMACOGENE CARD