RightMed® Comprehensive Test Report

The RightMed Comprehensive Test is a pharmacogenomic test that may aid healthcare providers in determining a therapeutic strategy for a patient. Providers may use this report, along with other clinical factors, to help them when selecting medications and dosages for this patient. This report is not intended to be used in isolation, and the provider needs to take into account all clinical considerations and FDA prescribing information before making any changes to treatment.

Patient and report summary

Patient name: **John Doe**
Patient date of birth: **1968-08-28**
OneOme report date: **2021-09-29**

Ordering provider: **Sample Doctor**
Ordering facility: **HealthCare Institution**
Product type: **Comprehensive**
Report type: **Original**

Report legend

Based on this patient's genetic profile, medications are reported and classified according to the gene-drug interactions described below.

Major gene-drug interaction	Major genotype-drug interaction identified that affects the metabolism of the medication and/or indicates an elevated risk of adverse reaction or loss of efficacy.
Moderate gene-drug interaction	Moderate genotype-drug interaction identified that affects the metabolism of the medication and/or indicates an elevated risk of adverse reaction or loss of efficacy.
Minimal gene-drug interaction	Minimal genotype-drug interaction identified that does not significantly affect medication metabolism nor indicate an elevated risk of adverse reaction or loss of efficacy.
Limited pharmacogenetic impact	No pharmacogenetic variants demonstrate a significant impact on medication response. Other types of genetic tests that may guide prescribing (e.g., tumor marker testing, diagnostic, or indication-establishing testing) are not taken into account.

Icon legend

Some medications are reported with icons to indicate that specific clinical annotations and/or dosing guidelines provided by FDA, CPIC, or other professional associations are available in Vantage.

FDA evidence	This medication is listed on the FDA Table of Pharmacogenetic Associations. Not all genetic variants or genetic variant-inferred phenotypes may be accounted for. Further information can be found at: https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations.
Increased exposure	Total exposure to active compound(s) may be increased. Monitor for adverse effects.
Decreased exposure	Total exposure to active compound(s) may be decreased. Monitor for lack of therapeutic response.
Difficult to predict	Total exposure to active compound(s) is difficult to predict. Monitor patient response.
Reduced response	Response to medication may be lowered due to genetic changes impacting mechanisms other than exposure (e.g. receptor function).
Additional testing	According to FDA labeling, additional laboratory testing may be indicated.
Professional guideline	Medication has professional guidelines associated with this patient's genetic test results. Avoidance, dose adjustment, or heightened monitoring may be indicated.

Report and laboratory comments

Secondary findings

This patient is a carrier for variants in UGT1A1, which may meet diagnostic criteria for Gilbert syndrome. The patient is also a carrier for one or more pathogenic or likely pathogenic variants in the following gene(s): DPYD, F5. Please review the *Gene and phenotype summary* for additional information and consider genetic counseling as appropriate.

Summary for medications of interest

This list was generated from the medications entered during the order process. Additional information about each of the medications listed below may be found in Vantage.

Provider decision support is available for certain gene-drug interactions reported. The information included is an abbreviated, synthesized summary of professional guideline(s) available along with the corresponding rationale and source(s). Additional information and expanded professional guidelines may be available in Vantage. Not all gene-drug interactions with professional guidelines have provider decision support available.

Medication	Gene-drug interaction	Details	Associated gene(s)
Tramadol (Ultram)	⚠ Moderate gene-drug interaction	✱ This medication is listed on the FDA Table of Pharmacogenetic Associations. Not all genetic variants or genetic variant-inferred phenotypes may be accounted for. Further information can be found at: https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations. ⬇ Reduced metabolism of tramadol predicted. ⊟ Decreased exposure to the active metabolite(s) of tramadol predicted. OPRM1 rs1799971 Asp/Asp (GG) genotype has been associated with decreased sensitivity to the analgesic effects of tramadol. Professional guidelines exist for the use of tramadol in patients with this genotype and/or phenotype.	CYP2D6 OPRM1

Genotype-predicted interactions for medications

Allergy/Pulmonology

Major gene-drug interaction

Moderate gene-drug interaction

- Dextromethorphan + 1 (Delsym®)

Minimal gene-drug interaction

Limited pharmacogenetic impact

- Desloratadine (Clarinex®)
- Montelukast (Singulair®)

Analgesic/Anesthesiology

Major gene-drug interaction

- Morphine 12, 20, 24, 25, 97, 107, 166, 183, 184, 198 (Kadian®, MS Contin®)

Moderate gene-drug interaction

- Alfentanil 1, 49, 90, 96, 145, 157 (Alfenta®)
- Carisoprodol * + 1, 52 (Soma®)
- Codeine * − 1, 2, 9, 20, 31, 32, 39, 185, 202
- Fentanyl 1, 42, 56, 74, 92, 100, 199, 219, 221, 226, 227, 228 (Duragesic®, Sublimaze®)
- Hydrocodone 1, 31, 32 (Hysingla®, Zohydro®)
- Oxycodone 1, 2, 31, 32, 39 (Oxycontin®, Roxicodone®)
- Tramadol * − 1, 2, 31, 32, 39, 111, 189, 191, 205 (Ultram®)

Minimal gene-drug interaction

- Buprenorphine 1 (Buprenex®, BuTrans®, Subutex®)

Limited pharmacogenetic impact

- Dexmedetomidine (Precedex®)
- Naloxone (Evzio®, Narcan®)

Anti-inflammatory

Major gene-drug interaction

Moderate gene-drug interaction

- Celecoxib * + 1 (Celebrex®)
- Diclofenac + 1 (Voltaren®)
- Flurbiprofen * + 1, 192 (Ansaid®)

Minimal gene-drug interaction

Limited pharmacogenetic impact

Anticoagulant/Antiplatelet

Major gene-drug interaction

Moderate gene-drug interaction

- Clopidogrel * + 1, 2, 39, 175, 176 (Plavix®)
- Warfarin * 1, 23, 78, 79 (Coumadin®, Jantoven®)

Minimal gene-drug interaction

- Apixaban 1 (Eliquis®)
- Cilostazol 1, 204 (Pletal®)
- Ticagrelor 1 (Brilinta®)

Limited pharmacogenetic impact

- Prasugrel (Effient®)

Cardiovascular

Major gene-drug interaction

Moderate gene-drug interaction

- Carvedilol * + 1 (Coreg®)
- Flecainide + 1, 2 (Tambocor®)

Minimal gene-drug interaction

- Amiodarone 1 (Cordarone®, Pacerone®)

Limited pharmacogenetic impact

- Digoxin (Digitek®, Digox®, Lanoxin®)
- Lisinopril (Prinivil®, Zestril®)

Cardiovascular (cont.)

Major gene-drug interaction

Moderate gene-drug interaction

- **Metoprolol** ✱ + 1, 2, 39 (Lopressor®, Toprol XL®)
- **Propafenone** ✱ + 1, 2, 39 (Rythmol®)

Minimal gene-drug interaction

- **Atorvastatin** ✱ 1, 15, 39, 153 (Lipitor®)
- **Disopyramide** 1 (Norpace®)
- **Dofetilide** 1 (Tikosyn®)
- **Pravastatin** 1, 58, 68, 125, 133, 137, 138, 139, 142, 161 (Pravachol®)
- **Quinidine** 1 (Quin-G®)
- **Simvastatin** ✱ 1, 39, 95, 161, 177, 204, 217 (Zocor®)

Limited pharmacogenetic impact

- **Spironolactone** (Aldactone®)

Endocrinology

Major gene-drug interaction

- **Ethinyl estradiol** 1, 2

Moderate gene-drug interaction

Minimal gene-drug interaction

Limited pharmacogenetic impact

- **Exenatide** (Bydureon®, Byetta®)
- **Metformin** (Fortamet®, Glucophage®)
- **Risedronate** (Actonel®, Atelvia®)

Gastroenterology

Major gene-drug interaction

- **Dexlansoprazole** ✱ − 1 (Dexilant®)
- **Lansoprazole** − 1, 2, 39, 88, 98, 104, 110, 200 (Prevacid®)
- **Omeprazole** ✱ − 1, 2, 39, 43, 45, 48, 172, 181, 194, 200, 201, 229 (Prilosec®)
- **Pantoprazole** ✱ − 1, 2, 39 (Protonix®)
- **Rabeprazole** ✱ − 1, 39, 44, 57, 71, 101, 105, 148, 194, 197 (Aciphex®)

Moderate gene-drug interaction

- **Dronabinol** ✱ + 1 (Marinol®, Syndros®)
- **Esomeprazole** ✱ − 1, 2, 39 (Nexium®)
- **Ondansetron** + 1, 13, 82, 207 (Zofran®)

Minimal gene-drug interaction

- **Aprepitant** 1, 128 (Cinvanti®, Emend®)
- **Fosaprepitant** 1, 128 (Emend Injection®)

Limited pharmacogenetic impact

Genetic disease

Major gene-drug interaction

Moderate gene-drug interaction

Minimal gene-drug interaction

- **Eliglustat** ✱ 1 (Cerdelga®)

Limited pharmacogenetic impact

Hematology/Oncology

Major gene-drug interaction

- **Belinostat** ✱ 1, 215 (Beleodaq®)
- **Capecitabine** ✱ 1, 2, 22 (Xeloda®)

Moderate gene-drug interaction

- **Tamoxifen** ✱ − 1, 2, 51 (Soltamox®)

Minimal gene-drug interaction

- **Brentuximab vedotin** 1 (Adcetris®)
- **Dasatinib** 1 (Sprycel®)
- **Docetaxel** 1 (Docefrez®, Taxotere®)

Limited pharmacogenetic impact

Hematology/Oncology (cont.)

Major gene-drug interaction

- Fluorouracil ✱ 📖 1, 2, 22 (Adrucil®)
- Irinotecan ✱ 📖 1, 2, 39, 40, 50, 94 (Camptosar®)
- Mercaptopurine ✱ 📖 1, 2, 18, 165 (Purixan®)
- Nilotinib ✱ 🖉 📖 1, 4 (Tasigna®)
- Pazopanib ✱ 📖 1 (Votrient®)
- Thioguanine ✱ 📖 1, 2, 18, 165 (Tabloid®)

Moderate gene-drug interaction

Minimal gene-drug interaction

- Gefitinib ✱ 🖉 1 (Iressa®)
- Lapatinib ✱ 🖉 1, 173 (Tykerb®)
- Methotrexate 1, 160, 162, 203, 224 (Rheumatrex®)
- Ruxolitinib 1 (Jakafi®)
- Temsirolimus 1 (Torisel®)

Limited pharmacogenetic impact

Immunosuppression

Major gene-drug interaction

- Azathioprine ✱ 📖 1, 2, 18, 165 (Imuran®)

Moderate gene-drug interaction

Minimal gene-drug interaction

- Cyclosporine 1 (Gengraf®, Neoral®, Sandimmune®)
- Sirolimus 1 (Rapamune®)
- Tacrolimus ✱ 📖 1, 14 (Prograf®)

Limited pharmacogenetic impact

- Mycophenolate sodium (Myfortic®)

Infectious disease

Major gene-drug interaction

- Atazanavir 📖 46, 77 (Reyataz®)
- Atovaquone/Proguanil ✚ 1 (Malarone®)
- Voriconazole ✱ ⊟ 📖 1, 2 (Vfend®)

Moderate gene-drug interaction

Minimal gene-drug interaction

- Abacavir ✱ 1, 2, 41, 114, 115, 119, 120, 169, 195 (Ziagen®)
- Efavirenz ✱ 📖 1, 2, 35, 39 (Sustiva®)
- Isavuconazole 1 (Cresemba®)
- Itraconazole 1 (Onmel®, Sporanox®)
- Peginterferon alfa-2a-containing regimens 1, 130 (Pegasys®)
- Peginterferon alfa-2b-containing regimens 1, 130 (Pegintron®)
- Quinidine 1 (Quin-G®)

Limited pharmacogenetic impact

- Fluconazole (Diflucan®)
- Levofloxacin (Levaquin®)
- Moxifloxacin (Avelox®)

Neurology

Major gene-drug interaction

- Clobazam ✱ ⊟ 1 (Onfi®)
- Fosphenytoin ✚ 📖 1, 2, 6, 21, 26, 116, 141 (Cerebyx®)
- Phenytoin ✚ 📖 1, 2, 6, 21, 26, 116, 141 (Dilantin®)

Moderate gene-drug interaction

Minimal gene-drug interaction

- Carbamazepine ✱ 1, 5, 6, 27, 28, 66, 106, 116, 124, 127, 140, 152, 156, 159, 178, 222 (Carbatrol®, Tegretol®)
- Eletriptan 1 (Relpax®)
- Eslicarbazepine 1, 6, 83, 156 (Aptiom®)

Limited pharmacogenetic impact

- Gabapentin (Neurontin®)
- Levetiracetam (Keppra®)
- Pramipexole (Mirapex®)
- Pregabalin (Lyrica®)

Neurology (cont.)

Major gene-drug interaction

Moderate gene-drug interaction

Minimal gene-drug interaction

- Lamotrigine 1, 6, 116, 156 (Lamictal®)
- Oxcarbazepine ✱ 1, 6, 156 (Trileptal®)
- Tetrabenazine ✱ 1 (Xenazine®)

Limited pharmacogenetic impact

Psychiatry

Major gene-drug interaction

- Amitriptyline ✱ 1, 2, 39, 61, 62, 216 (Elavil®)
- Citalopram ✱ 1, 2, 7, 37, 39, 60, 63, 64, 70, 86, 87, 99, 103, 108, 123, 129, 149, 155, 158, 170 (Celexa®)
- Clomipramine ✱ 1, 2, 62 (Anafranil®)
- Diazepam ✱ 1, 73 (Valium®)
- Doxepin ✱ 1, 2, 62 (Silenor®)
- Escitalopram ✱ 1, 17, 37, 39, 60, 65, 70, 118, 136, 218 (Lexapro®)
- Imipramine ✱ 1, 2, 62, 214 (Tofranil®)
- Trimipramine ✱ 1, 2, 62, 93 (Surmontil®)

Moderate gene-drug interaction

- Aripiprazole ✱ 1, 2, 81, 126 (Abilify®)
- Asenapine 1 (Saphris®)
- Chlorpromazine 1, 151, 190 (Thorazine®)
- Desipramine ✱ 1, 2, 62 (Norpramin®)
- Fluoxetine 1, 39, 47, 53, 60, 70, 76, 109, 112, 117, 154, 163, 174, 188, 220 (Prozac®, Sarafem®)
- Fluvoxamine ✱ 1, 60, 75, 84, 85, 179, 180, 186, 187, 188, 196, 223 (Luvox®)
- Haloperidol 1, 2, 150, 182, 209 (Haldol®)
- Nicotine 30, 33, 80, 131 (Nicoderm C-Q®, Nicorette®, Nicotrol®)
- Nortriptyline ✱ 1, 39, 62, 147, 210 (Pamelor®)
- Olanzapine 1, 2, 102, 113 (Zydis®, Zyprexa®)
- Paroxetine ✱ 1, 2, 39, 60 (Paxil®)
- Perphenazine ✱ 1, 146 (Etrafon®)
- Risperidone ✱ 1, 39, 81, 126, 225 (Risperdal®)
- Sertraline 1, 36, 38, 39, 60, 109, 132, 135, 143, 164, 168, 206, 213 (Zoloft®)
- Thioridazine ✱ 1
- Venlafaxine ✱ 1, 2, 39, 212 (Effexor®)
- Vortioxetine ✱ 1 (Trintellix®)

Minimal gene-drug interaction

- Amphetamine/ Dextroamphetamine mixed salts 1, 55, 69, 122 (Adderall®)
- Bupropion 1 (Wellbutrin®)
- Cariprazine 1, 3, 19, 29, 134 (Vraylar®)
- Clozapine ✱ 1, 8, 11, 193 (Clozaril®)
- Dextroamphetamine 1, 55, 69, 122 (Dexedrine®)
- Guanfacine 1, 121 (Intuniv®, Tenex®)
- Levomilnacipran 1 (Fetzima®)
- Lisdexamfetamine 1, 55, 69, 122 (Vyvanse®)
- Lurasidone 1 (Latuda®)
- Nefazodone 1, 167, 211 (Serzone®)
- Quetiapine 1, 10, 91, 204, 208 (Seroquel®)
- Trazodone 1 (Desyrel®)
- Vilazodone 1, 16 (Viibryd®)

Limited pharmacogenetic impact

- Desvenlafaxine (Pristiq®)
- Lithium (Lithobid®)
- Milnacipran (Savella®)
- Paliperidone (Invega®)
- Varenicline (Chantix®)

Rheumatology

Major gene-drug interaction	Moderate gene-drug interaction	Minimal gene-drug interaction	Limited pharmacogenetic impact
	▪ Lesinurad + 1 (Zurampic®)	▪ Allopurinol * 34, 59, 67, 89, 171 (Aloprim®, Zyloprim®) ▪ Cevimeline * 1 (Evoxac®) ▪ Methotrexate 1, 160, 162, 203, 224 (Rheumatrex®) ▪ Tofacitinib 1 (Xeljanz®)	

Sleep medicine

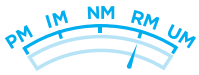
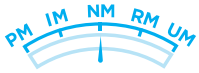
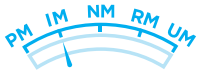
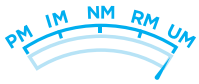
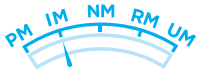
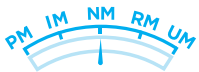
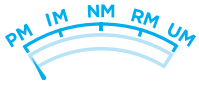
Major gene-drug interaction	Moderate gene-drug interaction	Minimal gene-drug interaction	Limited pharmacogenetic impact
			▪ Temazepam (Restoril®)

Urology

Major gene-drug interaction	Moderate gene-drug interaction	Minimal gene-drug interaction	Limited pharmacogenetic impact
	▪ Fesoterodine * + 1 (Toviaz®) ▪ Tamsulosin * + 1 (Flomax®)		

Genotype-derived classification of medications is provided as a service by OneOme and is intended solely for use by a medical professional who has reviewed and understands all sections within this report, including possible limitations of the services provided by OneOme. The relationships between the drugs and pharmacogenes annotated in this report are supported by scientific evidence that meets OneOme's criteria for inclusion. The order in which drugs are listed does not have any clinical or medical implications. Commonly used trade names for medications are listed for reference only. The list may not be inclusive of all trade names available and does not indicate preference or recommendation by OneOme of one medication product over another. For more information on these medications, for a list of additional medications curated but not annotated by OneOme, or to evaluate possible drug-to-drug interactions, please consult Vantage, which is accessible through the provider portal at portal.oneome.com.

Gene and phenotype summary

Gene	Genotype		Phenotype summary / Metabolic status
CYP1A2	*1A/*1C		**Rapid** Increased activity. Drugs converted to active metabolite(s) may have increased exposure. Active drugs converted to inactive metabolite(s) may have decreased exposure.
CYP2B6	*1/*1		**Normal** Normal activity. Drugs metabolized at a normal rate.
CYP2C9	*1/*3		**Intermediate** Decreased activity. Drugs converted to active metabolite(s) may have reduced exposure. Active drugs converted to inactive metabolite(s) may have increased exposure.
CYP2C19	*17/*17		**Ultrarapid** Increased activity. Drugs converted to active metabolite(s) may have increased exposure. Active drugs converted to inactive metabolite(s) may have decreased exposure.
CYP2C Cluster	rs12777823 GG		**Normal** CYP2C rs12777823 homozygous wild-type genotype consistent with normal clearance of a certain medication, independent of the impact of CYP2C9*2 and *3. CYP2C rs12777823, together with CYP4F2, CYP2C9, and VKORC1, may affect treatment management of a certain medication.
CYP2D6	*2/*5		**Intermediate** Decreased activity. Drugs converted to active metabolite(s) may have reduced exposure. Active drugs converted to inactive metabolite(s) may have increased exposure.
CYP3A4	*1/*1		**Normal** Normal activity. Drugs metabolized at a normal rate.
CYP3A5	*3/*3		**Poor** This CYP3A5 genotype is associated with the phenotype most prevalent in studies used to define standard dosing guidelines.
CYP4F2	*1/*1		**Normal activity** Genotype consistent with normal activity of the CYP4F2 enzyme, which catalyzes the metabolism of vitamin K, in counterpoint to the activity of VKORC1. CYP4F2, together with CYP2C9, VKORC1, and a variant in CYP2C Cluster, may affect treatment management of a certain medication.

Gene and phenotype summary (cont.)

COMT	rs4680 GG	⚠	**High activity** The COMT GG (Val/Val) genotype is predicted to yield higher COMT activity than the AA (Met/Met) or GA (Val/Met) genotypes at rs4680.
DPYD	*1/*2A	✋	**DPD activity score: 1** Genotype consistent with partial reduction of dihydropyrimidine dehydrogenase (DPD) activity with an activity score of 1, or an intermediate metabolizer phenotype. Partial DPD activity is associated with an increased risk of severe, life-threatening, or fatal adverse reactions related to the administration of certain medications.
DRD2	rs1799978 AA	✓	**Normal receptor expression** Homozygous wild-type dopamine receptor D2 (DRD2) rs1799978 AA genotype is consistent with normal receptor expression.
F2	rs1799963 GG	✓	**Normal risk** Normal risk of thrombosis associated with Factor II (prothrombin). Other genetic and clinical factors contribute to the risk for thrombosis.
F5	rs6025 GA	✋	**Increased risk** Increased risk of thrombosis associated with Factor V Leiden thrombophilia. Other genetic and clinical factors largely contribute to the risk for thrombosis.
GRIK4	rs1954787 CC	✓	**Normal receptor function** Glutamate ionotropic receptor kainate type subunit 4 (GRIK4) genotype is consistent with normal receptor function.
HLA-A	Negative	✓	**Normal risk** Negative for the presence of the HLA-A*31:01 allele. Normal risk of hypersensitivity induced by certain medications, and possibly others of structural similarity. Hypersensitivity and severe cutaneous reactions may occur regardless of the presence of the HLA-A*31:01 allele, in particular the presence of the HLA-B*15:02 allele is associated with severe cutaneous reactions induced by certain medications.
HLA-B	Negative	✓	**Normal risk** Negative for presence of the HLA-B*15:02, HLA-B*57:01, and HLA-B*58:01 alleles. Normal risk of hypersensitivity, severe cutaneous reactions, and severe hepatotoxicity induced by certain medications. Hypersensitivity, severe cutaneous reactions, and severe hepatotoxicity may occur regardless of the presence of HLA-B*15:02, HLA-B*57:01, or HLA-B*58:01 alleles. In particular, the presence of the HLA-A*31:01 allele is associated with hypersensitivity reactions induced by a certain medication, and possibly other medications of structural similarity.
HTR2A	rs7997012 AA	✓	**Intron 2 genotype AA** Homozygous wild-type HTR2A (5-hydroxytryptamine receptor 2A) genotype is consistent with normal HTR2A receptor function.

Gene and phenotype summary (cont.)

HTR2C	rs3813929 TT		**Protective influence** Homozygous variant HTR2C [5-hydroxytryptamine (serotonin) receptor 2C] genotype is associated with a protective influence on weight gain related to certain medications. The HTR2C gene is located on the X chromosome. In patients with only one X, result should read rs3813929 T;-.
IFNL4	rs12979860 CC		**Normal** Genotype consistent with a normal likelihood of hepatitis C sustained virologic response (SVR) with certain treatment options.
NUDT15	rs116855232 CC		**Normal metabolizer** NUDT15 genotype is consistent with normal enzyme activity and is not associated with an increased risk of thiopurine-induced toxicities. Toxicities with thiopurines can occur due to impaired TPMT activity independently from the NUDT15 activity.
OPRM1	rs1799971 GG		**Asp/Asp isoform** OPRM1 Asp/Asp (GG) genotype consistent with altered mu-1 opioid receptor function, and decreased sensitivity to the effects of certain substrates has been observed when compared to OPRM1 Asn/Asn (AA) and Asn/Asp (AG) genotypes at rs1799971. Decreased sensitivity has not been consistently observed in this genotype for all substrates that activate the mu-1 receptor.
SLC6A4	L/L (La/La)		**Typical to increased expression** Genotype consistent with a typical to increased expression of the SLC6A4 transporter compared to other genotypes. This genotype was shown to exhibit different phenotypes in East Asian populations, as opposite outcomes were observed for this genotype in East Asian populations when compared to Caucasian populations.
SLCO1B1	*1A/*1A		**Normal function** SLCO1B1 genotype consistent with normal function of the OATP1B1 transporter.
TPMT	*1/*3C		**Intermediate metabolizer** TPMT genotype is consistent with an intermediate metabolizer phenotype and is associated with an increased risk of thiopurine-induced toxicities.
UGT1A1	*28/*28		**Poor metabolizer (Homozygous *28)** Genotype consistent with little to no UGT1A1 enzyme activity, or a poor metabolizer phenotype, and is associated with an increased risk of certain drug-induced toxicities. Genotype is also consistent with Gilbert syndrome.

Gene and phenotype summary (cont.)

VKORC1	rs9923231 GA	⚠	**Intermediate activity** Genotype consistent with intermediate activity of the vitamin K epoxide reductase enzyme, associated with the c.-1639GA (rs9923231) variant. VKORC1, together with CYP2C9, CYP4F2, and a variant in CYP2C Cluster, may affect treatment management of a certain medication.

CYP phenotype abbreviations

PM	Poor metabolizer
IM	Intermediate metabolizer
NM	Normal metabolizer
RM	Rapid metabolizer
UM	Ultrarapid metabolizer

Test information

Specimen ID: **5733901983817**
Specimen type: **Buccal swab**
Collection date: **2021-09-29**
Receive date: **2021-09-29**

Clinical testing performed by:
OneOme
807 Broadway St. NE Suite 100
Minneapolis, MN 55412, United States

Reported by: **Lee Kaplan, PhD, FACMG**
CLIA: **24D2109855**
CAP: **9432670**
NY PFI: **9226**

Test results

The following analytical results were interpreted by OneOme to produce the pharmacogenomic interpretations and annotations described in the *Gene and phenotype summary*. Method-specific analytical limitations or inferred haplotypes may limit the ability to produce a definitive phenotype interpretation. See *Methodology and limitations* and/or the *Report and laboratory comments* sections for additional information.

CYP1A2 *1A/*1C

rs2069514	NG_008431.2:g.28338G>A	GA
rs2069526	NM_000761.4:c.-10+103T>G	TT
rs12720461	NM_000761.4:c.-10+113C>T	CC
rs35694136	NM_000761.4:c.-1635delT	TT
rs762551	NM_000761.4:c.-9-154C>A	CC

CYP2B6 *1/*1

rs3211371	NM_000767.4:c.1459C>T	CC
rs3745274	NM_000767.4:c.516G>T	GG
rs2279343	NM_000767.4:c.785A>G	AA
rs28399499	NM_000767.4:c.983T>C	TT

CYP2C9 *1/*3

rs28371685	NM_000771.3:c.1003C>T	CC
rs1057910	NM_000771.3:c.1075A>C	AC
rs56165452	NM_000771.3:c.1076T>C	TT
rs28371686	NM_000771.3:c.1080C>G	CC
rs1057911	NM_000771.3:c.1425A>T	AA
rs1799853	NM_000771.3:c.430C>T	CC
rs7900194	NM_000771.3:c.449G>A	GG
rs9332131	NM_000771.3:c.817delA	AA

CYP2C19 *17/*17

rs12248560	NM_000769.2:c.-806C>T	TT
rs28399504	NM_000769.2:c.1A>G	AA
rs4986893	NM_000769.2:c.636G>A	GG
rs6413438	NM_000769.2:c.680C>T	CC
rs4244285	NM_000769.2:c.681G>A	GG

CYP2C Cluster rs12777823 GG

rs12777823	NC_000010.10:g.96405502G>A	GG

CYP2D6 *2/*5

rs1080985	NM_000106.5:c.-1584C>G	CC
rs1065852	NM_000106.5:c.100C>T	CC
rs59421388	NM_000106.5:c.1012G>A	GG
rs72549346	NM_000106.5:c.1088_1089insGT	--
rs5030862	NM_000106.5:c.124G>A	GG
rs267608319	NM_000106.5:c.1319G>A	GG
rs774671100	NM_000106.5:c.137_138insT	--
rs765776661	NM_000106.5:c.1411_1412insTGCCCACTG	GTGCCCACGTGCCCAC
rs1135840	NM_000106.5:c.1457G>C	CC
rs201377835	NM_000106.5:c.181-1G>C	GG
rs769258	NM_000106.5:c.31G>A	GG
rs28371706	NM_000106.5:c.320C>T	CC
rs5030655	NM_000106.5:c.454delT	TT
rs5030865	NM_000106.5:c.505G>[A,T]	GG
rs3892097	NM_000106.5:c.506-1G>A	GG
rs72549353	NM_000106.5:c.765_768delAACT	AACTAACT
rs35742686	NM_000106.5:c.775delA	AA
rs5030656	NM_000106.5:c.841_843delAAG	AAGAAG
rs16947	NM_000106.5:c.886C>T	TT
rs5030867	NM_000106.5:c.971A>C	AA
rs79292917	NM_000106.5:c.975G>A	GG
rs28371725	NM_000106.5:c.985+39G>A	GG

CYP3A4 *1/*1

rs2740574	NM_017460.5:c.-392G>A	AA
rs35599367	NM_017460.5:c.522-191C>T	CC

CYP3A5 *3/*3

rs41303343	NM_000777.4:c.1035_1036insT	--
rs776746	NM_000777.4:c.219-237G>A	GG
rs10264272	NM_000777.4:c.624G>A	GG

CYP4F2 *1/*1

rs2108622	NM_001082.4:c.1297G>A	GG

COMT rs4680 GG

rs4680	NM_000754.3:c.472G>A	GG

DPYD *1/*2A

rs55886062	NM_000110.3:c.1679T>G	TT
rs3918290	NM_000110.3:c.1905+1G>A	GA
rs67376798	NM_000110.3:c.2846A>T	TT

DRD2 rs1799978 AA

rs1799978	NM_000795.3:c.-585A>G	AA

F2 rs1799963 GG

rs1799963	NM_000506.4:c.*97G>A	GG

F5 rs6025 GA

rs6025	NM_000130.4:c.1601G>A	GA

GRIK4 rs1954787 CC

rs1954787	NM_001282470.2:c.83-10039T>C	CC

HLA-A Negative

HLA00097	NM_002116 (interrogated at exon 2)	Negative

Test results (cont.)

HLA-B Negative

HLA00386	NM_005514 (interrogated at exon 2 and intron 2)	Negative
HLA00381	NM_005514 (interrogated at exon 3)	Negative
rs144012689	NM_005514.7:c.1012+104A>T	AA

HTR2A rs7997012 AA

rs7997012	NM_000621.4:c.614-2211T>C	TT

HTR2C rs3813929 TT

rs3813929	NM_000868.3:c.-759C>T	TT

IFNL4 rs12979860 CC

rs12979860	NM_001276254.2:c.151-152G>A	CC

NUDT15 rs116855232 CC

rs116855232	NM_018283.3:c.415C>T	CC

OPRM1 rs1799971 GG

rs1799971	NM_000914.4:c.118A>G	GG

SLC6A4 L/L (La/La)

rs774676466	NM_001045.5:c.-1917_-1875del43	LL
rs25531	NM_001045.5:c.-1936A>G	AA

SLCO1B1 *1A/*1A

rs4149015	NM_006446.4:c.-910G>A	GG
rs2306283	NM_006446.4:c.388A>G	AA
rs4149056	NM_006446.4:c.521T>C	TT

TPMT *1/*3C

rs1800462	NM_000367.3:c.238G>C	GG
rs1800460	NM_000367.3:c.460G>A	GG
rs1800584	NM_000367.3:c.626-1G>A	CC
rs1142345	NM_000367.3:c.719A>G	AG

UGT1A1 *28/*28

rs4148323	NM_001072.3:c.862-6536G>A	GG
rs1976391	NM_001072.3:c.862-9697A>G	GG

VKORC1 rs9923231 GA

rs9923231	NM_001311311.1:c.-1639G>A	GA
rs7200749	NM_024006.5:c.358C>T	GG

Electronically signed by:
Lee Kaplan, PhD, FACMG
2021-09-29

Methodology and limitations

Analytical results were produced using tests developed and validated by OneOme, LLC, a clinical laboratory located at 807 Broadway Street NE Suite 100, Minneapolis, MN 55413. These tests have not been cleared or approved by the U.S. Food and Drug Administration. OneOme is certified under CLIA-88 and accredited by the College of American Pathologists as qualified to perform high-complexity testing. This test is used for clinical purposes and should not be regarded as investigational or for research.

Genomic DNA was analyzed by PCR using Thermo Fisher TaqMan® and/or LGC Biosearch BHQ® probe-based methods to interrogate the variant locations listed in the *Test results* table above. In addition, CYP2D6 copy number status was assessed at sites within the promoter, intron 2, intron 6, and exon 9. The test detects CYP2D6 deletions, duplications/multiplications, and hybrid alleles, but cannot differentiate duplications in the presence of a deletion.

Haplotypes, or combinations of inherited variants on a chromosome, are annotated according to legacy nomenclature for the genes and alleles in the table below. Less frequent haplotypes or novel alleles may be reported when appropriate.

CYP1A2	*1C, *1D, *1E, *1F, *1J, *1K, *1L, *1V, *1W
CYP2B6	*4, *5, *6, *7, *9, *16, *18
CYP2C9	*2, *3, *4, *5, *6, *8, *11
CYP2C19	*2, *3, *4, *4B, *10, *17
CYP2D6	*2, *2A, *3, *4, *4M, *4N, *5, *6, *6C, *7, *8, *9, *10, *11, *12, *13, *14, *15, *17, *18, *19, *20, *29, *31, *34, *35, *36, *39, 41, *42, *59, *63, *64, *65, *68, *69, *70, *91, *109, *114
CYP3A4	*1B, *22
CYP3A5	*3, *6, *7
CYP4F2	*3
DPYD	*2A, *13
SLCO1B1	*1B, *5, *15, *17, *21
TPMT	*2, *3A, *3B, *3C, *4
UGT1A1	*6, *28

The test does not detect all known and unknown variations in the gene(s) tested, nor does absence of a detectable variant (designated as *1 for genes encoding drug metabolizing enzymes) rule out the presence of other, non-detected variants.

As with other common SNP genotyping techniques, these assays cannot differentiate between the maternal and paternal chromosomes. In cases where observed variants are associated with more than one haplotype, OneOme infers and reports the most likely diplotype based on published allele frequency and/or ethnicity data. Inferences with potential clinical impact are reported in the *Report and laboratory comments* section.

The variant detection methods validated by OneOme provide >99.9% accuracy; however, PCR may be subject to general interference by factors such as reaction inhibitors and low quality or quantity of extracted DNA. When present, these interferents typically yield no result rather than an inaccurate one. Very infrequent variants or polymorphisms occurring in primer- or probe-binding regions may also affect testing and could produce an erroneous result or assay failure. Variant locations tested by the assay but not assigned a genotype call are reported as “No Call.” Test results and clinical interpretation may be inaccurate for individuals who have undergone or are receiving non-autologous blood transfusions, tissue, and/or organ transplant therapies. Although extremely rare, results could also be impacted by other factors not addressed above, such as laboratory error.

Due to the complexity of interpreting some genetic test results, such as those that may carry a probabilistic risk of disease, patients and providers should consider the benefits of consulting with a trained genetic counseling professional, physician, or pharmacogenomic specialist. For additional support, contact OneOme through the website or by calling 844-663-6635.

OneOme liability disclaimer

The interpretations and clinical annotations provided by OneOme are intended solely for use by a medical professional and do not constitute medical advice by OneOme. The treating provider remains ultimately responsible for all diagnosis and treatment decisions for the patient. OneOme disclaims liability for any errors, omissions or ambiguities in any translation or interpretation of a report by a third party, including without limitation direct, indirect, incidental, special, consequential or exemplary damages, whether such damages arise in contract, negligence, tort, under statute, in equity, at law or otherwise. Information included in this report is based upon scientific literature, including information from and guidelines published by professional associations (e.g., CPIC, FDA, DPWG), and does not take into account other genetic variants and environmental or social factors that may affect a patient's response. Other factors not included in this report include, but are not limited to, environmental factors (e.g., smoking), health factors (e.g., diet), social and familial factors, various medical conditions, and drug-to-drug interactions. Administration of any medication, including the ones listed in the OneOme reports, requires careful therapeutic monitoring regardless of the phenotype or genotype-predicted interaction reported. As a matter of practice, OneOme will routinely update its pharmacogenomic database as new information becomes available to the scientific community. Genotype-predicted interactions and annotations found on the patient's RightMed Comprehensive Test Report, Vantage Reports, or RightMed specialty reports are therefore dependent on the date of generation and/or the database version used to generate that report. Providers may access these reports with updated annotations using OneOme's latest released version through the provider portal at portal.oneome.com.

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