PredictScript™ POLY
Pharmacogenomic Test

Phenomics HEALTH™

## James Doe

DOB: 1956-01-01
Clinician: Ima Test
Order No: SA0000001-A01

Sample Analysis: Jan. 28, 2022 11:25 EST
Sample Collection: Jan. 01, 2022 22:13 EST

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

*This pharmacogenomics 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, ATORVASTATIN, CLOPIDOGREL, ESCITALOPRAM, GLIPIZIDE, METOPROLOL, TRAMADOL

**PRESCRIBE AS DIRECTED**

### Cardiovascular, Metabolic, and Gastrointestinal Agents

- Amlodipine (Norvasc®)
- Amiodarone (Cordarone®, Pacerone®)
- Apixaban (Eliquis®)
- Atenolol (Tenormin®)
- ***Atorvastatin (Lipitor®)**
- Bisoprolol (Zebeta®)
- Carvedilol (Coreg®)
- Dexlansoprazole (Dexilant®)
- Esomeprazole (Nexium®)
- Fluvastatin (Lescol®)
- Glimepiride (Amaryl®)
- ***Glipizide (Glucotrol®)**
- Glyburide (Diabeta®, Micronase®)
- Labetalol (Normodyne®, Trandate®)
- Losartan (Cozaar®)
- Nebivolol (Bystolic®)
- Nifedipine (Procardia® XL)
- Ondansetron (Zofran®)
- Propranolol (Inderal®)
- Rabeprazole (AcipHex®)
- Rivaroxaban (Xarelto®)
- Rosuvastatin (Crestor®)
- Simvastatin (Zocor®)
- Ticagrelor (Brilinta®)
- Torsemide (Demadex®)
- Tropisetron (Novoban®)
- Valsartan (Diovan®)
- Verapamil (Calan®, Isoptin®, Verelan®)

### Antidepressants and Anxiolytics

- Alprazolam (Xanax®)
- Amoxapine (Asendin®)
- Bupropion (Wellbutrin SR®)
- Buspirone (BuSpar®)
- Citalopram (Celexa®)
- Clobazam (Onfi®)
- Clonazepam (Klonopin®)
- Desvenlafaxine (Pristiq®)
- Diazepam (Valium®)
- Duloxetine (Cymbalta®)
- ***Escitalopram (Lexapro®)**
- Esketamine (Spravato®)
- Eszopiclone (Lunesta®)
- Ketamine (Ketalar®)
- Lorazepam (Ativan®)
- Fluoxetine (Prozac®)
- Fluvoxamine (Luvox®)
- Imipramine (Tofranil®)
- Mirtazapine (Remeron®)
- Oxazepam (Serax®)
- Paroxetine (Paxil®)
- Protriptyline (Vivactil®)
- Temazepam (Restoril®)
- Trazodone (Desyrel®)
- Trimipramine (Surmontil®)
- Zolpidem (Ambien®)

### Analgesics and Other CNS Agents

- Buprenorphine (Subutex®)
- Celecoxib (Celebrex®)
- Clonidine (Catapres®)
- Dexmethylphenidate (Focalin®)
- Dextroamphetamine(Adderall®)
- Diclofenac (Voltaren®)
- Fentanyl (Sublimaze®)
- Flurbiprofen (Ansaid®)
- Guanfacine (Intuniv®)
- Hydromorphone (Exalgo®)
- Ibuprofen (IBU, Motrin®)
- Indomethacin (Indocin SR)
- Lisdexamfetamine (Vyvanse®)
- Lofexidine (Lucemyra®)
- Lornoxicam (Xefocam®)
- Meloxicam (Mobic®)
- Methadone (Dolophine®, Methadose®)
- Methylphenidate (Concerta®)
- Morphine (MS Contin®)
- Naloxone (Narcan®)
- Naltrexone (ReVia®)
- Naproxen (Naprosyn®)
- Oxycodone (Roxicodone®)
- Piroxicam (Feldene®)
- Tenoxicam (Mobiflex®)

### Antipsychotics and Anticonvulsants

- Carbamazepine (Epitol®, Tegretol®)
- Cariprazine (Vraylar®)
- Chlorpromazine (Thorazine®)
- Clozapine (Clozaril®, FazaClo®)
- Fluphenazine (Prolixin®)
- Lurasidone (Latuda®)
- Olanzapine (Zyprexa®)
- Paliperidone (Invega®)
- Phenytoin (Dilantin®)
- Pimozide (Orap®)
- Primidone (Mysoline®)
- Quetiapine (Seroquel®)
- Risperidone (Risperdal®)
- Thioridazine (Mellaril®)
- Topiramate (Topamax®, Topiragen®)

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### MAJOR GENE-DRUG INTERACTIONS

| Cardiometabolic and Gastrointestinal Agents | | Antidepressants and Anxiolytics | | Analgesics and Other CNS Agents | | Antipsychotics and Anticonvulsants | |
|---|---|---|---|---|---|---|---|
| ***Clopidogrel (Plavix®)** | 3,5 | Amitriptyline (Elavil®) | 5 | Donepezil (Aricept®) | 4 | Brexpiprazole (Rexulti®) | 4 |
| Lovastatin (Mevacor®) | 2 | Clomipramine (Anafranil®) | 5 | Codeine (Fioricet®) | 4 | Brivaracetam (Briviact®) | 4 |
| Meclizine (Antivert®, Bonine®) | 4 | Desipramine (Norpramin®) | 2, 5 | ***Tramadol (Ultram®)** | 3 | Fosphenytoin (Cerebyx®) | 1,2,4 |
| Metoclopramide (Reglan®) | 2,4 | Vilazodone (Viibryd®) | 3 | | | Haloperidol (Haldol®) | 4 |
| Pravastatin (Pravachol®) | 2 | | | | | Iloperidone (Fanapt®) | 2,4 |
| Repaglinide (Prandin®) | 2 | | | | | Lamotrigine (Lamictal®) | 3 |
| Timolol (Betimol®) | 4 | | | | | Ziprasidone (Geodon®) | 3 |

### MODERATE GENE-DRUG INTERACTIONS

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Diltiazem (Cardizem®, Diltzac®, Taztia XT®, Tiazac®) | 3,5 | Doxepin (Sinequan®) | 1,4 | Amphetamine(Adderall®) | 2,4 | ***Aripiprazole (Abilify®)** | 2,4 |
| Flecainide (Tambocor®) | 4 | Nortriptyline (Pamelor®) | 5 | Atomoxetine (Strattera®) | 2,4 | Oxcarbazepine (Trileptal®) | 1,2 |
| Irbesartan (Avapro®) | 4 | Sertraline (Zoloft®) | 4 | Hydrocodone (Lorcet HD®, Lortab®, Norco®) | 3 | Perphenazine (Trilafon®) | 2,4 |
| Lansoprazole (Prevacid®) | 4 | Venlafaxine (Effexor XR®) | 4 | Galantamine | 4 | Valproic Acid (Depakene®) | 2 |
| ***Metoprolol (Lopressor®)** | 4 | Vortioxetine (Trintellix®) | 4 | Lithium (Eskalith®, Lithobid®) | 2 | | |
| Nateglinide (Starlix®) | 2 | | | | | | |
| Omeprazole (Zofran®) | 4 | | | | | | |
| Pantoprazole (Protonix®) | 4 | | | | | | |
| Propafenone (Rythmol®) | 4 | | | | | | |
| Ranolazine (Ranexa®) | 4 | | | | | | |
| Warfarin (Coumadin®, Jantoven®) | 3 | | | | | | |

### 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 8 |
| 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 |
| ***Clopidogrel** | *CYP2C19* | Consider alternative antiplatelet therapy (e.g., prasugrel, ticagrelor). | 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 10, 11 |
| 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 |

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| Medication | Genes | Recommendations | Source |
|---|---|---|---|
| Lamotrigine | *ABCB1* | May cause a variable drug response. Consider an alternative | Ref 1, 2, 3 |
| Lovastatin | *SLCO1B1* | May increase risk of statin-related myopathy | CPIC |
| Meclizine | *CYP2D6* | May affect systemic concentrations. Monitor for adverse reactions. | FDA |
| Metoclopramide | *CYP2D6* | Potential increase in the risk for adverse reactions, reduce dose. | FDA |
| Omeprazole | *CYP2C19* | Initiate standard starting daily dose. For chronic therapy (>12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy. | CPIC |
| Pravastatin | *CYP3A4* | May reduce drug response | CPIC |
| Repaglinide | *SLCO1B1* | May cause an increased risk of adverse drug reaction. Consider an alternative. | Ref 4, 5 |
| Timolol | *CYP2D6* | May require a lower dose due to increased systemic concentrations | Ref 6 |
| ***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 7, 8 |
| Ziprasidone | *DRD2* | May cause a decrease in drug efficacy | Ref 8, 9 |

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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 |
| Diltiazem | *CYP3A5* | May require a lower dose due to decreased drug metabolism | Ref 15, 20 |
| Doxepin | *CYP2C19, CYP2D6* | Avoid use. If warranted, consider a 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments. | CPIC |
| Flecainide | *CYP2D6* | Reduce the dose to 50% of the standard dose and record an ECG. | DPWG |
| 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 |
| Irbesartan | *CYP2C9* | May require a lower dose due to decreased drug metabolism | Ref 16, 19, 30 |
| Lansoprazole | *CYP2C19* | Initiate standard starting daily dose. For chronic therapy (>12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy. | 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 |
| ***Metoprolol** | *CYP2D6* | If a gradual reduction in heart is desired, or in the event of symptomatic bradycardia, increase the dose in smaller steps and/or prescribe no more than 25% of the standard dose. | DPWG |

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| Medication | Genes | Recommendations | Source |
|---|---|---|---|
| Nateglinide | *SLCO1B1* | May cause an increased risk of adverse drug reaction. Consider an alternative. | Ref 3, 4 |
| 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 |
| Omeprazole | *CYP2C19* | Initiate standard starting daily dose. For chronic therapy (>12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy. | CPIC |
| Oxcarbazepine | *HLA-B* | If patient is oxcarbazepine naïve, do not use oxcarbazepine. | CPIC |
| Pantoprazole | *CYP2C19* | Initiate standard starting daily dose. For chronic therapy (>12 weeks) and efficacy achieved, consider 50% reduction in daily doe and monitor for continued efficacy. | CPIC |
| Perphenazine | *CYP2D6* | Greater risk of side effects due to higher drug concentrations | FDA |
| Propafenone | *CYP2D6* | Reduce the dose to 30% of the standard dose, perform an ECG and monitor plasma concentrations. | DPWG |
| Ranolazine | *CYP2D6* | May cause increased systemic concentrations and risk of adverse drug reaction. Consider an alternative | Ref # |
| Sertraline | *CYP2C19*<br>*HTR2A* | Initiate therapy with recommended starting dose (25mg/d or 50mg/d, depending on age and indication).<br>May cause an increased risk of adverse drug reaction. Consider an alternative | CPIC<br>Ref 6, 8, 9 |
| Valproic Acid | *CPS1* | May cause an increased risk of severe adverse drug reaction. Avoid use | Ref 20 |
| RefVenlafaxine | *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 |
| Warfarin | *VKORC1, CYP2C9,*<br>*CYP4F2* | Calculate warfarin dose using a validated pharmacogenetic algorithm (e.g., http://warfarindosing.org).<br>May require a 5 - 10% increase in dose among individuals of European ancestry | CPIC |

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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 |
| *CYP4F2* | | *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 |
| *SLCO1B1* | rs4149056 | *5/*5 | Decreased Function |
| *UGT1A1* | rs35350960 | *27/*27 | Decreased Function |
| *UGT2B15* | | *1/*1 | Normal Function |
| *VKORC1* | rs9923231 | *2/*2 | Decreased 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); 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 Srinivas Narayan, Ph.D.

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## PATIENT PHARMACOGENE CARD