Pharmacogenomics Actionable & Research Review

Individual's genetic information provided by
PHD LABORATORY LLC
5104 Reagan Dr Suite 8 Charlotte NC 28206
(704) 565-0870
https://www.phdlaboratory.com/

The results of the systematic review performed by Genetica Consulting Services (GCS) of available pharmacogenomics (PGx) actionable guidelines and research literature is presented here for your consideration. The GCS PGx Review is a tool intended to provide users with relevant medical reference information related to identified multiple factors (including gene variations) and their drug associations. This review reflects the professional opinions of the GCS team and clearly indicates content intended for clinical use and for research use. Review of the same evidence can be found with references documented at geneticaconsulting.com/refs.

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I. Pharmacogenomics Genetic Summary

Gene	Genotype(s)	Phenotype(s)
CYP2B6	*1/*5	Normal Metabolizer
CYP2C19	*17/*17	Ultrarapid Metabolizer
CYP2C9	*1/*1	Normal Metabolizer
CYP2D6	*2/*4E	Intermediate Metabolizer
CYP3A5	*3/*3	Poor Metabolizer

Gene	Genotype(s)	Phenotype(s)
DPYD	*1/*1	Normal Metabolizer
NUDT15	*1/*1	Normal Metabolizer
SLCO1B1	*37/*5 or *1/*15	Decreased Function
TPMT	*1/*1	Normal Metabolizer

Gene	Genotype(s)/Individual Impact
ABCB1	c.2887T>G(A) Heterozygous, AC c.3645T>C Heterozygous, AG c.1446T>C Heterozygous, AG
ABCG2	c.421C>A Negative, GG
ADRB2	c.46G>A Negative, GG
APOE	E3/E3
COMT	c.472G>A Negative, GG
CYP1A2	*1F/*1F
CYP2C	g.94645745G>A Negative, GG
CYP3A4	*1A/*1A
CYP4F2	c.1297G>A Negative, CC

Gene	Genotype(s)/Individual Impact
DRD2	c.-31-870T>C Heterozygous, AG g.4651A>G Heterozygous, CT c.2137G>A Heterozygous, AG c.1139-134T>G Heterozygous, AC g.4750dup Heterozygous, GdupG
F2	c.*97G>A Negative, GG/Average Risk of ADR
F5	c.1601G>A Negative, CC/Average Risk of ADR
HTR1A	g.4555G>C Negative, CC
HTR2A	c.614-2211T>C Heterozygous, AG g.4692G>A Negative, CC
HTR2C	g.4963C>T Negative, CC c.551-3008C>G Homozygous, GG
MTHFR	c.788C>T Heterozygous, AG c.1409A>C Negative, TT
OPRM1	c.118A>G Negative, AA
VKORC1	g.3588G>A Heterozygous, CT

IMPORTANT! Individuals should not alter their medication(s) unless directly instructed by their healthcare provider.

Pharmacogenomics Actionable & Research Review
II. Definitions

A. General Definitions

- **Allele:** A variant form of a gene; one of two or more versions of DNA sequence (a single base or a segment of bases) at a given genomic location.
- **Genotype:** The genetic makeup of an organism (e.g., a Individual's genotype is CYP2C19*2/*2).
- **Inducer:** A drug or substrate that increases the metabolic activity of an enzyme by decreasing the rate of degradation or by increasing the expression of the gene coding for the enzyme.
- **Inhibitor:** A drug or substrate that decreases the metabolic activity of an enzyme by binding with the active site of the enzyme.
- **Phenoconversion:** A drug-gene-drug interaction that causes a mismatch between an individual's genotype and their true capacity to metabolize medications due to non-genetic factors.
- **Phenotype(s)/Individual Impact:** The potential outcome of an individual associated with a particular genotype (e.g., Phenotype: Normal metabolizer (NM), Intermediate Metabolizer (IM), Poor Metabolizer (PM), Rapid Metabolizer (RM), Ultra-rapid Metabolizer (UM) phenotype, or Individual Impact: Average or High Risk Status).
- **Star (*) Allele:** The consensus allele classification based on the protein functional impact of a variant.
- **Substrate:** A drug or substance on which an enzyme acts.

B. Gene-Drug Interaction Types

Normal Response Expected: The corresponding drug response (toxicity and efficacy) is like that of the general population.

Use with Caution: Medication may result in a mild adverse drug reaction and/or lack of efficacy. Medication can still be on the individual, however, may require additional clinical judgment by a healthcare professional.

Consider Alternatives: Medication may result in a clinically severe adverse drug reaction and/or lack of efficacy. Medication can still be used for the individual, however, may require additional clinical adjustment by a healthcare professional.

Decrease Dose: The standard dose of the medication may cause a negative drug response (adverse drug reaction). “This dosing direction is taken directly from the FDA label for these medications”

Increase Dose: The standard dose of the medication may not achieve therapeutic success. “This dosing direction is taken directly from the FDA label for these medications”

Multiple Indicators: Medications with primary (box in color) and secondary (icon on the left) gene-drug interactions imply that additional factors must be considered when using the medication. Individual iconography is present in medication when gene-drug interactions with different levels of evidence simultaneously occur.

C. Drug Interactions

- **Contraindicated:** Medications that when simultaneously administered may produce a life threatening undesired effect.
- **Severe:** Medications that when simultaneously administered may produce a strong undesired effect.
- **Moderate:** Medications that when simultaneously administered may produce a non-life threatening undesired effect.

D. Organ Function Dependent-Drug Interactions

Certain medications can impact or be impacted by liver and kidney function. Altered organ function should be considered when prescribing certain medications as it may affect pharmacokinetic processes such as metabolism and excretion.

Hepatic: Please consider liver function when prescribing this medication as it may impact metabolism.

Renal: Please consider renal function when prescribing this medication as it may impact excretion.

Hepatic and Renal: Please consider liver and renal function when prescribing this medication as it may impact metabolism and excretion.

E. Evidence

- **Robust:** Includes gene-drug pairs supported by established actionable pharmacogenomics content (see sources). Primarily determines the overall color of the gene-drug interaction box.
  - FDA (Food and Drug Administration) Drug Labeling with actionable detailed pharmacogenomics content.
  - Clinical Pharmacogenomics Implementation Consortium (CPIC) Guidelines.
- **Modest:** Includes gene-drug pairs supported by pharmacogenomics content (see sources) regarding detailed pharmacological consequences (increased or decreased pharmacokinetics, drug metabolism, transporting; pharmacodynamics, affinity; circulating drug levels, and excretion rates) statements as dictated per the individual's genotype(s) affecting drug behavior. Secondarily determines the overall color of the gene-drug interaction box.
  - FDA (Food and Drug Administration) Drug Labeling with actionable pharmacogenomics content.
- **Developing:** Includes gene-drug pairs supported by pharmacogenomics content (see sources) regarding general pharmacological changes as dictated per the individual's genotype(s) affecting drug behavior. Does not determine the overall color of the gene-drug interaction box (Interpretative boxes with black borders). Interactions are indicated by the green check or exclamation marks.
  - FDA (Food and Drug Administration) Drug Labeling with informative pharmacogenomics content.
  - Clinical Pharmacogenomics Implementation Consortium (CPIC) without Guidelines Levels A, B, and, B/C.
  - Pharmacogenomics Knowledge Database (PharmGKB) Levels, 1, 2, and selected medications level 3.

The results of the systematic review performed by Genetica Consulting Services (GCS) of available pharmacogenomics (PGx) actionable guidelines and research literature is presented here for your consideration. The GCS PGx Review is a tool intended to provide users with relevant medical reference information related to identified multiple factors (including gene variations) and their drug associations. This review reflects the professional opinions of the GCS team and clearly indicates content intended for clinical use and for research use. Review of the same evidence can be found with references documented at geneticaconsulting.com/refs. © 2024 Genetica Consulting Services

Pharmacogenomics Actionable & Research Review

III. At a Glance

A. Current Medications & Medications Being Considered

Gene-drug interactions for current medications and medications being considered for treatment.

Refer to Section IV for additional details regarding medication response.

NORMAL RESPONSE EXPECTED	USE WITH CAUTION	CONSIDER ALTERNATIVES	INCREASE DOSE	DECREASE DOSE
DERMATOLOGY **Immunosuppressant** Tacrolimus	**CARDIOLOGY** **Beta-Blocker** Metoprolol	**CARDIOLOGY** **Antilipemic** Simvastatin		**PSYCHIATRY** **Antidepressant** Paroxetine
IMMUNOLOGY **Immunosuppressant** Tacrolimus	**GASTROENTEROLOGY** **Acid Reducing Agent** Omeprazole	**INFECTIOUS DISEASES** **Antifungal** Voriconazole		**Tricyclic Antidepressant** Desipramine
PAIN MANAGEMENT **Non-Steroidal Anti-Inflammatory Drug** Celecoxib	**PSYCHIATRY** **Antipsychotic** Brexpiprazole	**PSYCHIATRY** **Antipsychotic** Thioridazine		
RHEUMATOLOGY **Non-Steroidal Anti-Inflammatory Drug** Celecoxib				

Pharmacogenomics Actionable & Research Review
III. At a Glance

B. Comprehensive Medications

Comprehensive summary of all medications which have been assessed for gene-drug interactions.

Refer to Section IV for additional information regarding the Individual's medication response.

✓ Normal Response Expected | ! Use With Caution | ✗ Consider Alternatives | ↓ Decrease Dose | ↑ Increase Dose

CARDIOLOGY

Alpha and Beta Adrenergic Blocker
- ! Carvedilol
- ! Labetalol

Antiarrhythmic
- ! Digoxin
- ! Flecainide
- ! Propafenone

Anticoagulant
- ! Acenocoumarol
- ! Dabigatran
- ! Phenprocoumon
- ! Warfarin

Antihypertensive
- ✓ Irbesartan
- ✓ Losartan

Antilipemic
- ↓ Atorvastatin
- ! Fluvastatin
- ✗ Lovastatin
- ↓ Pitavastatin
- ! Pravastatin
- ! Rosuvastatin

Antiplatelet
- ✓ Clopidogrel
- ✓ Prasugrel
- ! Ticagrelor

Antiplatelet/Non-Steroidal Anti-Inflammatory Drug
- ✓ Aspirin

Antithrombotic
- ✓ Rivaroxaban

Beta-Blocker
- ! Acebutolol
- ! Betaxolol
- ! Bisoprolol
- ✓ Nebivolol
- ! Propranolol
- ! Timolol

CARDIOLOGY

Cardiovascular Agent
- ! Mavacamten

DENTAL

Cholinergic Agonist
- ! Cevimeline

DERMATOLOGY

Antineoplastic, Antimetabolite
- ✓ Fluorouracil

Dermatological Agent
- ! Abrocitinib
- ✗ Doxepin

ENDOCRINOLOGY

Endocrine Metabolic Agent
- ! Eliglustat

Meglitinide Analog
- ✓ Nateglinide

Sulfonylurea
- ✓ Glimepiride

GASTROENTEROLOGY

Acid Reducing Agent
- ! Dexlansoprazole
- ! Esomeprazole
- ! Lansoprazole
- ! Pantoprazole
- ! Rabeprazole

Antiemetic
- ✓ Dronabinol
- ! Meclizine
- ! Metoclopramide
- ! Ondansetron
- ✓ Palonosetron
- ! Tropisetron

GYNECOLOGY

Central Nervous System Agent
- ! Flibanserin

Contraceptive
- ! Drospirenone and Ethinyl Estradiol

GYNECOLOGY

Contraceptive
- ✓ Hormonal Contraceptives For Systemic Use

Endocrine Metabolic Agent
- ! Elagolix

HEMATOLOGY

Colony Stimulating Factor
- ✓ Avatrombopag
- ✓ Eltrombopag
- ✓ Lusutrombopag

IMMUNOLOGY

Cholinergic Agonist
- ! Cevimeline

Immunomodulatory Agent
- ✓ Siponimod

Immunosuppressant
- ✓ Azathioprine
- ! Methotrexate
- ! Sirolimus

INFECTIOUS DISEASES

Antimalarial Agent
- ! Quinine Sulfate

Antiretroviral
- ✓ Efavirenz
- ✓ Nevirapine

NEUROLOGY

Anti-Amyloid Monoclonal Antibody
- ✓ Aducanumab
- ✓ Lecanemab

Anticholinergic
- ! Donepezil
- ! Galantamine

Anticonvulsant
- ! Brivaracetam
- ✓ Fosphenytoin
- ! Lacosamide
- ✓ Phenytoin

NEUROLOGY

Antimigraine
- ✓ Rimegepant

Benzodiazepine
- ! Clobazam
- ! Diazepam
- ! Midazolam

Central Monoamine-Depleting Agent
- ! Deutetrabenazine
- ! Tetrabenazine
- ! Valbenazine

Central Nervous System Agent
- ! Dextromethorphan and Quinidine

Immunomodulatory Agent
- ✓ Siponimod

ONCOLOGY

Antiestrogen
- ✗ Tamoxifen

Antineoplastic
- ! Belzutifan
- ✓ Cisplatin
- ✓ Erdafitinib
- ! Gefitinib
- ✓ Rucaparib
- ✓ Tegafur

Antineoplastic, Antimetabolite
- ✓ Capecitabine
- ✓ Fluorouracil
- ✓ Mercaptopurine
- ! Methotrexate
- ✓ Thioguanine

OPHTHALMOLOGY

Antiglaucoma
- ! Timolol

PAIN MANAGEMENT

Antiplatelet/Non-Steroidal Anti-Inflammatory Drug
- ✓ Aspirin

Pharmacogenomics Actionable & Research Review
III. At a Glance

B. Comprehensive Medications

Comprehensive summary of all medications which have been assessed for gene-drug interactions.

Refer to Section IV for additional information regarding the Individual's medication response.

✓ Normal Response Expected | ! Use With Caution | ✗ Consider Alternatives | ↓ Decrease Dose | ↑ Increase Dose

PAIN MANAGEMENT

Non-Steroidal Anti-Inflammatory Drug
- ✓ Aceclofenac
- ✓ Diclofenac
- ✓ Flurbiprofen
- ✓ Ibuprofen
- ✓ Indomethacin
- ✓ Lornoxicam
- ✓ Lumiracoxib
- ✓ Meloxicam
- ✓ Metamizole
- ✓ Naproxen
- ✓ Piroxicam
- ✓ Tenoxicam

Opioid
- ✓ Alfentanil
- ✓ Buprenorphine
- ! Codeine
- ✓ Fentanyl
- ! Hydrocodone
- ✓ Hydromorphone
- ✓ Levomethadone
- ! Methadone
- ✓ Morphine
- ! Oliceridine
- ! Oxycodone
- ✓ Remifentanil
- ✓ Sufentanil
- ! Tramadol

Opioid Antagonist
- ✓ Naltrexone

Opioid Dependency
- ! Lofexidine

PSYCHIATRY

Antidepressant
- ✓ Bupropion
- ✗ Citalopram
- ! Duloxetine
- ✗ Escitalopram
- ✓ Fluoxetine
- ! Fluvoxamine
- ✓ Milnacipran
- ! Mirtazapine
- ! Nefazodone
- ! Sertraline
- ! Venlafaxine
- ! Vortioxetine

Antipsychotic
- ! Aripiprazole
- ! Aripiprazole Lauroxil
- ! Cariprazine
- ! Clozapine
- ! Haloperidol
- ! Iloperidone
- ✓ Lurasidone
- ! Olanzapine
- ✓ Paliperidone
- ! Perphenazine
- ! Pimozide
- ✓ Quetiapine
- ! Risperidone
- ! Zuclopenthixol

Benzodiazepine
- ! Diazepam

Central Nervous System Agent
- ! Atomoxetine
- ! Viloxazine

Central Nervous System Stimulant
- ! Amphetamine
- ! Modafinil
- ! Pitolisant

First Generation Antipsychotic
- ! Prochlorperazine

Tricyclic Antidepressant
- ✗ Amitriptyline
- ! Amoxapine
- ✗ Clomipramine
- ✗ Imipramine
- ↓ Nortriptyline
- ! Protriptyline
- ✗ Trimipramine

Tricyclic Antidepressant, Sleep Aid
- ✗ Doxepin

RESPIRATORY

Anticholinergic
- ✓ Umeclidinium

Antitussive
- ! Dextromethorphan

Bronchodilator
- ✓ Arformoterol
- ✓ Salmeterol

RHEUMATOLOGY

Antigout
- ✓ Lesinurad

Antiplatelet/Non-Steroidal Anti-Inflammatory Drug
- ✓ Aspirin

Antirheumatic
- ✓ Azathioprine
- ! Methotrexate
- ✓ Upadacitinib

Muscle Relaxant
- ! Carisoprodol

Non-Steroidal Anti-Inflammatory Drug
- ✓ Aceclofenac
- ✓ Diclofenac
- ✓ Flurbiprofen
- ✓ Ibuprofen
- ✓ Indomethacin
- ✓ Lornoxicam
- ✓ Lumiracoxib
- ✓ Meloxicam
- ✓ Nabumetone
- ✓ Naproxen
- ✓ Piroxicam
- ✓ Tenoxicam

SMOKING CESSATION

Smoking Cessation Aid
- ✓ Bupropion

SUPPLEMENTS

Vitamins
- ! L-methylfolate

TOXICOLOGY

Opioid Antagonist
- ✓ Naltrexone

UROLOGY

Alpha-1 Blocker
- ! Tamsulosin

Anticholinergic
- ! Darifenacin
- ! Fesoterodine
- ! Tolterodine

Genitourinary Agent
- ! Mirabegron

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C. Medications with Limited or No Pharmacogenomics Evidence

Medications, if listed in the table below, are not included in the report due to limited or no PGx evidence.

Medications, Supplements, and Others

Fluconazole	Grapefruit juice	Alprazolam	Buspirone

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Cardiology

Drug Class: Antilipemic **MOA:** HMG-CoA Reductase Inhibitor

Simvastatin (Zocor) — Consider Alternatives

This individual has a decreased SLCO1B1 function, which may reduce the transport of simvastatin into the liver. Additionally, this individual has a normal CYP2C9 enzymatic activity.

This individual may experience a subsequent increase in simvastatin concentrations, which may translate to an increased risk of simvastatin-induced myopathy.

The risk of adverse reaction is higher for individuals on 80 mg than those on lower doses. Alternative statin may be considered depending on the desired potency. However, if simvastatin is used, please limit the dose to <20mg/day. Physicians should evaluate drug-drug interactions, hepatic, and renal function prior to initiating a statin.

Gene: SLCO1B1, CYP2C9 **Robust**

This individual may have a normal simvastatin response and whole blood concentrations.

Gene: CYP3A4 **Developing**

This individual is not associated with type III hyperlipoproteinemia, which is a rare autosomal recessive inherited disorder characterized by increased plasma cholesterol and triglyceride levels.

In addition, APOE has been used to assess susceptibility to Alzheimer's disease. However, according to the American College of Medical Genetics, the use of APOE analysis is not clinically recommended due to limited clinical utility and poor predictive value. Although, individuals with Alzheimer's disease may have a decreased response to treatment with statins.

Gene: APOE **Developing**

Phenoconversion

Drug-Gene-Drug

Phenoconverters	Gene Property	Outcome
Grapefruit Juice, Voriconazole	CYP3A4/5 Strong Inhibitor	This results in elevated simvastatin plasma levels, and increased risk of myopathy. Concomitant use should be avoided.
Fluconazole	CYP3A4/5 Moderate Inhibitor	This results in elevated simvastatin plasma levels, and increased risk of myopathy.

Non-Genetic Interactions

Drug-Drug

Drug	Severity	Interaction
FLUCONAZOLE	MAJOR	Concurrent use of FLUCONAZOLE and SIMVASTATIN may result in increased simvastatin exposure and an increased risk of myopathy and rhabdomyolysis.

Drug-Food

Food	Severity	Interaction
GRAPEFRUIT JUICE	MAJOR	Concurrent use of SIMVASTATIN and GRAPEFRUIT JUICE may result in increased bioavailability of simvastatin resulting in an increased risk of myopathy or rhabdomyolysis.
CRANBERRY JUICE	MAJOR	Concurrent use of SIMVASTATIN and CRANBERRY JUICE may result in increased risk of hepatitis and myopathy/rhabdomyolysis.

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Cardiology

Drug Class: Beta-Blocker

MOA: Beta-1 Adrenergic Receptor Antagonist

! Metoprolol (Lopressor, Toprol XL)

Use with Caution

This individual metabolizes metoprolol slower.

This may result in higher systemic concentrations of metoprolol and a greater risk of adverse effects, including worsening of heart disease, tiredness, dizziness, hypotension, diarrhea, and rash.

This individual may have increased metoprolol blood levels, decreasing metoprolol's cardioselectivity. Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation while monitoring for any adverse events.

Gene: CYP2D6

Modest

Phenoconversion

Drug-Gene-Drug

Phenoconverters	Gene Property	Outcome
Celecoxib, Desipramine, Thioridazine	CYP2D6 Weak Inhibitor	May decrease metoprolol metabolism leading to reduced cardioselectivity.
Paroxetine	CYP2D6 Strong Inhibitor	May decrease metoprolol metabolism leading to reduced cardioselectivity.

Non-Genetic Interactions

Drug-Drug

Drug	Severity	Interaction
CELECOXIB	MODERATE	Concurrent use of BETA-ADRENERGIC BLOCKERS and NSAIDS may result in reduced antihypertensive effect.
PAROXETINE HYDROCHLORIDE	MODERATE	Concurrent use of METOPROLOL and STRONG CYP2D6 INHIBITORS may result in increased metoprolol exposure.

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Dermatology

Drug Class: Immunosuppressant **MOA:** Calcineurin Inhibitor

Tacrolimus (Astagraf XL, Prograf, Protopic, Envarsus XR) — Normal Response Expected

This individual is expected to have a normal response to tacrolimus.

This individual has poor CYP3A5 enzyme activity and is likely to metabolize tacrolimus slowly. This may result in higher tacrolimus concentrations and a higher probability of achieving therapeutic levels. Physicians should measure drug concentrations and adjust dosage based on trough whole blood tacrolimus concentrations.

Gene: CYP3A5 **Robust**

This individual may have a normal tacrolimus response and whole blood concentrations.

Gene: CYP3A4 **Developing**

Phenoconversion

Drug-Gene-Drug

Phenoconverters	Gene Property	Outcome
Grapefruit Juice, Voriconazole	CYP3A4/5 Strong Inhibitor	Results in increased tacrolimus whole blood concentrations. Monitor and adjust the dose as needed.
Fluconazole	CYP3A4/5 Moderate Inhibitor	Results in increased tacrolimus whole blood concentrations. Monitor and adjust the dose as needed.

Non-Genetic Interactions

Drug-Drug

Drug	Severity	Interaction
FLUCONAZOLE	CONTRAINDICATED	Concurrent use of FLUCONAZOLE and TACROLIMUS may result in increased tacrolimus exposure and toxicity and an increased risk of QT interval prolongation.
CELECOXIB	MAJOR	Concurrent use of TACROLIMUS and NONSTEROIDAL ANTIINFLAMMATORY AGENTS may result in acute renal failure.
OMEPRAZOLE	MAJOR	Concurrent use of OMEPRAZOLE and TACROLIMUS may result in increased tacrolimus exposure and an increased risk of toxicity.
VORICONAZOLE	MAJOR	Concurrent use of TACROLIMUS and VORICONAZOLE may result in increased tacrolimus exposure and an increased risk of QT interval prolongation.

Drug-Food

Food	Severity	Interaction
GRAPEFRUIT JUICE	MAJOR	Concurrent use of TACROLIMUS and GRAPEFRUIT JUICE may result in increased tacrolimus exposure.

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Gastroenterology

Drug Class: Acid Reducing Agent **MOA:** Proton Pump Inhibitor

Omeprazole (Prilosec) — Use with Caution

This individual metabolizes omeprazole fast.

Increased activity may expose the individual to lower levels of omeprazole at standard dosing and may require dose adjustment due to a lack of pharmacotherapy success.

Increasing the starting daily dose may be required while closely monitoring for efficacy.

Gene: CYP2C19 Robust

Phenoconversion

Drug-Gene-Drug

Phenoconverters	Gene Property	Outcome
Voriconazole, Desipramine, Paroxetine	CYP2C19 Weak Inhibitor	This results in decreased metabolism and increased omeprazole exposure.
Grapefruit Juice, Voriconazole	CYP3A4/5 Strong Inhibitor	This results in decreased drug metabolism and increased omeprazole exposure. In patients with Zollinger-Ellison syndrome, dose adjustment may be considered when combining omeprazole and voriconazole.
Fluconazole	CYP2C19 Strong Inhibitor	This results in decreased metabolism and increased omeprazole exposure.
Fluconazole	CYP3A4/5 Moderate Inhibitor	This results in decreased drug metabolism and increased omeprazole exposure.

Non-Genetic Interactions

Drug-Drug

Drug	Severity	Interaction
FLUCONAZOLE	MAJOR	Concurrent use of FLUCONAZOLE and OMEPRAZOLE may result in increased omeprazole exposure.
VORICONAZOLE	MAJOR	Concurrent use of OMEPRAZOLE and VORICONAZOLE may result in increased plasma concentrations of omeprazole.
TACROLIMUS	MAJOR	Concurrent use of OMEPRAZOLE and TACROLIMUS may result in increased tacrolimus exposure and an increased risk of toxicity.

Drug-Food

Food	Severity	Interaction
CRANBERRY	MODERATE	Concurrent use of PROTON PUMP INHIBITORS and CRANBERRY may result in reduced effectiveness of proton pump inhibitors.

Drug-Lab

Lab	Severity	Interaction
URINE SUBSTANCE MEASUREMENT	MODERATE	PROTON PUMP INHIBITORS may result in false-positive urine screening tests for tetrahydrocannabinol (THC) due to an unknown mechanism.

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Immunology

Drug Class: Immunosuppressant **MOA:** Calcineurin Inhibitor

Tacrolimus (Astagraf XL, Prograf, Protopic, Envarsus XR) — Normal Response Expected

This individual is expected to have a normal response to tacrolimus.

This individual has poor CYP3A5 enzyme activity and is likely to metabolize tacrolimus slowly. This may result in higher tacrolimus concentrations and a higher probability of achieving therapeutic levels. Physicians should measure drug concentrations and adjust dosage based on trough whole blood tacrolimus concentrations.

Gene: CYP3A5 **Robust**

This individual may have a normal tacrolimus response and whole blood concentrations.

Gene: CYP3A4 **Developing**

Phenoconversion

Drug-Gene-Drug

Phenoconverters	Gene Property	Outcome
Grapefruit Juice, Voriconazole	CYP3A4/5 Strong Inhibitor	Results in increased tacrolimus whole blood concentrations. Monitor and adjust the dose as needed.
Fluconazole	CYP3A4/5 Moderate Inhibitor	Results in increased tacrolimus whole blood concentrations. Monitor and adjust the dose as needed.

Non-Genetic Interactions

Drug-Drug

Drug	Severity	Interaction
FLUCONAZOLE	CONTRAINDICATED	Concurrent use of FLUCONAZOLE and TACROLIMUS may result in increased tacrolimus exposure and toxicity and an increased risk of QT interval prolongation.
CELECOXIB	MAJOR	Concurrent use of TACROLIMUS and NONSTEROIDAL ANTIINFLAMMATORY AGENTS may result in acute renal failure.
OMEPRAZOLE	MAJOR	Concurrent use of OMEPRAZOLE and TACROLIMUS may result in increased tacrolimus exposure and an increased risk of toxicity.
VORICONAZOLE	MAJOR	Concurrent use of TACROLIMUS and VORICONAZOLE may result in increased tacrolimus exposure and an increased risk of QT interval prolongation.

Drug-Food

Food	Severity	Interaction
GRAPEFRUIT JUICE	MAJOR	Concurrent use of TACROLIMUS and GRAPEFRUIT JUICE may result in increased tacrolimus exposure.

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Infectious Diseases

Drug Class: Antifungal **MOA:** Ergosterol Synthesis Inhibitor

✕ Voriconazole (Vfend) — Consider Alternatives

This individual metabolizes voriconazole fast, which may reduce the probability of pharmacotherapy success.

An alternative therapy may be required in adult and pediatric individuals.

Gene: CYP2C19 Robust

Phenoconversion

Drug-Gene-Drug

Phenoconverters	Gene Property	Outcome
Omeprazole, Desipramine, Paroxetine	CYP2C19 Weak Inhibitor	This results in reduced drug metabolism and increased voriconazole plasma concentrations which may lead to an increased risk of adverse events. Adjust voriconazole dosage and monitor for adverse reactions.
Grapefruit Juice	CYP3A4/5 Strong Inhibitor	This results in reduced metabolism and increased voriconazole plasma concentrations which may lead to an increased risk of adverse events. Adjust voriconazole dosage and monitor for adverse reactions.
Fluconazole	CYP2C9 Moderate Inhibitor	This results in reduced drug metabolism and increased voriconazole plasma concentrations which may lead to an increased risk of adverse events. Adjust voriconazole dosage and monitor for adverse reactions.
Fluconazole	CYP2C19 Strong Inhibitor	This results in reduced drug metabolism and increased voriconazole plasma concentrations which may lead to an increased risk of adverse events. Adjust voriconazole dosage and monitor for adverse reactions.
Fluconazole	CYP3A4/5 Moderate Inhibitor	This results in reduced metabolism and increased voriconazole plasma concentrations which may lead to an increased risk of adverse events. Adjust voriconazole dosage and monitor for adverse reactions.
Paroxetine	CYP2C9 Weak Inhibitor	This results in reduced drug metabolism and increased voriconazole plasma concentrations which may lead to an increased risk of adverse events. Adjust voriconazole dosage and monitor for adverse reactions.

Non-Genetic Interactions

Drug-Drug

Drug	Severity	Interaction
ALPRAZOLAM	CONTRAINDICATED	Concurrent use of ALPRAZOLAM and STRONG CYP3A4 INHIBITORS may result in increased alprazolam exposure.
FLUCONAZOLE	CONTRAINDICATED	Concurrent use of FLUCONAZOLE and VORICONAZOLE may result in increased voriconazole exposure and an increased risk of QT interval prolongation.
OMEPRAZOLE	MAJOR	Concurrent use of OMEPRAZOLE and VORICONAZOLE may result in increased plasma concentrations of omeprazole.
TACROLIMUS	MAJOR	Concurrent use of TACROLIMUS and VORICONAZOLE may result in increased tacrolimus exposure and an increased risk of QT interval prolongation.

Drug-Food

Food	Severity	Interaction
FOOD	MODERATE	Concurrent use of VORICONAZOLE and FOOD may result in decreased voriconazole exposure.

PHD LABORATORY

Pain Management

Drug Class: Non-Steroidal Anti-Inflammatory Drug **MOA:** Selective COX-2 Inhibitor

Celecoxib (Celebrex) — Normal Response Expected

This individual is expected to have a normal response to celecoxib.

Gene: CYP2C9 Robust

Phenoconversion

Drug-Gene-Drug

Phenoconverters	Gene Property	Outcome
Fluconazole	CYP2C9 Moderate Inhibitor	This results in decreased drug metabolism and increased celecoxib exposure. Likely leading to an increased risk of adverse events. Monitor for adverse events and adjust the dose accordingly.
Voriconazole, Paroxetine	CYP2C9 Weak Inhibitor	This results in decreased drug metabolism and increased celecoxib exposure. Likely leading to an increased risk of adverse events. Monitor for adverse events and adjust the dose accordingly.

Non-Genetic Interactions

Drug-Drug

Drug	Severity	Interaction
FLUCONAZOLE	MAJOR	Concurrent use of CELECOXIB and FLUCONAZOLE may result in increased celecoxib exposure.
DESIPRAMINE HYDROCHLORIDE	MAJOR	Concurrent use of NSAID and TRICYCLIC ANTIDEPRESSANTS may result in an increased risk of bleeding.
PAROXETINE HYDROCHLORIDE	MAJOR	Concurrent use of NSAIDS and SSRI may result in an increased risk of bleeding.
TACROLIMUS	MAJOR	Concurrent use of TACROLIMUS and NONSTEROIDAL ANTIINFLAMMATORY AGENTS may result in acute renal failure.
METOPROLOL TARTRATE	MODERATE	Concurrent use of BETA-ADRENERGIC BLOCKERS and NSAIDS may result in reduced antihypertensive effect.

PHD LABORATORY

Psychiatry

Drug Class: Antidepressant

MOA: Selective Serotonin Reuptake Inhibitor

Paroxetine (Paxil, Pexeva, Brisdelle)

Decrease Dose

This individual metabolizes paroxetine slower, which can lead to an increased probability of adverse events due to higher plasma concentrations.

The adverse events may include nervousness, insomnia, decreased libido, impotence, and dry mouth.

A lower starting dose and a slower titration schedule may be considered.

The recommended initial dosage is 10 mg per day for individuals with severe renal impairment and severe hepatic impairment. The dosage should not exceed 40 mg/day.

Gene: CYP2D6 — **Robust**

This individual may have a reduced response.

Gene: HTR1A ! — **Developing**

This individual may have an increased risk of nausea or sexual dysfunctions.

Gene: HTR2A ! — **Developing**

Non-Genetic Interactions

Drug-Drug

Drug	Severity	Interaction
THIORIDAZINE HYDROCHLORIDE	CONTRAINDICATED	Concurrent use of PAROXETINE and THIORIDAZINE may result in an increased risk of thioridazine toxicity, cardiotoxicity (QT interval prolongation, torsades de pointes, cardiac arrest).
CELECOXIB	MAJOR	Concurrent use of NSAIDS and SSRI may result in an increased risk of bleeding.
METOPROLOL TARTRATE	MODERATE	Concurrent use of METOPROLOL and STRONG CYP2D6 INHIBITORS may result in increased metoprolol exposure.

PHD LABORATORY

Psychiatry

Drug Class: Antipsychotic

MOA: D2 and 5-HT1A Receptor Partial Agonist and 5-HT2A Receptor Antagonist

! Brexpiprazole (Rexulti) — Use with Caution

This individual metabolizes brexpiprazole slower, which may lead to an increased probability of adverse events.

Adverse effects of brexpiprazole therapy can include weight gain, feeling the urge to move constantly (akathisia), and cerebrovascular reactions such as stroke and transient ischemic attack.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Gene: CYP2D6 — **Robust**

This individual may have a normal response to brexpiprazole.

Gene: CYP3A4 — **Developing**

Phenoconversion

Drug-Gene-Drug

Phenoconverters	Gene Property	Outcome
Celecoxib, Desipramine, Thioridazine	CYP2D6 Weak Inhibitor	This results in decreased drug metabolism and higher brexpiprazole exposure.
Grapefruit Juice, Voriconazole	CYP3A4/5 Strong Inhibitor	May result in higher brexpiprazole exposure. Administer half of the usual dose of brexpiprazole. With concomitant use of brexpiprazole with a strong CYP3A4 inhibitor and a strong/moderate CYP2D6 inhibitor, administer a quarter of the usual brexpiprazole dose.
Fluconazole	CYP3A4/5 Moderate Inhibitor	May result in higher brexpiprazole exposure. With concomitant use of brexpiprazole with a moderate CYP3A4 inhibitor and a strong/moderate CYP2D6 inhibitor, administer a quarter of the usual brexpiprazole dose.
Paroxetine	CYP2D6 Strong Inhibitor	Increased exposure of brexpiprazole. Administer half of the usual dose of brexpiprazole. With concomitant use of brexpiprazole with a strong CYP2D6 inhibitor and a strong/moderate CYP3A4 inhibitor, administer a quarter of the recommended brexpiprazole dose.

PHD LABORATORY

Psychiatry

Drug Class: Antipsychotic

MOA: D2 Receptor Blocker

✕ Thioridazine (Mellaril)

Consider Alternatives

This individual may metabolize thioridazine slower, which results in increased exposure to thioridazine and a greater risk of QT prolongation.

Thioridazine is contraindicated in this individual. However, if thioridazine is used, please consider conducting a baseline and subsequent electrocardiograms to evaluate QT segment status.

Gene: CYP2D6

Robust

Phenoconversion

Drug-Gene-Drug

Phenoconverters	Gene Property	Outcome
Celecoxib, Desipramine	CYP2D6 Weak Inhibitor	Higher levels of thioridazine may lead to an increased risk of QT prolongation and cardiac arrhythmias. Concomitant use is not recommended.
Paroxetine	CYP2D6 Strong Inhibitor	Higher levels of thioridazine may lead to an increased risk of QT prolongation and cardiac arrhythmias. Concomitant use is not recommended.

Non-Genetic Interactions

Drug-Drug

Drug	Severity	Interaction
PAROXETINE HYDROCHLORIDE	CONTRAINDICATED	Concurrent use of PAROXETINE and THIORIDAZINE may result in an increased risk of thioridazine toxicity, cardiotoxicity (QT interval prolongation, torsades de pointes, cardiac arrest).

Drug-Lab

Lab	Severity	Interaction
URINE CHORIONIC GONADOTROPHIN MEASUREMENT	MODERATE	PHENOTHIAZINES may result in false positive or negative pregnancy test results due to interference based on immunological reactions between human chorionic gonadotropin (HCG) and anti-HCG.

Drug-Alcohol

Alcohol	Severity	Interaction
ETHANOL	MODERATE	Concurrent use of THIORIDAZINE and ETHANOL may result in increased central nervous system depression and an increased risk of extrapyramidal reactions.

PHD LABORATORY

Psychiatry

Drug Class: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor

Desipramine (Norpramin) — Decrease Dose

This individual metabolizes desipramine slower, which may lead to an increased probability of adverse events due to higher plasma concentrations of desipramine when given usual doses.

The adverse events may include cardiotoxicity, blurred vision, constipation, dizziness, central nervous system toxicities, and suicide risk.

A dose reduction of the recommended starting dose may be required. Physicians may adjust the dose based on the individual's clinical presentation.

Gene: CYP2D6 — Robust

Phenoconversion

Drug-Gene-Drug

Phenoconverters	Gene Property	Outcome
Celecoxib, Thioridazine	CYP2D6 Weak Inhibitor	May result in decreased drug metabolism and higher plasma concentration of desipramine. Lower doses for either desipramine or the CYP2D6 inhibitor are recommended. Monitor desipramine plasma levels.
Paroxetine	CYP2D6 Strong Inhibitor	May result in decreased drug metabolism and increased plasma concentration of desipramine. Lower doses for either desipramine or the CYP2D6 inhibitor are recommended. Monitor desipramine plasma levels.

Non-Genetic Interactions

Drug-Drug

Drug	Severity	Interaction
CELECOXIB	MAJOR	Concurrent use of NSAID and TRICYCLIC ANTIDEPRESSANTS may result in an increased risk of bleeding.

PHD LABORATORY

Rheumatology

Drug Class: Non-Steroidal Anti-Inflammatory Drug **MOA:** Selective COX-2 Inhibitor

Celecoxib (Celebrex) — Normal Response Expected

This individual is expected to have a normal response to celecoxib.

Gene: CYP2C9 Robust

Phenoconversion

Drug-Gene-Drug

Phenoconverters	Gene Property	Outcome
Fluconazole	CYP2C9 Moderate Inhibitor	This results in decreased drug metabolism and increased celecoxib exposure. Likely leading to an increased risk of adverse events. Monitor for adverse events and adjust the dose accordingly.
Voriconazole, Paroxetine	CYP2C9 Weak Inhibitor	This results in decreased drug metabolism and increased celecoxib exposure. Likely leading to an increased risk of adverse events. Monitor for adverse events and adjust the dose accordingly.

Non-Genetic Interactions

Drug-Drug

Drug	Severity	Interaction
FLUCONAZOLE	MAJOR	Concurrent use of CELECOXIB and FLUCONAZOLE may result in increased celecoxib exposure.
DESIPRAMINE HYDROCHLORIDE	MAJOR	Concurrent use of NSAID and TRICYCLIC ANTIDEPRESSANTS may result in an increased risk of bleeding.
PAROXETINE HYDROCHLORIDE	MAJOR	Concurrent use of NSAIDS and SSRI may result in an increased risk of bleeding.
TACROLIMUS	MAJOR	Concurrent use of TACROLIMUS and NONSTEROIDAL ANTIINFLAMMATORY AGENTS may result in acute renal failure.
METOPROLOL TARTRATE	MODERATE	Concurrent use of BETA-ADRENERGIC BLOCKERS and NSAIDS may result in reduced antihypertensive effect.

PHD LABORATORY

Cardiology

Drug Class: Alpha and Beta Adrenergic Blocker

MOA: Nonselective Beta Adrenergic Blocker and Alpha 1 Adrenergic Blocker

! Carvedilol (Coreg) — Use with Caution

This individual may metabolize carvedilol slower, which results in a greater risk of adverse effects, including dizziness, due to higher concentrations of the a-blocking R (+) enantiomer of carvedilol.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation while monitoring for any vasodilating effects.

Gene: CYP2D6 — **Modest**

Drug Class: Alpha and Beta Adrenergic Blocker

MOA: Nonselective Beta Adrenergic Blocker and Alpha 1 Adrenergic Blocker

Labetalol (Normodyne, Trandate) !

This individual metabolizes labetalol slower, leading to higher concentrations.

This may lead to an increased risk of adverse events. Adverse events may include jaundice, Intraoperative Floppy Iris Syndrome (IFIS), orthostatic hypotension, dizziness, and nausea.

Gene: CYP2D6 — **Developing**

Drug Class: Antiarrhythmic

MOA: Sodium and Potassium ATPase Pump Inhibitor

Digoxin (Digitek, Digox, Lanoxin, Lanoxin Pediatric) !

This individual may have altered metabolism and altered serum concentrations of digoxin.

There is no mention of the drug response and/or drug exposure associated with this genotype and how it may affect pharmacotherapy success or increase the risk of adverse drug reactions.

Gene: ABCB1 — **Developing**

Drug Class: Antiarrhythmic

MOA: Sodium Channel Blocker

Flecainide (Tambocor) !

This individual metabolizes flecainide slower, leading to higher concentrations of the drug, which may increase the risk of adverse events.

Adverse events may include dizziness, vision changes, and cardiovascular effects.

Gene: CYP2D6 — **Developing**

Drug Class: Antiarrhythmic

MOA: Sodium Channel Blocker

! Propafenone (Rythmol SR) — Use with Caution

This individual metabolizes propafenone slower, resulting in higher systemic concentrations which can lead to a greater risk of adverse effects including cardiac arrhythmias.

Gene: CYP2D6 — **Robust**

This individual may have a normal response to propafenone.

Gene: CYP3A4 ✓ — **Developing**

Drug Class: Anticoagulant

MOA: Direct Thrombin Inhibitor

Dabigatran (Pradaxa) !

This individual may have increased exposure to dabigatran.

Gene: ABCB1 — **Developing**

PHD LABORATORY

Cardiology

Drug Class: Anticoagulant

MOA: Synthesis of Vitamin K-Dependent Coagulation Factors II, VII, IX, and X, Protein C and S Inhibitor

Acenocoumarol

This individual may have increased sensitivity to acenocoumarol.

Gene: VKORC1 **Developing**

This individual's genotype is associated with lower levels of active vitamin K likely requiring a reduced dose.

Gene: CYP4F2 **Developing**

This individual may have a decreased risk of over-anticoagulation and a decreased risk of bleeding.

Gene: CYP2C9 **Developing**

Drug Class: Anticoagulant

MOA: Synthesis of Vitamin K-Dependent Coagulation Factors II, VII, IX, and X, Protein C and S Inhibitor

Phenprocoumon

This individual may have increased sensitivity to phenprocoumon and an increased risk of adverse events (bleeding, over-anticoagulation, or increased time above therapeutic range).

Gene: VKORC1 **Developing**

This individual's genotype is associated with lower levels of active vitamin K likely requiring a reduced dose.

Gene: CYP4F2 **Developing**

Drug Class: Anticoagulant

MOA: Synthesis of Vitamin K-Dependent Coagulation Factors II, VII, IX, and X, Protein C and S Inhibitor

Warfarin (Coumadin, Jantoven) — Use with Caution

CYP2C9 and VKORC1

This individual is expected to have a normal response to warfarin.

CYP4F2 (c.1297G>A Negative, CC)

Carriers of one copy (heterozygous) or two copies (homozygous) of CYP4F2 variants have higher levels of active vitamin K likely requiring a 5 - 10% dose increase respectively.

CYP2C (g.94645745G>A Negative, GG)

Carriers of one copy (heterozygous) or two copies (homozygous) of CYP2C variants have decreased warfarin clearance likely requiring a 10 - 25% dose reduction respectively. This pharmacokinetic change affecting dosing was observed to have a significant impact in individuals of African ancestry, and less significant in those individuals of European or Asian ancestry.

It is recommended to establish an INR baseline and to monitor INR periodically until reaching a steady protective value.

Gene: CYP2C9, VKORC1, CYP4F2, CYP2C **Robust**

Drug Class: Antihypertensive

MOA: Angiotensin II Receptor Antagonist

Irbesartan (Avapro)

This individual may have normal therapeutic levels of irbesartan.

Gene: CYP2C9 **Developing**

Drug Class: Antihypertensive

MOA: Angiotensin II Receptor Antagonist

Losartan (Cozaar)

This individual may have normal therapeutic levels of losartan and its active metabolite.

Gene: CYP2C9 **Developing**

PHD LABORATORY

Cardiology

Drug Class: Antilipemic **MOA:** HMG-CoA Reductase Inhibitor

Atorvastatin (Lipitor) — Decrease Dose

This individual has a decreased SLCO1B1 function, which may reduce the transport of atorvastatin into the liver. Additionally, this individual has a normal CYP2C9 enzymatic activity.

This individual may experience a subsequent increase in atorvastatin concentrations, which may translate to an increased risk of atorvastatin-induced myopathy.

Physicians may prescribe </=40 mg as a starting dose and adjust the dose based on the individual's clinical presentation and disease-specific guidelines. However, if >40 mg is needed for desired efficacy, please consider combination therapy. Physicians should evaluate drug-drug interactions, hepatic, and renal function prior to initiating a statin.

Gene: SLCO1B1, CYP2C9 **Robust**

This individual may have a normal response to atorvastatin.

Gene: CYP3A4 **Developing**

This individual is not associated with type III hyperlipoproteinemia, which is a rare autosomal recessive inherited disorder characterized by increased plasma cholesterol and triglyceride levels.

In addition, APOE has been used to assess susceptibility to Alzheimer's disease. However, according to the American College of Medical Genetics, the use of APOE analysis is not clinically recommended due to limited clinical utility and poor predictive value. Moreover, individuals with this genotype may have a decreased response to treatment with atorvastatin.

Gene: APOE **Developing**

Drug Class: Antilipemic **MOA:** HMG-CoA Reductase Inhibitor

Fluvastatin (Lescol) — Use with Caution

This individual has a decreased SLCO1B1 function, which may reduce the transport of fluvastatin into the liver.

Additionally, this individual has a normal CYP2C9 enzymatic activity.

This individual may experience a subsequent increase in fluvastatin concentrations, which may translate to an increased risk of fluvastatin-induced myopathy, especially with doses >40mg per day.

When using this medication, it is recommended to monitor individuals for myopathy symptoms (muscle pain and tenderness) and evaluate drug-drug interactions as well as hepatic and renal function prior to initiating a statin. Physicians may adjust the dose based on the individual's clinical presentation, creatine kinase (CK) levels, and cholesterol levels.

Gene: SLCO1B1, CYP2C9 **Robust**

This individual is not associated with type III hyperlipoproteinemia, which is a rare autosomal recessive inherited disorder characterized by increased plasma cholesterol and triglyceride levels.

In addition, APOE has been used to assess susceptibility to Alzheimer's disease. However, according to the American College of Medical Genetics, the use of APOE analysis is not clinically recommended due to limited clinical utility and poor predictive value. Although, individuals with Alzheimer's disease may have a decreased response to treatment with statins.

Gene: APOE **Developing**

Cardiology

Drug Class: Antilipemic **MOA:** HMG-CoA Reductase Inhibitor

Lovastatin (Altoprev, Mevacor) — Consider Alternatives

This individual has a decreased SLCO1B1 function, which may reduce the transport of lovastatin into the liver. Additionally, this individual has a normal CYP2C9 enzymatic activity.

This individual may experience a subsequent increase in lovastatin concentrations, which may translate to an increased risk of lovastatin-induced myopathy.

Alternative statin may be considered depending on the desired potency. However, if lovastatin is used, please limit the dose to </= 20mg/day. Physicians should evaluate drug-drug interactions, hepatic, and renal function prior to initiating a statin.

Gene: SLCO1B1, CYP2C9 **Robust**

This individual may have a normal response to lovastatin.

Gene: CYP3A4 **Developing**

This individual is not associated with type III hyperlipoproteinemia, which is a rare autosomal recessive inherited disorder characterized by increased plasma cholesterol and triglyceride levels.

In addition, APOE has been used to assess susceptibility to Alzheimer's disease. However, according to the American College of Medical Genetics, the use of APOE analysis is not clinically recommended due to limited clinical utility and poor predictive value. Although, individuals with Alzheimer's disease may have a decreased response to treatment with statins.

Gene: APOE **Developing**

Drug Class: Antilipemic **MOA:** HMG-CoA Reductase Inhibitor

Pitavastatin (Livalo, Zypitamag) — Decrease Dose

This individual has a decreased SLCO1B1 function, which may reduce the transport of pitavastatin into the liver. Additionally, this individual has a normal CYP2C9 enzymatic activity.

This individual may experience a subsequent increase in pitavastatin concentrations, which may translate to an increased risk of pitavastatin-induced myopathy.

Physicians may prescribe </=2 mg as a starting dose and adjust the dose based on the individual's clinical presentation and disease-specific guidelines. However, if >2 mg is needed for desired efficacy, please consider an alternative statin or combination therapy. Physicians should evaluate drug-drug interactions, hepatic, and renal function prior to initiating a statin.

Gene: SLCO1B1, CYP2C9 **Robust**

This individual is not associated with type III hyperlipoproteinemia, which is a rare autosomal recessive inherited disorder characterized by increased plasma cholesterol and triglyceride levels.

In addition, APOE has been used to assess susceptibility to Alzheimer's disease. However, according to the American College of Medical Genetics, the use of APOE analysis is not clinically recommended due to limited clinical utility and poor predictive value. Although, individuals with Alzheimer's disease may have a decreased response to treatment with statins.

Gene: APOE **Developing**

Cardiology

Drug Class: Antilipemic **MOA:** HMG-CoA Reductase Inhibitor

! Pravastatin (Pravachol) — Use with Caution

This individual has a decreased SLCO1B1 function, which may reduce the transport of pravastatin into the liver. Additionally, this individual has a normal CYP2C9 enzymatic activity.

This individual may experience a subsequent increase in pravastatin concentrations, which may translate to an increased risk of pravastatin-induced myopathy, especially with doses >40mg per day.

When using this medication, it is recommended to monitor individuals for myopathy symptoms (muscle pain and tenderness) and evaluate drug-drug interactions as well as hepatic and renal function prior to initiating a statin. Physicians may adjust the dose based on the individual's clinical presentation, creatine kinase (CK) levels, and cholesterol levels.

Gene: SLCO1B1, CYP2C9 **Robust**

This individual is not associated with type III hyperlipoproteinemia, which is a rare autosomal recessive inherited disorder characterized by increased plasma cholesterol and triglyceride levels.

In addition, APOE has been used to assess susceptibility to Alzheimer's disease. However, according to the American College of Medical Genetics, the use of APOE analysis is not clinically recommended due to limited clinical utility and poor predictive value. Although, individuals with Alzheimer's disease may have a decreased response to treatment with statins.

Gene: APOE ! **Developing**

Drug Class: Antilipemic **MOA:** HMG-CoA Reductase Inhibitor

! Rosuvastatin (Crestor, Ezallor Sprinkle) — Use with Caution

This individual has a decreased SLCO1B1 function, which may reduce the transport of rosuvastatin into the liver, and a normal ABCG2 function.

Additionally, this individual has a normal CYP2C9 enzymatic activity that does not affect the pharmacokinetics of rosuvastatin.

This individual may experience a subsequent increase in rosuvastatin concentrations, which may translate to an increased risk of rosuvastatin-induced myopathy, especially with doses >20mg per day.

When using this medication, it is recommended to monitor individuals for myopathy symptoms (muscle pain and tenderness) and evaluate drug-drug interactions, Asian ancestry as well as hepatic and renal function prior to initiating a statin. Physicians may adjust the dose based on the individual's clinical presentation, creatine kinase (CK) levels, and cholesterol levels.

Gene: SLCO1B1, CYP2C9, ABCG2 **Robust**

This individual is not associated with type III hyperlipoproteinemia, which is a rare autosomal recessive inherited disorder characterized by increased plasma cholesterol and triglyceride levels.

In addition, APOE has been used to assess susceptibility to Alzheimer's disease. However, according to the American College of Medical Genetics, the use of APOE analysis is not clinically recommended due to limited clinical utility and poor predictive value. Although, individuals with Alzheimer's disease may have a decreased response to treatment with statins.

Gene: APOE ! **Developing**

Drug Class: Antiplatelet **MOA:** P2Y12 Inhibitor

! Clopidogrel (Plavix) — Normal Response Expected

This individual metabolizes clopidogrel fast leading to increased clopidogrel active metabolite formation and lower on-treatment platelet reactivity.

For individuals with acute coronary syndromes (ACS) and/or undergoing percutaneous coronary intervention (PCI), clopidogrel should be used at the standard dose because there is no increased risk of bleeding or ischemic events compared to individuals who are normal metabolizers.

For individuals with neurovascular disease, there is insufficient data on ischemic outcomes and bleeding risk. In addition, there are no recommendations for non-ACS, non-PCI cardiovascular indications. Physicians may initiate therapy with the recommended starting dose and adjust the dose based on the individual's clinical presentation.

Gene: CYP2C19 **Robust**

PHD LABORATORY

Cardiology

Drug Class: Antiplatelet
MOA: P2Y12 Inhibitor

! Prasugrel (Effient) — Normal Response Expected

Physicians may initiate the recommended starting dose and adjust the dose based on the individual's clinical presentation.

Gene: CYP2C19, CYP2C9, CYP3A5, CYP2B6 — Modest

Drug Class: Antiplatelet
MOA: P2Y12 Inhibitor

! Ticagrelor (Brilinta) — Use with Caution

This individual metabolizes ticagrelor fast.

However, there is no mention of the drug response and/or drug exposure associated with increased activity of this enzyme and how it may affect pharmacotherapy success or increase the risk of adverse drug reactions.

Physicians may initiate the recommended starting dose and adjust the dose based on the individual's clinical presentation.

Gene: CYP2C19 — Modest

This individual may have a normal response to standard dosing of ticagrelor.

Gene: CYP3A4 — Developing

Drug Class: Antiplatelet/Non-Steroidal Anti-Inflammatory Drug
MOA: Prostaglandin Synthesis and Platelet Aggregation Inhibitor

Aspirin (Ecotrin, Bayer, Asctiptin, Durlaza) — Normal Response Expected

This individual may have normal therapeutic levels of aspirin.

Avoid aspirin in individuals with severe hepatic insufficiency or severe renal failure (GFR <10 mL/min).

Gene: CYP2C9 — Robust

Drug Class: Antithrombotic
MOA: Selective Factor Xa Inhibitor

Rivaroxaban (Xarelto) — Normal Response Expected

This individual is expected to have an average risk of thrombotic and thromboembolic complications when administering rivaroxaban.

Gene: F5 — Modest

This individual may have a normal response to standard dosing of rivaroxaban.

Gene: CYP3A4 — Developing

Drug Class: Beta-Blocker
MOA: Beta-1 Adrenergic Receptor Antagonist

! Acebutolol — Use with Caution

This individual has reduced CYP2D6 enzyme activity and likely metabolizes acebutolol slower.

There is insufficient evidence regarding drug exposure and clinical effectiveness.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation while monitoring blood pressure and heart rate.

Gene: CYP2D6 — Robust

Cardiology

Drug Class: Beta-Blocker
MOA: Beta-1 Adrenergic Receptor Antagonist

! Betaxolol — Use with Caution

This individual has reduced CYP2D6 enzyme activity and likely metabolizes betaxolol slower.

There is insufficient evidence regarding drug exposure and clinical effectiveness.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation while monitoring blood pressure and heart rate.

Gene: CYP2D6 — Robust

Drug Class: Beta-Blocker
MOA: Beta-1 Adrenergic Receptor Antagonist

! Bisoprolol — Use with Caution

This individual has reduced CYP2D6 enzyme activity and likely metabolizes bisoprolol slower.

There is insufficient evidence regarding drug exposure and clinical effectiveness.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation while monitoring blood pressure and heart rate.

Gene: CYP2D6 — Robust

Drug Class: Beta-Blocker
MOA: Beta-1 Adrenergic Receptor Antagonist

! Nebivolol (Bystolic) — Normal Response Expected

This individual may metabolize nebivolol slower, which may result in higher systemic concentrations of nebivolol.

However, the clinical effect and safety profile observed in poor metabolizers were similar to those of normal metabolizers.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

However, nebivolol exposure increases with inhibition of CYP2D6. The dose of nebivolol may need to be reduced.

In individuals with severe renal impairment (CrCl < 30 mL/min) or moderate hepatic impairment, the recommended initial dose is 2.5 mg once daily; titrate up slowly if needed. Nebivolol is not recommended in individuals with severe hepatic impairment.

Gene: CYP2D6 — Robust

Drug Class: Beta-Blocker
MOA: Nonselective Beta-Adrenergic Receptor Antagonist

! Propranolol (Inderal, Inderal LA, InnoPran XL, Propranolol HCl Intensol, Inderal XL, Hemangeol) — Use with Caution

This individual may metabolize propranolol slower, which may affect systemic concentrations of propranolol.

No difference was observed between CYP2D6 normal metabolizers and poor metabolizers with respect to oral clearance or elimination half-life.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

CYP2D6 inhibitors, CYP1A2 inhibitors, and CYP2C19 inhibitors increase exposure to propranolol when co-administered with propranolol. Monitor individuals for bradycardia and hypotension. CYP1A2 inducers and CYP2C19 inducers decrease the plasma levels of propranolol resulting in a loss of efficacy.

Initiate propranolol in individuals with impaired renal or hepatic function at the lowest dose (80 mg) once daily and monitor individuals for marked bradycardia and hypotension.

Gene: CYP2D6 — Modest

PHD LABORATORY

Cardiology

Drug Class: Beta-Blocker

MOA: Nonselective Beta-Adrenergic Receptor Antagonist

Timolol (Betimol) !

This individual metabolizes timolol slower, which may lead to increased exposure to timolol, and increased exercise heart rate reduction.

Gene: CYP2D6 **Developing**

Drug Class: Cardiovascular Agent

MOA: Cardiac Myosin Inhibitor

! Mavacamten (Camzyos) — Use with Caution

This individual may metabolize mavacamten fast, which may reduce the probability of pharmacotherapy success.

Physicians may initiate the recommended starting dose and adjust the dose based on the individual's clinical presentation while closely monitoring for therapeutic effects.

Gene: CYP2C19 **Robust**

Dental

Drug Class: Cholinergic Agonist

MOA: Cholinergic Receptor Agonist

! Cevimeline (Evoxac) — Use with Caution

This individual metabolizes cevimeline slower, which may lead to an increased probability of adverse events.

Adverse effects of cevimeline therapy can include increased sweating, excessive salivation, nausea, diarrhea, headache, and a stuffy nose. Therefore, cevimeline should be used with caution.

Physicians may initiate therapy at a recommended dose, adjust the dose as needed, or consider an alternative drug therapy based on the individual's clinical presentation.

Gene: CYP2D6 **Robust**

This individual may have a normal response to cevimeline.

Gene: CYP3A4 ✓ **Developing**

Dermatology

Drug Class: Antineoplastic, Antimetabolite

MOA: DNA and RNA Synthesis Inhibitor

✓ Fluorouracil (Adrucil, Carac, Efudex, Fluoroplex) — Normal Response Expected

This individual is expected to have a normal response to fluorouracil.

Gene: DPYD **Robust**

Drug Class: Dermatological Agent

MOA: Janus Kinase Inhibitor

! Abrocitinib (Cibinqo) — Use with Caution

This individual may metabolize abrocitinib fast, which may reduce the probability of pharmacotherapy success.

Physicians may initiate the recommended starting dose and adjust the dose based on the individual's clinical presentation while closely monitoring for therapeutic effect.

A dosage reduction in individuals with moderate renal impairment is recommended. No dosage adjustment is required in individuals with mild renal impairment (eGFR 60-89 mL/min). Abrocitinib is not recommended for use in individuals with severe renal or hepatic impairment.

Gene: CYP2C19 **Robust**

PHD LABORATORY

Dermatology

Drug Class: Dermatological Agent

MOA: Serotonin and Norepinephrine Reuptake Inhibitor, Histamine Receptor Antagonist

! Doxepin (Silenor, Zonalon, Sinequan, Prudoxin) — Consider Alternatives

This individual has an increased CYP2C19 enzymatic activity and a decreased CYP2D6 enzymatic activity which may alter doxepin metabolism.

Alternative drug therapy may be considered. However, if doxepin is used, please monitor for drug toxicities and therapeutic response, and adjust the dose based on the individual's clinical presentation.

Gene: CYP2D6, CYP2C19 — Robust

Endocrinology

Drug Class: Endocrine Metabolic Agent

MOA: Glucosylceramide Synthase Inhibitor

! Eliglustat (Cerdelga) — Use with Caution

This individual metabolizes eliglustat slower, which results in an increased risk of cardiac arrhythmias from prolongation of the PR, QT, and/or QRS cardiac intervals.

The recommended dose is 84 mg twice daily.

Gene: CYP2D6 — Robust

This individual may have a normal response to eliglustat.

Gene: CYP3A4 ✓ — Developing

Drug Class: Meglitinide Analog

MOA: Insulin Secretion Stimulator

✓ Nateglinide (Starlix) — Normal Response Expected

This individual is expected to have a normal response to nateglinide.

Gene: CYP2C9 — Robust

Drug Class: Sulfonylurea

MOA: Insulin Release Stimulator

Glimepiride (Amaryl) ✓

This individual is expected to have a normal response to glimepiride.

Gene: CYP2C9 — Developing

Gastroenterology

Drug Class: Acid Reducing Agent

MOA: Proton Pump Inhibitor

↑ Dexlansoprazole (Dexilant) — Use with Caution

This individual metabolizes dexlansoprazole fast.

Increased activity may expose the individual to lower levels of dexlansoprazole at standard dosing and may require dose adjustment due to a lack of pharmacotherapy success.

Increasing the starting daily dose may be required while closely monitoring for efficacy.

Gene: CYP2C19 — Robust

PHD LABORATORY

Gastroenterology

Drug Class: Acid Reducing Agent **MOA:** Proton Pump Inhibitor

Esomeprazole (Nexium) — Use with Caution

This individual metabolizes esomeprazole fast which may lead to lower levels of esomeprazole.

However, there is no mention of the drug response associated with the increased activity of this enzyme and how it may affect pharmacotherapy success or increase the risk of adverse drug reactions.

Physicians may initiate the recommended starting dose and adjust the dose based on the individual's clinical presentation while closely monitoring for adverse events and therapeutic response.

Gene: CYP2C19 Robust

Drug Class: Acid Reducing Agent **MOA:** Proton Pump Inhibitor

Lansoprazole (Prevacid, Prevacid SoluTab) — Use with Caution

This individual metabolizes lansoprazole fast.

Increased activity may expose the individual to lower levels of lansoprazole at standard dosing and may require dose adjustment due to a lack of pharmacotherapy success.

Increasing the starting daily dose may be required while closely monitoring for efficacy.

Gene: CYP2C19 Robust

Drug Class: Acid Reducing Agent **MOA:** Proton Pump Inhibitor

Pantoprazole (Protonix) — Use with Caution

This individual metabolizes pantoprazole fast.

Increased activity may expose the individual to lower levels of pantoprazole at standard dosing and may require dose adjustment due to a lack of pharmacotherapy success.

Increasing the starting daily dose may be required while closely monitoring for efficacy.

Gene: CYP2C19 Robust

Drug Class: Acid Reducing Agent **MOA:** Proton Pump Inhibitor

Rabeprazole (AcipHex) — Use with Caution

This individual metabolizes rabeprazole fast which may lead to lower levels of rabeprazole.

However, there is no mention of the drug response associated with the increased activity of this enzyme and how it may affect pharmacotherapy success or increase the risk of adverse drug reactions.

Physicians may initiate the recommended starting dose and adjust the dose based on the individual's clinical presentation while closely monitoring for adverse events and therapeutic response.

Gene: CYP2C19 Robust

PHD LABORATORY

Gastroenterology

Drug Class: Antiemetic **MOA:** 5-HT3 Receptor Antagonist

! Ondansetron (Zofran, Zuplenz) — Use with Caution

This individual metabolizes ondansetron slower and has reduced CYP2D6 activity.

Reduced activity may expose the individual to higher levels of ondansetron and lead to adverse events such as headaches, constipation, and QT prolongation. However, individuals who are CYP2D6 intermediate metabolizers are not expected to differ from those who are CYP2D6 normal metabolizers in their ondansetron metabolism.

Physicians may initiate therapy with the recommended starting dose and adjust the dose based on the individual's clinical presentation.

Gene: CYP2D6 **Robust**

This individual may have a normal response to ondansetron.

Gene: CYP3A4 **Developing**

This individual may have increased risk of nausea and vomiting shortly after being treated with ondansetron.

Gene: ABCB1 ! **Developing**

Drug Class: Antiemetic **MOA:** 5-HT3 Receptor Antagonist

! Palonosetron (Aloxi) — Normal Response Expected

This individual may metabolize palonosetron slower.

However, the clinical pharmacokinetic parameters are not significantly different between poor and normal metabolizers of CYP2D6 substrates. Therefore, the individual is expected to have a standard response to the recommended dosing of palonosetron.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Gene: CYP2D6 **Modest**

Drug Class: Antiemetic **MOA:** 5-HT3 Receptor Antagonist

! Tropisetron — Use with Caution

This individual metabolizes tropisetron slower.

However, there is insufficient evidence to demonstrate clinical impact based on the CYP2D6 genotype.

Physicians may initiate therapy with the recommended starting dose and adjust the dose based on the individual's clinical presentation while monitoring for adverse events and therapeutic response.

Gene: CYP2D6 **Robust**

Drug Class: Antiemetic **MOA:** Cannabinoid Receptor Agonist

Dronabinol (Syndros, Marinol) — Normal Response Expected

This individual is expected to have a normal response to dronabinol.

Gene: CYP2C9 **Modest**

This individual may have a normal response to dronabinol.

Gene: CYP3A4 **Developing**

PHD LABORATORY

Gastroenterology

Drug Class: Antiemetic

MOA: Dopamine and Serotonin Receptors Blocker

! Metoclopramide (Reglan)

Use with Caution

This individual may metabolize metoclopramide slower, which may lead to dystonic and other adverse reactions due to higher systemic concentrations of the medication.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Reduce the dosage in individuals with moderate and severe renal impairment (CrCl </= 60 mL/minute), including those receiving hemodialysis and continuous ambulatory peritoneal dialysis, and in individuals with moderate or severe hepatic impairment.

Gene: CYP2D6

Modest

Drug Class: Antiemetic

MOA: H1 Receptor Antagonist

! Meclizine (Antivert, Bonine, Dramamine Less Drowsy, Motion-Time, Travel Sickness, Travel-Easy)

Use with Caution

This individual may metabolize meclizine slower, which results in higher systemic concentrations.

This may lead to a greater risk of adverse effects, including anaphylactic reaction, drowsiness, dry mouth, headache, fatigue, and vomiting.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation while monitoring for any adverse events.

Gene: CYP2D6

Robust

Gynecology

Drug Class: Central Nervous System Agent

MOA: Mixed 5-HT1A Agonist and 5-HT2A Antagonist

! Flibanserin (Addyi)

Use with Caution

This individual metabolizes flibanserin fast. Increased activity may expose the individual to lower levels of flibanserin at standard dosing.

Physicians may initiate the recommended starting dose and adjust the dose based on the individual's clinical presentation while closely monitoring for therapeutic effect.

The use of flibanserin is contraindicated in individuals with hepatic impairment.

Gene: CYP2C19

Modest

Drug Class: Contraceptive

MOA: Follicle-Stimulating Hormone and Luteinizing Hormone Inhibitor

! Drospirenone and Ethinyl Estradiol (Jasmiel, Lo-Zumandimine, Loryna, Nikki, Ocella, Syeda, Vestura, Yasmin 28, YAZ, Zarah, Zumandimine)

Use with Caution

This individual metabolizes drospirenone and ethinyl estradiol fast.

Increased activity may expose the individual to lower levels of drospirenone and ethinyl estradiol at standard dosing.

Physicians may initiate the recommended starting dose and adjust the dose based on the individual's clinical presentation while monitoring for therapeutic effect.

The medication is contraindicated in individuals with renal impairment or hepatic disease.

Gene: CYP2C19

Modest

PHD LABORATORY

Gynecology

Drug Class: Contraceptive

MOA: Follicle-Stimulating Hormone and Luteinizing Hormone Inhibitor

Hormonal Contraceptives For Systemic Use

This individual may have a decreased risk of experiencing thrombosis when receiving oral contraceptives.

Gene: F5 **Developing**

Drug Class: Endocrine Metabolic Agent

MOA: Gonadotropin-Releasing Hormone Antagonist

Elagolix (Orilissa) — Use with Caution

This individual may have higher plasma concentrations of elagolix after treatment with a standard dose.

However, the adverse events of elagolix have not been evaluated in individuals with this genotype.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Gene: SLCO1B1 **Modest**

Hematology

Drug Class: Colony Stimulating Factor

MOA: Thrombopoietin Receptor Agonist

Avatrombopag (Doptelet) — Normal Response Expected

This individual has an average risk for thrombotic and thromboembolic events and is expected to have a normal response to avatrombopag.

Gene: F2, F5, CYP2C9 **Modest**

This individual may have a normal response to avatrombopag.

Gene: CYP3A4 **Developing**

Drug Class: Colony Stimulating Factor

MOA: Thrombopoietin Receptor Agonist

Eltrombopag (Promacta) — Normal Response Expected

This individual is expected to have an average risk of thrombotic and thromboembolic complications when administering eltrombopag.

Gene: F5 **Modest**

Drug Class: Colony Stimulating Factor

MOA: Thrombopoietin Receptor Agonist

Lusutrombopag (Mulpleta) — Normal Response Expected

This individual has an average risk for thrombotic and thromboembolic events and is expected to have a normal response to lusutrombopag.

Gene: F2, F5 **Modest**

PHD LABORATORY

Immunology

Drug Class: Cholinergic Agonist **MOA:** Cholinergic Receptor Agonist

! Cevimeline (Evoxac) — Use with Caution

This individual metabolizes cevimeline slower, which may lead to an increased probability of adverse events.

Adverse effects of cevimeline therapy can include increased sweating, excessive salivation, nausea, diarrhea, headache, and a stuffy nose. Therefore, cevimeline should be used with caution.

Physicians may initiate therapy at a recommended dose, adjust the dose as needed, or consider an alternative drug therapy based on the individual's clinical presentation.

Gene: CYP2D6 **Robust**

This individual may have a normal response to cevimeline.

Gene: CYP3A4 **Developing**

Drug Class: Immunomodulatory Agent **MOA:** Sphingosine-1 Phosphate Receptor Modulator

Siponimod (Mayzent) — Normal Response Expected

This individual is expected to have a normal response to siponimod.

After treatment titration (see FDA MAYZENT package insert for treatment initiation tables), the recommended maintenance dosage for this individual is 2 mg taken orally once daily starting on Day 6.

Gene: CYP2C9 **Robust**

This individual may have a normal response to siponimod.

Gene: CYP3A4 **Developing**

Drug Class: Immunosuppressant **MOA:** Dihydrofolate Reductase Inhibitor

Methotrexate (Otrexup, Rasuvo, Trexall, Xatmet) !

This individual is a carrier of a partial methylenetetrahydrofolate reductase (MTHFR) deficiency.

An autosomal recessive inborn error of metabolism featuring higher homocysteine levels and lower serum folate levels should be managed according to the standard of care for those disorders (clinical genetics and genetic counselor consults). First-degree family members of the individual (parents, siblings, offerings, and first cousins) should be clinically assessed by a geneticist and/or a genetic counselor, and seek molecular testing for the variant(s) found positive in this individual.

This individual has an intermediate risk of toxicity such as the increased risk of bone marrow, liver, lung, and kidney toxicities when treated with methotrexate for arthritis, and would benefit from methylfolate supplementation therapy.

Gene: MTHFR **Developing**

Drug Class: Immunosuppressant **MOA:** mTOR Kinase Inhibitor

Sirolimus (Rapamune) !

This individual may have decreased metabolism of sirolimus.

Gene: CYP3A5 **Developing**

Drug Class: Immunosuppressant **MOA:** Purine Antagonist

Azathioprine (Azasan, Imuran) — Normal Response Expected

This individual is expected to have a normal response to azathioprine.

Gene: TPMT, NUDT15 **Robust**

PHD LABORATORY

Infectious Diseases

Drug Class: Antimalarial Agent

MOA: Nucleic Acid Synthesis, Protein Synthesis, and Glycolysis in Plasmodium Falciparum Inhibitor

! Quinine Sulfate (Qualaquin) — Use with Caution

This individual may metabolize quinine slower, which results in potentially increased concentrations of quinine.

However, there is no mention of the drug response associated with the reduced activity of this enzyme and how it may affect pharmacotherapy success or increase the risk of adverse drug reactions.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Gene: CYP2D6 — **Modest**

Drug Class: Antiretroviral

MOA: Non-Nucleoside Reverse Transcriptase Inhibitor

Efavirenz (Sustiva) — Normal Response Expected

This individual is expected to have a normal response to efavirenz.

Efavirenz is not recommended for individuals with moderate or severe hepatic impairment. Use caution in individuals with mild hepatic impairment.

Gene: CYP2B6 — **Robust**

Drug Class: Antiretroviral

MOA: Non-Nucleoside Reverse Transcriptase Inhibitor

Nevirapine (Viramune, Viramune XR)

This individual may have normal therapeutic levels of nevirapine and an average risk of adverse effects including Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN).

Gene: CYP2B6 — **Developing**

This individual may have an average risk for nevirapine hepatotoxicity.

Gene: ABCB1 — **Developing**

Neurology

Drug Class: Anti-Amyloid Monoclonal Antibody

MOA: Amyloid Beta Plaque Antagonist

Aducanumab (Aduhelm) — Normal Response Expected

This individual is not associated with type III hyperlipoproteinemia, which is a rare autosomal recessive inherited disorder characterized by increased plasma cholesterol and triglyceride levels.

This individual has an average risk of developing ARIA (amyloid related imaging abnormalities). Testing for ApoE E4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA.

In addition, APOE has been used to assess susceptibility to Alzheimer's disease. However, according to the American College of Medical Genetics, the use of APOE analysis is not clinically recommended due to limited clinical utility and poor predictive value.

Gene: APOE — **Modest**

PHD LABORATORY

Neurology

Drug Class: Anti-Amyloid Monoclonal Antibody **MOA:** Amyloid Beta Plaque Antagonist

Lecanemab (Leqembi) — Normal Response Expected

This individual is not associated with type III hyperlipoproteinemia, which is a rare autosomal recessive inherited disorder characterized by increased plasma cholesterol and triglyceride levels.

This individual has an average risk of developing ARIA (amyloid related imaging abnormalities). Testing for ApoE E4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA.

In addition, APOE has been used to assess susceptibility to Alzheimer's disease. However, according to the American College of Medical Genetics, the use of APOE analysis is not clinically recommended due to limited clinical utility and poor predictive value.

Gene: APOE **Modest**

Drug Class: Anticholinergic **MOA:** Acetylcholinesterase Inhibitor

Donepezil (Aricept) — Use with Caution

This individual may metabolize donepezil slower, which results in increased systemic concentrations.

This may lead to a greater risk of adverse effects, including cardiovascular conditions, weight loss, nausea, and vomiting.

Individuals with this genotype may have slower clearance.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Gene: CYP2D6 **Modest**

Drug Class: Anticholinergic **MOA:** Acetylcholinesterase Inhibitor

Galantamine (Razadyne, Razadyne ER) — Use with Caution

This individual metabolizes galantamine slower.

This individual may have a higher exposure to the medication; however, dosage adjustment is not necessary as the dose of the drug is individually titrated to tolerability.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Gene: CYP2D6 **Robust**

Drug Class: Anticonvulsant **MOA:** Sodium Channel Blocker

Fosphenytoin (Cerebyx) — Normal Response Expected

This individual is expected to have a normal response to fosphenytoin. Fosphenytoin is a phosphate ester prodrug that is converted to phenytoin by peripheral esterases (phosphatases).

Gene: CYP2C9, CYP2C19 **Robust**

Drug Class: Anticonvulsant **MOA:** Sodium Channel Blocker

Phenytoin (Dilantin, Phenytek) — Normal Response Expected

This individual is expected to have a normal response to phenytoin. Phenytoin is mainly metabolized by CYP2C9 (95%).

Gene: CYP2C9, CYP2C19 **Robust**

PHD LABORATORY

Neurology

Drug Class: Anticonvulsant

MOA: Sodium Channel Blocker and Collapsin Response Mediator Protein-2 (CRMP-2) Binder

! Lacosamide (Vimpat) — Use with Caution

This individual metabolizes lacosamide fast.

However, there is no mention of the drug response associated with the increased activity of this enzyme and how it may affect pharmacotherapy success or increase the risk of adverse drug reactions.

Physicians may initiate the recommended starting dose and adjust the dose based on the individual's clinical presentation while monitoring for therapeutic effects and adverse events.

Gene: CYP2C19 — Modest

Drug Class: Anticonvulsant

MOA: Synaptic Vesicle Protein 2A Binder

! Brivaracetam (Briviact) — Use with Caution

This individual metabolizes brivaracetam fast, which may reduce the probability of pharmacotherapy success.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Gene: CYP2C19 — Robust

Drug Class: Antimigraine

MOA: ï¿½Calcitonin Gene-Related Peptide Receptor Antagonist

Rimegepant (Nurtec) — Normal Response Expected

This individual is expected to have a normal response to standard dosing of rimegepant.

Gene: CYP2C9 — Modest

Drug Class: Benzodiazepine

MOA: GABA-A Agonist

! Clobazam (Onfi, Sympazan) — Use with Caution

This individual metabolizes clobazam fast, which can lead to decreased levels of N-desmethylclobazam, clobazam's active metabolite, and potentially result in therapeutic failure.

Physicians may initiate the recommended starting dose and adjust the dose based on the individual's clinical presentation while monitoring for therapeutic response.

Gene: CYP2C19 — Robust

Drug Class: Benzodiazepine

MOA: GABA-A Agonist

! Diazepam (Valium, Diastat AcuDial, Diazepam Intensol, Diastat Pediatric) — Use with Caution

This individual metabolizes diazepam fast.

However, there is no mention of the drug response associated with the increased activity of this enzyme and how it may affect pharmacotherapy success or increase the risk of adverse drug reactions.

Physicians may initiate the recommended starting dose and adjust the dose based on the individual's clinical presentation while monitoring for therapeutic effects and adverse events.

Gene: CYP2C19 — Modest

Drug Class: Benzodiazepine

MOA: GABA-A Agonist

Midazolam (Nayzilam) !

This individual may metabolize midazolam slowly and have slower clearance rates.

Gene: CYP3A5 — Developing

PHD LABORATORY

Neurology

Drug Class: Central Monoamine-Depleting Agent **MOA:** Vesicular Monoamine Transporter 2 Inhibitor

! Deutetrabenazine (Austedo) — Use with Caution

This individual metabolizes deutetrabenazine slower, which can affect the QT prolongation.

Other known adverse effects associated with increased exposure to the active dihydro-metabolites of deutetrabenazine include CNS reactions (sedation, dizziness/vertigo, headache, and tremor); cardiovascular reactions (tachycardia, hypotension, and syncope); autonomic nervous system reactions (hypersalivation, sweating, dry mouth, and visual disturbances); gastrointestinal reactions (constipation and nausea); and fever.

When using this medication, it is recommended to conduct a baseline and subsequent electrocardiograms to evaluate QT/QTc interval status.

Gene: CYP2D6 **Robust**

Drug Class: Central Monoamine-Depleting Agent **MOA:** Vesicular Monoamine Transporter 2 Inhibitor

! Tetrabenazine (Xenazine) — Use with Caution

This individual metabolizes tetrabenazine slower.

This may lead to an increased probability of adverse events due to increased systemic concentrations of the primary drug metabolites. The adverse events may include akathisia, restlessness, parkinsonism, depression, anxiety, insomnia, and sedation.

The dosage of tetrabenazine can be titrated to a maximum single dose of 37.5 mg and a recommended maximum daily dose of 100 mg.

Gene: CYP2D6 **Robust**

Drug Class: Central Monoamine-Depleting Agent **MOA:** Vesicular Monoamine Transporter 2 Inhibitor

! Valbenazine (Ingrezza) — Use with Caution

This individual metabolizes valbenazine slower.

This may lead to an increased probability of adverse events including QT prolongation due to increased exposure to valbenazine's active metabolite.

Physicians may initiate therapy with the recommended starting dose and adjust the dose based on the individual's clinical presentation.

Gene: CYP2D6 **Robust**

This individual may have a normal response to valbenazine.

Gene: CYP3A4 **Developing**

Drug Class: Central Nervous System Agent **MOA:** N-Methyl-D-Aspartate (NMDA) Receptor Antagonist

! Dextromethorphan and Quinidine (Nuedexta) — Use with Caution

This individual may have an increased probability of adverse events after treatment with dextromethorphan and quinidine.

The quinidine component is not expected to contribute to therapeutic effectiveness, but adverse events of the quinidine are still possible.

Gene: CYP2D6 **Modest**

This individual may have a normal response to dextromethorphan and quinidine.

Gene: CYP3A4 **Developing**

PHD LABORATORY

Neurology

Drug Class: Immunomodulatory Agent **MOA:** Sphingosine-1 Phosphate Receptor Modulator

Siponimod (Mayzent) — Normal Response Expected

This individual is expected to have a normal response to siponimod.

After treatment titration (see FDA MAYZENT package insert for treatment initiation tables), the recommended maintenance dosage for this individual is 2 mg taken orally once daily starting on Day 6.

Gene: CYP2C9 **Robust**

This individual may have a normal response to siponimod.

Gene: CYP3A4 **Developing**

Oncology

Drug Class: Antiestrogen **MOA:** Selective Estrogen Receptor Modulator

Tamoxifen (Soltamox) — Consider Alternatives

This individual may metabolize tamoxifen slower.

The impact of CYP2D6 polymorphisms on the efficacy of tamoxifen is not well established. However, the individual may have lower endoxifen concentrations which may lead to a higher risk of disease recurrence in tamoxifen adjuvant therapy for early breast cancer.

Alternative hormonal treatment (aromatase inhibitor for postmenopausal women or aromatase inhibitor along with ovarian function suppression in premenopausal women) may be required. Please consider monitoring serum levels of tamoxifen and endoxifen to ensure both are within therapeutic levels.

In addition, the individual has average risk factors for thrombotic and thromboembolic events.

Gene: CYP2D6, F2, F5 **Robust**

This individual may have a normal response to tamoxifen.

Gene: CYP3A4 **Developing**

Drug Class: Antineoplastic **MOA:** DNA Synthesis Inhibitor

Cisplatin (Platinol-AQ) — Normal Response Expected

This individual is expected to have a normal response to cisplatin.

Gene: TPMT **Modest**

Drug Class: Antineoplastic **MOA:** Epidermal Growth Factor Receptor Inhibitor

Gefitinib (Iressa) — Use with Caution

This individual metabolizes gefitinib slower, which results in an increased risk for adverse events due to higher systemic concentrations.

Adverse events may include interstitial lung disease, pulmonary symptoms, diarrhea, ocular disorder, and higher skin reactions.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Discontinue gefitinib if the individual has severe hepatic impairment.

Gene: CYP2D6 **Robust**

This individual may have a normal response to gefitinib.

Gene: CYP3A4 **Developing**

PHD LABORATORY

Oncology

Drug Class: Antineoplastic

MOA: Fibroblast Growth Factor Receptor Kinase Inhibitor

Erdafitinib (Balversa) — Normal Response Expected

This individual is expected to have a normal response to erdafitinib.

Gene: CYP2C9 — **Modest**

This individual may have a normal response to erdafitinib.

Gene: CYP3A4 — **Developing**

Drug Class: Antineoplastic

MOA: HIF-2-alpha Inhibitor

Belzutifan (Welireg) — Use with Caution

This individual may metabolize belzutifan fast, which may reduce the probability of pharmacotherapy success.

Physicians may initiate the recommended starting dose and adjust the dose based on the individual's clinical presentation while closely monitoring for therapeutic effect.

Gene: CYP2C19 — **Modest**

Drug Class: Antineoplastic

MOA: Poly (ADP-ribose) polymerase (PARP) inhibitor

Rucaparib (Rubraca) — Normal Response Expected

This individual has a decreased CYP2D6 enzymatic activity which may alter rucaparib metabolism.

However, steady-state concentrations did not differ significantly across CYP2D6 or CYP1A2 genotype subgroups.

The individual is expected to have a standard response to the recommended dosing of rucaparib. Physicians may initiate the recommended starting dose and adjust the dose based on the individual's clinical presentation.

Gene: CYP2D6, CYP1A2 — **Modest**

Drug Class: Antineoplastic

MOA: Thymidylate Synthase Inhibitor

Tegafur — Normal Response Expected

This individual may have normal therapeutic levels of tegafur.

Gene: DPYD — **Robust**

Drug Class: Antineoplastic, Antimetabolite

MOA: Dihydrofolate Reductase Inhibitor

Methotrexate (Otrexup, Rasuvo, Trexall, Xatmet)

This individual is a carrier of a partial methylenetetrahydrofolate reductase (MTHFR) deficiency.

An autosomal recessive inborn error of metabolism featuring higher homocysteine levels and lower serum folate levels should be managed according to the standard of care for those disorders (clinical genetics and genetic counselor consults). First-degree family members of the individual (parents, siblings, offerings, and first cousins) should be clinically assessed by a geneticist and/or a genetic counselor, and seek molecular testing for the variant(s) found positive in this individual.

This individual has an intermediate risk of toxicity such as the increased risk of bone marrow, liver, lung, and kidney toxicities when treated with methotrexate for arthritis, and would benefit from methylfolate supplementation therapy.

Gene: MTHFR — **Developing**

Drug Class: Antineoplastic, Antimetabolite

MOA: DNA and RNA Synthesis Inhibitor

Capecitabine (Xeloda) — Normal Response Expected

This individual is expected to have a normal response to capecitabine.

Gene: DPYD — **Robust**

PHD LABORATORY

Oncology

Drug Class: Antineoplastic, Antimetabolite
MOA: DNA and RNA Synthesis Inhibitor

Fluorouracil (Adrucil, Carac, Efudex, Fluoroplex) — **Normal Response Expected**

This individual is expected to have a normal response to fluorouracil.

Gene: DPYD — **Robust**

Drug Class: Antineoplastic, Antimetabolite
MOA: Purine Antagonist

Mercaptopurine (Purinethol, Purixan) — **Normal Response Expected**

This individual is expected to have a normal response to mercaptopurine.

Gene: TPMT, NUDT15 — **Robust**

Drug Class: Antineoplastic, Antimetabolite
MOA: Purine Antagonist

Thioguanine (Tabloid) — **Normal Response Expected**

This individual is expected to have a normal response to thioguanine.

Gene: TPMT, NUDT15 — **Robust**

Ophthalmology

Drug Class: Antiglaucoma
MOA: Nonselective Beta-Adrenergic Receptor Antagonist

Timolol (Betimol) !

This individual metabolizes timolol slower, which may lead to increased exposure to timolol, and increased exercise heart rate reduction.

Gene: CYP2D6 — **Developing**

Pain Management

Drug Class: Antiplatelet/Non-Steroidal Anti-Inflammatory Drug
MOA: Prostaglandin Synthesis and Platelet Aggregation Inhibitor

Aspirin (Ecotrin, Bayer, Asctiptin, Durlaza) — **Normal Response Expected**

This individual may have normal therapeutic levels of aspirin.

Avoid aspirin in individuals with severe hepatic insufficiency or severe renal failure (GFR <10 mL/min).

Gene: CYP2C9 — **Robust**

Drug Class: Non-Steroidal Anti-Inflammatory Drug
MOA: Cyclooxygenase 1 and 2 Inhibitor

Diclofenac (Diclozor, Flector, Pennsaid, Voltaren, Xrylix, Cambia, Zipsor, Zorvolex) — **Normal Response Expected**

This individual may have normal therapeutic levels of diclofenac.

Individuals with hepatic disease may require reduced doses of diclofenac. Treatment with diclofenac is not recommended in individuals with advanced renal disease.

Gene: CYP2C9 — **Robust**

Drug Class: Non-Steroidal Anti-Inflammatory Drug
MOA: Cyclooxygenase 1 and 2 Inhibitor

Flurbiprofen (Ansaid) — **Normal Response Expected**

This individual is expected to have a normal response to flurbiprofen.

Gene: CYP2C9 — **Robust**

PHD LABORATORY

Pain Management

Drug Class: Non-Steroidal Anti-Inflammatory Drug **MOA:** Cyclooxygenase 1 and 2 Inhibitor

Ibuprofen (Addaprin, Advil Junior Strength, Advil Migraine, Advil, Caldolor, Childrens Advil, Childrens Motrin, Dyspel, Genpril, GoodSense Ibuprofen Childrens, GoodSense Ibuprofen, IBU, Ibuprofen Childrens, Infants Advil , KS Ibuprofen, Motrin Childrens, Motrin IB, Motrin Infants Drops, NeoProfen, Provil)

Normal Response Expected

This individual is expected to have a normal response to ibuprofen.

Avoid use in individuals with advanced renal disease; discontinue use with persistent or worsening abnormal renal function tests. Additionally, use with caution in individuals with hepatic impairment; individuals with advanced hepatic disease are at an increased risk of GI bleeding with NSAIDs.

Gene: CYP2C9 Robust

Drug Class: Non-Steroidal Anti-Inflammatory Drug **MOA:** Cyclooxygenase 1 and 2 Inhibitor

Indomethacin (Indocin, Tivorbex)

Normal Response Expected

This individual may have normal therapeutic levels of indomethacin.

Gene: CYP2C9 Robust

Drug Class: Non-Steroidal Anti-Inflammatory Drug **MOA:** Cyclooxygenase 1 and 2 Inhibitor

Lornoxicam

Normal Response Expected

This individual is expected to have a normal response to lornoxicam.

Gene: CYP2C9 Robust

Drug Class: Non-Steroidal Anti-Inflammatory Drug **MOA:** Cyclooxygenase 1 and 2 Inhibitor

Meloxicam (Anjeso, Mobic, Qmiiz ODT, Vivlodex)

Normal Response Expected

This individual is expected to have a normal response to meloxicam.

The use of meloxicam in individuals with severe renal impairment is not recommended. In individuals on hemodialysis, the maximum dosage of meloxicam is 7.5 mg per day. It is recommended to use meloxicam with caution in individuals with hepatic impairment.

Gene: CYP2C9 Robust

Drug Class: Non-Steroidal Anti-Inflammatory Drug **MOA:** Cyclooxygenase 1 and 2 Inhibitor

Naproxen (Aleve, EC-Naprosyn, EC-Naproxen, GoodSense Naproxen Sodium, Mediproxen, Naprelan, Naprosyn, Naproxen DR)

Normal Response Expected

This individual may have normal therapeutic levels of naproxen.

Naproxen is not recommended for use in individuals with moderate to severe and severe renal impairment (CrCl < 30 mL/min). A lower dose should be considered in individuals with renal or hepatic impairment.

Gene: CYP2C9 Robust

Drug Class: Non-Steroidal Anti-Inflammatory Drug **MOA:** Cyclooxygenase 1 and 2 Inhibitor

Piroxicam (Feldene)

Normal Response Expected

This individual is expected to have a normal response to piroxicam.

Gene: CYP2C9 Robust

PHD LABORATORY

Pain Management

Drug Class: Non-Steroidal Anti-Inflammatory Drug
MOA: Cyclooxygenase 1 and 2 Inhibitor

Tenoxicam — Normal Response Expected

This individual is expected to have a normal response to tenoxicam.

Gene: CYP2C9 — Robust

Drug Class: Non-Steroidal Anti-Inflammatory Drug
MOA: Prostaglandin Synthesis Inhibitor

Metamizole — Normal Response Expected

This individual may have normal therapeutic levels of metamizole.

Gene: CYP2C9 — Robust

Drug Class: Non-Steroidal Anti-Inflammatory Drug
MOA: Selective COX-2 Inhibitor

Aceclofenac — Normal Response Expected

This individual may have normal therapeutic levels of aceclofenac.

Gene: CYP2C9 — Robust

Drug Class: Non-Steroidal Anti-Inflammatory Drug
MOA: Selective COX-2 Inhibitor

Lumiracoxib — Normal Response Expected

This individual may have normal therapeutic levels of lumiracoxib.

Gene: CYP2C9 — Robust

Drug Class: Opioid
MOA: MU-Opioid Receptor Agonist

Alfentanil (Alfenta) — Normal Response Expected

This individual may have normal therapeutic levels of the medication.

However, following the initiation of this medication, physicians should still monitor individuals for analgesic effectiveness, adverse events, individual-specific factors, and adjust the dose accordingly.

Gene: COMT, OPRM1 — Robust

Drug Class: Opioid
MOA: MU-Opioid Receptor Agonist

Codeine — Use with Caution

This individual has a decreased CYP2D6 enzymatic activity and may metabolize codeine slower.

This may result in reduced morphine formation following codeine administration, and insufficient pain relief.

Physicians may initiate a recommended age-specific or weight-specific dosing. Following the initiation of this medication, physicians should monitor individuals for analgesic effectiveness, adverse events, and individual-specific factors. However, if there is no response to codeine, physicians may consider an alternative treatment.

Lower initial doses or longer dosing intervals followed by careful titration while monitoring for signs of respiratory depression, sedation, and hypotension are recommended for individuals with renal or hepatic impairment.

Gene: COMT, OPRM1, CYP2D6 — Robust

This individual may have a normal response to codeine.

Gene: CYP3A4 — Developing

PHD LABORATORY

Pain Management

Drug Class: Opioid **MOA:** MU-Opioid Receptor Agonist

Fentanyl (Abstral, Actiq, Duragesic, Fentora, Ionsys, Lazanda, Sublimaze, Subsys) — Normal Response Expected

This individual may have normal therapeutic levels of the medication.

However, following the initiation of this medication, physicians should still monitor individuals for analgesic effectiveness, adverse events, individual-specific factors, and adjust the dose accordingly.

Gene: COMT, OPRM1 Robust

Drug Class: Opioid **MOA:** MU-Opioid Receptor Agonist

Hydrocodone (Hysingla ER, Zohydro ER) — Use with Caution

This individual has a decreased CYP2D6 enzymatic activity and may metabolize hydrocodone slower.

This may result in reduced hydromorphone formation following hydrocodone administration. However, there is insufficient evidence on whether there is an association between opioid adverse events and/or analgesia and the individual's genotype.

When using this medication, physicians should monitor individuals for analgesic effectiveness, adverse events, and individual-specific factors. However, if there is no response to hydrocodone, physicians may consider an alternative treatment.

Gene: COMT, OPRM1, CYP2D6 Robust

Drug Class: Opioid **MOA:** MU-Opioid Receptor Agonist

Hydromorphone (Dilaudid) — Normal Response Expected

This individual may have normal therapeutic levels of the medication.

However, following the initiation of this medication, physicians should still monitor individuals for analgesic effectiveness, adverse events, individual-specific factors, and adjust the dose accordingly.

Gene: COMT, OPRM1 Robust

Drug Class: Opioid **MOA:** MU-Opioid Receptor Agonist

Levomethadone — Normal Response Expected

This individual may have normal therapeutic levels of the medication.

However, following the initiation of this medication, physicians should still monitor individuals for analgesic effectiveness, adverse events, individual-specific factors, and adjust the dose accordingly.

Gene: COMT, OPRM1 Robust

Drug Class: Opioid **MOA:** MU-Opioid Receptor Agonist

Morphine (Arymo ER, Duramorph, Infumorph 200, Infumorph 500, Kadian, Mitigo, MorphaBond ER, MS Contin) — Normal Response Expected

This individual may have normal therapeutic levels of the medication.

However, following the initiation of this medication, physicians should still monitor individuals for analgesic effectiveness, adverse events, individual-specific factors, and adjust the dose accordingly.

Gene: COMT, OPRM1 Robust

PHD LABORATORY

Pain Management

Drug Class: Opioid
MOA: MU-Opioid Receptor Agonist

! Oliceridine (Olinvyk) — Use with Caution

This individual metabolizes oliceridine slower.

This can result in increased plasma concentrations of oliceridine, and increased risk for adverse events including respiratory depression and sedation.

Physicians may initiate therapy at a recommended dose and adjust the dose as needed based on the individual's clinical presentation while monitoring the severity of pain and response to treatment.

Gene: CYP2D6 — Robust

Drug Class: Opioid
MOA: MU-Opioid Receptor Agonist

! Oxycodone (Oxaydo, OxyCONTIN, Roxicodone, Xtampza ER) — Use with Caution

This individual has a decreased CYP2D6 enzymatic activity and may metabolize oxycodone slower.

This may result in reduced oxymorphone formation following oxycodone administration. However, there is insufficient evidence on whether there is an association between opioid adverse events and/or analgesia and the individual's genotype. Following the initiation of this medication, physicians should monitor individuals for analgesic effectiveness, adverse events, individual-specific factors, and adjust the dose accordingly.

Gene: COMT, OPRM1, CYP2D6 — Robust

Drug Class: Opioid
MOA: MU-Opioid Receptor Agonist

✓ Remifentanil (Ultiva) — Normal Response Expected

This individual may have normal therapeutic levels of the medication.

However, following the initiation of this medication, physicians should still monitor individuals for analgesic effectiveness, adverse events, individual-specific factors, and adjust the dose accordingly.

Gene: COMT, OPRM1 — Robust

Drug Class: Opioid
MOA: MU-Opioid Receptor Agonist

✓ Sufentanil (Dsuvia, Sufenta) — Normal Response Expected

This individual may have normal therapeutic levels of the medication.

However, following the initiation of this medication, physicians should still monitor individuals for analgesic effectiveness, adverse events, individual-specific factors, and adjust the dose accordingly.

Gene: COMT, OPRM1 — Robust

Drug Class: Opioid
MOA: MU-Opioid Receptor Agonist and N-Methyl-D-Aspartate Receptor Antagonist

! Methadone (Dolophine, Methadone HCL Intensol, Methadose, Diskets Dispersible) — Use with Caution

This individual has decreased CYP2D6 but normal CYP2B6 enzymatic activity and may metabolize methadone slower.

However, the clinical impact is unknown. There is insufficient evidence on whether there is an association between opioid adverse events and/or analgesia and the individual's genotype. Following the initiation of this medication, physicians should monitor individuals for analgesic effectiveness, adverse events, individual-specific factors, and adjust the dose accordingly.

Gene: COMT, OPRM1, CYP2D6, CYP2B6 — Robust

PHD LABORATORY

Pain Management

Drug Class: Opioid

MOA: MU-Opioid Receptor Agonist and Norepinephrine and Serotonin Reuptake Inhibitor

! Tramadol (Ultram, ConZip) — Use with Caution

This individual metabolizes tramadol slower, which results in reduced O-desmethyltramadol formation following tramadol administration, and insufficient pain relief.

Physicians may initiate a recommended age-specific or weight-specific dosing. Following the initiation of this medication, physicians should monitor for analgesic effectiveness, adverse events, and individual-specific factors. However, if there is no response to tramadol, physicians may consider an alternative treatment.

The recommended dose for adult individuals with severe hepatic impairment is 50 mg every 12 hours. In individuals with CrCl < 30 mL/min, it is recommended that the dosing interval be increased to 12 hours, with a maximum daily dose of 200 mg.

Gene: CYP2D6, CYP3A4, CYP2B6, COMT, OPRM1

Robust

Drug Class: Opioid

MOA: Partial MU-Opioid Receptor Agonist and Kappa-Opioid Receptor Antagonist

Buprenorphine (Belbuca, Buprenex, Butrans, Probuphine Implant Kit, Sublocade) — Normal Response Expected

This individual may have normal therapeutic levels of the medication.

However, following the initiation of this medication, physicians should still monitor individuals for analgesic effectiveness, adverse events, individual-specific factors, and adjust the dose accordingly.

Gene: COMT, OPRM1

Robust

Drug Class: Opioid Antagonist

MOA: Opioid Receptor Antagonist

Naltrexone (Vivitrol) — Normal Response Expected

This individual may have normal therapeutic levels of the medication.

However, following the initiation of this medication, physicians should still monitor individuals for analgesic effectiveness, adverse events, individual-specific factors, and adjust the dose accordingly.

Gene: COMT, OPRM1

Robust

Drug Class: Opioid Dependency

MOA: Alpha-2 Adrenergic Agonist

! Lofexidine (Lucemyra) — Use with Caution

This individual may metabolize lofexidine slower, likely resulting in higher systemic concentrations.

This may lead to a greater risk of adverse effects. Monitor for adverse events such as orthostatic hypotension and bradycardia.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Gene: CYP2D6

Robust

Psychiatry

Drug Class: Antidepressant

MOA: 5-HT Reuptake Inhibitor, 5-HT1A Receptor Agonist, and 5-HT3 Receptor Antagonist

! Vortioxetine (Trintellix) — Use with Caution

This individual metabolizes vortioxetine slower, which results in an increased risk of adverse events due to increased plasma concentrations.

The adverse events may include serotonin syndrome, activation of mania/hypomania, and angle-closure glaucoma.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed while monitoring for any adverse events.

Gene: CYP2D6

Robust

PHD LABORATORY

Psychiatry

MOA: Alpha-2 Adrenergic Antagonist, 5-HT2 and 5-HT3 Serotonin Receptor and H1 Histamine Antagonist, and Moderate Peripheral Alpha-1 Adrenergic and Muscarinic Antagonist

Drug Class: Antidepressant

Mirtazapine (Remeron)

This individual metabolizes mirtazapine slower, leading to higher concentrations.

This may lead to an increased risk of adverse events. Adverse events may include somnolence, constipation, xerostomia, and weight gain.

Gene: CYP2D6 — **Developing**

MOA: Dopamine and Norepinephrine Reuptake Inhibitor

Drug Class: Antidepressant

Bupropion (Aplenzin, Forfivo XL, Wellbutrin SR, Wellbutrin XL)

This individual may have normal therapeutic levels of hydroxybupropion, a metabolite of bupropion.

Gene: CYP2B6 — **Developing**

Drug Class: Antidepressant

MOA: Selective Serotonin Reuptake Inhibitor

Citalopram (Celexa) — Consider Alternatives

This individual may metabolize citalopram fast, which reduces the probability of pharmacotherapy success.

Alternative therapy may be considered after evaluating other individual characteristics. However, if citalopram is used, consider titrating to a higher maintenance dose.

Gene: CYP3A4, CYP2C19, CYP2D6 — **Robust**

This individual may be more likely to have improvement in symptoms but may be more likely to experience nausea, vomiting, or sexual dysfunction.

Gene: HTR2A — **Developing**

Drug Class: Antidepressant

MOA: Selective Serotonin Reuptake Inhibitor

Escitalopram (Lexapro) — Consider Alternatives

This individual may metabolize escitalopram fast, which reduces the probability of pharmacotherapy success.

Alternative therapy may be considered after evaluating other individual characteristics. However, if escitalopram is used, consider titrating to a higher maintenance dose.

The recommended dosage of escitalopram in individuals with hepatic impairment is 10 mg daily. No dosage adjustment is necessary for individuals with mild or moderate renal impairment.

Gene: CYP3A4, CYP2C19, CYP2D6 — **Robust**

This individual may have an average risk of adverse cognitive effects and sexual dysfunctions.

Gene: HTR2A — **Developing**

PHD LABORATORY

Psychiatry

Drug Class: Antidepressant **MOA:** Selective Serotonin Reuptake Inhibitor

! Fluoxetine (Prozac, Sarafem) — Normal Response Expected

This individual metabolizes the S-enantiomer metabolite of fluoxetine slower.

Because fluoxetine metabolism, like that of several other compounds, including tricyclics and selective serotonin reuptake inhibitors, involves the CYP2D6 system; concomitant therapy with drugs also metabolized by the CYP2D6 system, including certain antidepressants, antipsychotics, and antiarrhythmics, may lead to detrimental drug-enzyme interactions and should be approached with caution.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Please use a lower or less frequent dosage in individuals with hepatic impairment. Use with caution in individuals with severe renal impairment.

Gene: CYP2D6 **Modest**

This individual may have an increased response.

Gene: HTR1A **Developing**

Drug Class: Antidepressant **MOA:** Selective Serotonin Reuptake Inhibitor

! Fluvoxamine (Luvox, Luvox CR) — Use with Caution

This individual metabolizes fluvoxamine slower, which can lead to an increased probability of adverse events due to higher plasma concentrations.

The adverse events may include abnormal ejaculation, anorexia, anorgasmia, asthenia, diarrhea, nausea, somnolence, sweating, and tremor.

Fluvoxamine should be used with caution. Physicians may initiate therapy with the recommended starting dose and adjust the dose based on the individual's clinical presentation.

Gene: CYP2D6 **Robust**

Drug Class: Antidepressant **MOA:** Selective Serotonin Reuptake Inhibitor

! Sertraline (Zoloft) — Use with Caution

This individual may metabolize sertraline faster, which may reduce the probability of pharmacotherapy success.

However, physicians may initiate therapy at the standard starting dose and adjust the dose accordingly.

Gene: CYP2B6, CYP2C19 **Robust**

Drug Class: Antidepressant **MOA:** Serotonin and Norepinephrine Reuptake Inhibitor

! Duloxetine (Cymbalta, Drizalma Sprinkle) — Use with Caution

This individual may metabolize duloxetine slower, which results in higher exposure to duloxetine.

This may lead to a greater risk of adverse effects, including hepatoxicity, orthostatic hypotension, abnormal bleeding, and serotonin syndrome.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Similar to CYP2D6 poor metabolizer individuals, these individuals may also have an increase in AUC and Cmax when administering duloxetine in combination with a potent CYP1A2 inhibitor. Potent CYP2D6 inhibitors may increase duloxetine concentrations as well. Additionally, duloxetine is a moderate inhibitor of CYP2D6.

Avoid use in individuals with chronic liver disease or cirrhosis or in individuals with severe renal impairment, GFR <30 mL/min.

Gene: CYP2D6 **Modest**

PHD LABORATORY

Psychiatry

Drug Class: Antidepressant

MOA: Serotonin and Norepinephrine Reuptake Inhibitor

Milnacipran (Savella, Savella Titration Pack)

This individual may have an increased response.

Gene: HTR1A — **Developing**

Drug Class: Antidepressant

MOA: Serotonin and Norepinephrine Reuptake Inhibitor

! Venlafaxine (Effexor) — Use with Caution

This individual metabolizes venlafaxine slower, resulting in reduced conversion of venlafaxine to the active metabolite O-desmethylvenlafaxine.

However, there is insufficient evidence to demonstrate clinical impact based on the CYP2D6 genotype.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed while monitoring for any adverse events and therapeutic responses.

Gene: CYP2D6 — **Robust**

This individual may be more likely to respond to venlafaxine.

Gene: HTR2A — **Developing**

Drug Class: Antidepressant

MOA: Serotonin and Norepinephrine Reuptake Inhibitor, and 5-HT2 and Alpha1 Receptor Antagonist

! Nefazodone (Serzone) — Use with Caution

This individual may metabolize nefazodone slower, which may result in an increased probability of adverse effects, including hypotension and mania/hypomania.

However, the pharmacokinetics of nefazodone and its major metabolites are not altered but the plasma concentrations of one minor metabolite may be increased.

Physicians may initiate therapy with the recommended starting dose and adjust the therapy based on the individual's clinical presentation.

Nefazodone should not be initiated in individuals with active liver disease or with elevated baseline serum transaminases. Use with caution in individuals with renal impairment.

Gene: CYP2D6 — **Robust**

Drug Class: Antipsychotic

MOA: 5-HT2A and Dopamine-D2 Receptor Antagonist

! Iloperidone (Fanapt) — Use with Caution

This individual metabolizes iloperidone slower, which results in increased systemic concentrations and a greater risk of adverse effects such as QT prolongation.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Iloperidone is not recommended for individuals with severe hepatic impairment.

Gene: CYP2D6 — **Robust**

This individual may have a normal response to iloperidone.

Gene: CYP3A4 — **Developing**

PHD LABORATORY

Psychiatry

Drug Class: Antipsychotic **MOA:** 5-HT2A and Dopamine-D2 Receptor Antagonist

! Paliperidone (Invega) — Normal Response Expected

This individual may metabolize paliperidone slower.

Population pharmacokinetics analyses indicated no difference in exposure or clearance of paliperidone.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Gene: CYP2D6 **Modest**

Drug Class: Antipsychotic **MOA:** 5-HT2A and Dopamine-D2 Receptor Antagonist

Quetiapine (Seroquel) ✓

This individual may have a normal response to quetiapine.

Gene: CYP3A4 **Developing**

Drug Class: Antipsychotic **MOA:** 5-HT2A and Dopamine-D2 Receptor Antagonist

! Risperidone (Risperdal) — Use with Caution

This individual may metabolize risperidone slower, which results in increased risperidone plasma concentrations and decreased 9-hydroxyrisperidone (paliperidone) concentrations.

However, the pharmacokinetics of risperidone and 9-hydroxyrisperidone combined, after single and multiple doses, are similar in normal and poor metabolizers.

In addition, clinical studies suggest that poor and normal metabolizers do not have different rates of adverse events. Physicians should still monitor for risk of adverse events (cerebrovascular effects, tardive dyskinesia, and neuroleptic malignant syndrome) and therapeutic response.

Physicians may initiate therapy with the recommended starting dose and adjust the dose accordingly.

Additionally, the dose of risperidone should be adjusted when used in combination with CYP2D6 inhibitors and enzyme inducers.

Individuals with severe renal (CrCl < 30 ml/min) or severe hepatic impairment should use a lower starting dose of 0.5 mg twice daily and may increase to dosages above 1.5 mg twice daily at intervals of one week or longer.

Gene: CYP2D6 **Modest**

This individual may have an undetermined response and an increased risk of hyperprolactinemia.

Gene: DRD2 ! **Developing**

This individual may have a reduced response.

Gene: HTR2A ! **Developing**

Female (XX) and Male (XY) individuals may have an increased risk of weight gain but an average risk of developing metabolic syndrome.

Gene: HTR2C ! **Developing**

Drug Class: Antipsychotic **MOA:** Central Dopamine Receptor Antagonist

! Pimozide (Orap) — Use with Caution

This individual metabolizes pimozide slower, which may result in an increased risk of adverse events such as neuroleptic malignant syndrome, tardive dyskinesia, and extrapyramidal symptoms.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Gene: CYP2D6 **Robust**

This individual may have a normal response to pimozide.

Gene: CYP3A4 ✓ **Developing**

PHD LABORATORY

Psychiatry

Drug Class: Antipsychotic

MOA: D1 and D2, Alpha 1 Adrenergic and 5-HT2 Receptor Antagonist

Zuclopenthixol

This individual metabolizes zuclopenthixol slower, leading to higher concentrations.

This may lead to an increased risk of adverse events. Adverse events may include drowsiness, hypertonia, tremor, weakness, and xerostomia.

Gene: CYP2D6 — **Developing**

Drug Class: Antipsychotic

MOA: D2 and 5-HT1A Receptor Partial Agonist and 5-HT2A Receptor Antagonist

Aripiprazole (Abilify)

Use with Caution

This individual metabolizes aripiprazole slower, which may lead to an increased probability of adverse events.

The adverse events may include anxiety, weight gain, constipation, sleep problems, and cerebrovascular reactions such as stroke and transient ischemic attack.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Gene: CYP2D6 — **Robust**

This individual may have a normal response to aripiprazole.

Gene: CYP3A4 — **Developing**

Drug Class: Antipsychotic

MOA: D2 and 5-HT1A Receptor Partial Agonist and 5-HT2A Receptor Antagonist

Aripiprazole Lauroxil (Aristada, Aristada Initio)

Use with Caution

This individual metabolizes aripiprazole lauroxil slower, which may lead to an increased probability of adverse events due to higher concentrations.

Adverse effects of aripiprazole lauroxil therapy can include feeling the urge to move constantly (akathisia), injection site reactions, weight gain, insomnia, and cerebrovascular reactions.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Gene: CYP2D6 — **Robust**

This individual may have a normal response to aripiprazole lauroxil.

Gene: CYP3A4 — **Developing**

Drug Class: Antipsychotic

MOA: D2 and 5-HT1A Receptor Partial Agonist and 5-HT2A Receptor Antagonist

Cariprazine (Vraylar)

Use with Caution

This individual may metabolize cariprazine slowly, which results in potentially higher concentrations of cariprazine and a greater risk of adverse effects.

The adverse events may include tardive dyskinesia, neuroleptic malignant syndrome, and cerebrovascular effects.

This individual may not have a clinically relevant effect on the pharmacokinetics of cariprazine and its active metabolites. Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Usage of cariprazine is not recommended in individuals with severe hepatic impairment (Child-Pugh score between 10 and 15) or with severe renal impairment (CrCL < 30 mL/min).

Gene: CYP2D6 — **Modest**

PHD LABORATORY

Psychiatry

Drug Class: Antipsychotic

MOA: D2 Receptor Blocker

! Perphenazine (Trilafon) — Use with Caution

This individual metabolizes perphenazine slower, which results in higher systemic concentrations.

This may lead to a greater risk of adverse effects, especially during the first 10 days of treatment, such as tardive dyskinesia, extrapyramidal reactions, neuroleptic malignant syndrome, drowsiness, and dystonia.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Monitor hepatic function during use; discontinue if abnormalities occur; contraindicated in individuals with liver damage. Use with caution in individuals with renal impairment.

Gene: CYP2D6 — **Modest**

Drug Class: Antipsychotic

MOA: Dopamine-D2, Serotonin 5-HT2A, and 5-HT7 Receptor Antagonist

Lurasidone (Latuda) ✓

This individual may have an increased response.

Gene: HTR1A — **Developing**

Drug Class: Antipsychotic

MOA: Nonselective Postsynaptic Dopaminergic D2 Receptor Blocker

Haloperidol (Haldol) !

This individual metabolizes haloperidol slower, potentially may to higher concentrations of haloperidol and the active metabolite.

This may lead to an increased risk of adverse events. Adverse events may include cardiovascular effects, extrapyramidal symptoms, dystonia, and tardive dyskinesia.

Gene: CYP2D6 — **Developing**

Drug Class: Antipsychotic

MOA: Serotonin 5-HT2A and 5-HT2C, Dopamine D1-4, Histamine H1 and Alpha 1-Adrenergic Receptor Antagonist

Olanzapine (ZyPREXA, ZyPREXA Relprevv, ZyPREXA Zydis) !

This individual may have an average risk of side effects.

Gene: HTR2A ✓ — **Developing**

Female (XX) and Male (XY) individuals may have an increased risk of weight gain.

Gene: HTR2C ! — **Developing**

PHD LABORATORY

Psychiatry

MOA: Serotonin Type 2A, Dopamine Type 2, Histamine H1 and Alpha Adrenergic, Cholinergic and Other Dopaminergic and Serotonergic Receptor Antagonist

Drug Class: Antipsychotic

! Clozapine (Clozaril, Versacloz) — Use with Caution

This individual metabolizes clozapine slower, which can lead to an increased probability of adverse events.

Adverse effects of clozapine therapy can include CNS reactions (sedation, dizziness/vertigo, headache, and tremor); cardiovascular reactions (tachycardia, hypotension, and syncope); autonomic nervous system reactions (hypersalivation, sweating, dry mouth, and visual disturbances); gastrointestinal reactions (constipation and nausea); and fever.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation. Physicians should also monitor the blood absolute neutrophil count (ANC) to reduce the risk of developing severe neutropenia.

Gene: CYP2D6 — **Robust**

This individual is expected to have a normal response to clozapine.

Physicians should monitor the blood absolute neutrophil count (ANC) to reduce the risk of developing severe neutropenia.

Gene: CYP3A4 — **Developing**

This individual may have a reduced response.

Gene: HTR1A ! — **Developing**

Female (XX) and Male (XY) individuals may have an increased risk of weight gain but an average risk of developing metabolic syndrome.

Gene: HTR2C ! — **Developing**

Drug Class: Benzodiazepine

MOA: GABA-A Agonist

! Diazepam (Valium, Diastat AcuDial, Diazepam Intensol, Diastat Pediatric) — Use with Caution

This individual metabolizes diazepam fast.

However, there is no mention of the drug response associated with the increased activity of this enzyme and how it may affect pharmacotherapy success or increase the risk of adverse drug reactions.

Physicians may initiate the recommended starting dose and adjust the dose based on the individual's clinical presentation while monitoring for therapeutic effects and adverse events.

Gene: CYP2C19 — **Modest**

Drug Class: Central Nervous System Agent

MOA: Selective Norepinephrine Reuptake Inhibitor

Atomoxetine (Strattera) — Use with Caution

This individual metabolizes atomoxetine slower, which may result in higher concentrations.

This may lead to an increased probability of adverse events including blurred vision, dry mouth, constipation, tremor, insomnia, and weight decrease.

In children, atomoxetine may be initiated with a dose of 0.5 mg/kg/day and adjusted thereafter based on the individual's clinical presentation while closely monitoring for adverse events and clinical response. Additionally, in adults, atomoxetine should be initiated with a dose of 40 mg/day, and if no clinical response and in the absence of adverse events after 2 weeks increase the dose to 80 mg/day.

Gene: CYP2D6 — **Robust**

PHD LABORATORY

Psychiatry

Drug Class: Central Nervous System Agent
MOA: Selective Norepinephrine Reuptake Inhibitor

! Viloxazine (Qelbree) — Use with Caution

This individual may metabolize viloxazine slower, which results in higher viloxazine systemic concentrations.This may lead to a greater risk of adverse effects, including somnolence, fatigue, activation of mania, increased heart rate, insomnia, and irritability. In-vitro studies show that viloxazine is not an inhibitor of SLCO1B1. Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

In individuals with severe renal impairment (eGFR < 30 mL/min/1.73m2), the recommended starting dosage is 100 mg once daily. Dosage may be titrated in weekly increments of 50 to 100 mg once daily, to a maximum recommended dosage of 200 mg once daily.

Gene: CYP2D6, SLCO1B1 — **Modest**

Drug Class: Central Nervous System Stimulant
MOA: Dopamine Reuptake Inhibitor

! Modafinil (Provigil) — Use with Caution

This individual metabolizes modafinil slower.

Caution should be taken when co-administering modafinil with another drug that is a CYP2D6 substrate and has ancillary routes of elimination through CYP2C19 (TCAs and SSRIs) due to increased rsk of adverse events.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

In individuals with severe hepatic impairment, the dosage of modafinil should be reduced to one-half of the recommended dosage. Use with caution in individuals with renal impairment.

Gene: CYP2D6 — **Modest**

This individual may have a normal response to modafinil.

Gene: CYP3A4 — **Developing**

Drug Class: Central Nervous System Stimulant
MOA: Histamine-3 (H3) Receptor Antagonist/Inverse Agonist

! Pitolisant (Wakix) — Use with Caution

This individual metabolizes pitolisant slower, which results in higher pitolisant concentrations.

This may lead to an increased risk for adverse events including QT prolongation, insomnia, and nausea.

Physicians may initiate therapy at a recommended dose and adjust the dose accordingly.

Gene: CYP2D6 — **Robust**

Drug Class: Central Nervous System Stimulant
MOA: Norepinephrine and Dopamine Reuptake Inhibitor

! Amphetamine (Dyanavel XR, Adzenys XR-ODT, Adzenys ER) — Use with Caution

This individual may metabolize amphetamine slower.

This may affect systemic concentrations and increase the risk of adverse events such as serious cardiovascular, psychiatric, growth suppression, including serotonin syndrome a potentially life-threatening condition.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Gene: CYP2D6 — **Robust**

Drug Class: First Generation Antipsychotic
MOA: Dopamine-D2 Receptor Antagonist

Prochlorperazine (Compro) !

This individual may have an increased incidence of nausea following treatment with prochlorperazine.

Gene: DRD2 — **Developing**

PHD LABORATORY

Psychiatry

Drug Class: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor

! Amitriptyline (Elavil, Vanatrip)

Consider Alternatives

This individual has an increased CYP2C19 enzymatic activity and a decreased CYP2D6 enzymatic activity which may alter amitriptyline metabolism.

Alternative drug therapy may be considered. However, if amitriptyline is used, please monitor for drug toxicities and therapeutic response, and adjust the dose based on the individual's clinical presentation.

Gene: CYP2D6, CYP2C19

Robust

Drug Class: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor

! Imipramine (Tofranil)

Consider Alternatives

This individual has an increased CYP2C19 enzymatic activity and a decreased CYP2D6 enzymatic activity which may alter imipramine metabolism.

Alternative drug therapy may be considered. However, if imipramine is used, please monitor for drug toxicities and therapeutic response, and adjust the dose based on the individual's clinical presentation.

Gene: CYP2D6, CYP2C19

Robust

Drug Class: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor

! Protriptyline (Vivactil)

Use with Caution

This individual metabolizes protriptyline slower, which can lead to an increased probability of adverse events due to higher systemic concentrations.

The adverse events may include aggravating agitation and anxiety, producing cardiovascular reactions such as tachycardia and hypotension, and an increased risk of suicide.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Gene: CYP2D6

Modest

Drug Class: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor

! Trimipramine (Surmontil)

Consider Alternatives

This individual has an increased CYP2C19 enzymatic activity and a decreased CYP2D6 enzymatic activity which may alter trimipramine metabolism.

Alternative drug therapy may be considered. However, if trimipramine is used, please monitor for drug toxicities and therapeutic response, and adjust the dose based on the individual's clinical presentation.

Gene: CYP2D6, CYP2C19

Robust

PHD LABORATORY

Psychiatry

Drug Class: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor, and Dopamine Receptor Blocker

! Amoxapine (Asendin) — Use with Caution

This individual metabolizes amoxapine slower, which can lead to an increased probability of adverse events due to increased concentrations.

The adverse events may include cardiotoxicity, blurred vision due to pupillary dilation in individuals with angle-closure glaucoma, constipation, tardive dyskinesia, and dizziness.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Gene: CYP2D6 — Modest

Drug Class: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor; Histamine, 5-Hydroxytryptamine, and Acetylcholine Receptor Blocker

Nortriptyline (Pamelor) — Decrease Dose

This individual metabolizes nortriptyline slower, which can lead to an increased probability of adverse events due to higher plasma concentrations of nortriptyline when given usual doses.

The adverse events may include cardiotoxicity, blurred vision, constipation, dizziness, central nervous system toxicities, and suicide risk.

A dose reduction of the recommended starting dose may be required. Physicians may adjust the dose based on the individual's clinical presentation.

Gene: CYP2D6 — Robust

Drug Class: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Uptake Inhibitor

! Clomipramine (Anafranil) — Consider Alternatives

This individual has an increased CYP2C19 enzymatic activity and a decreased CYP2D6 enzymatic activity which may alter clomipramine metabolism.

Alternative drug therapy may be considered. However, if clomipramine is used, please monitor for drug toxicities and therapeutic response, and adjust the dose based on the individual's clinical presentation.

Gene: CYP2D6, CYP2C19 — Robust

Drug Class: Tricyclic Antidepressant, Sleep Aid

MOA: Serotonin and Norepinephrine Reuptake Inhibitor, Histamine Receptor Antagonist

! Doxepin (Silenor, Zonalon, Sinequan, Prudoxin) — Consider Alternatives

This individual has an increased CYP2C19 enzymatic activity and a decreased CYP2D6 enzymatic activity which may alter doxepin metabolism.

Alternative drug therapy may be considered. However, if doxepin is used, please monitor for drug toxicities and therapeutic response, and adjust the dose based on the individual's clinical presentation.

Gene: CYP2D6, CYP2C19 — Robust

PHD LABORATORY

Respiratory

Drug Class: Anticholinergic

MOA: M3 Receptor Inhibitor

! Umeclidinium (Incruse Ellipta) — Normal Response Expected

This individual may metabolize umeclidinium slower.

However, no clinically meaningful difference in systemic exposure to umeclidinium (500 mcg) was observed. Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Gene: CYP2D6 — **Modest**

Drug Class: Antitussive

MOA: N-Methyl-D-Aspartate (NMDA) Receptor Antagonist

Dextromethorphan (Robitussin, Delsym, Pediacare, Robafen) !

This individual metabolizes dextromethorphan slower, leading to higher concentrations.

This may lead to an increased risk of adverse events. Adverse events may include dizziness and somnolence.

Gene: CYP2D6 — **Developing**

Drug Class: Bronchodilator

MOA: Long-Acting Beta2-Adrenergic Agonist

! Arformoterol (Brovana) — Normal Response Expected

This individual has decreased CYP2D6 enzymatic activity and may metabolize arformoterol slower.

However, there is no impact on systemic exposure to arformoterol in individuals with reduced CYP2D6 enzyme activity. Normal drug response is expected.

Physicians may initiate the recommended starting dose and adjust the dose based on the individual's clinical presentation.

Gene: CYP2D6 — **Modest**

Drug Class: Bronchodilator

MOA: Long-Acting Beta2-Adrenergic Agonist

Salmeterol (Serevent Diskus)

This individual may have an increased response to salmeterol.

Gene: ADRB2 — **Developing**

Rheumatology

Drug Class: Antigout

MOA: URAT1 Inhibitor

Lesinurad (Zurampic) — Normal Response Expected

This individualis expected to have a normal response to lesinurad.

Lesinurad should not be initiated in individuals with CrCl < 45 mL/min. No dose adjustment is recommended in individuals with CrCl 45-60 mL/min, however, more frequent renal function monitoring is recommended. Lesinurad is not recommended for individuals with severe hepatic impairment.

Gene: CYP2C9 — **Modest**

Drug Class: Antiplatelet/Non-Steroidal Anti-Inflammatory Drug

MOA: Prostaglandin Synthesis and Platelet Aggregation Inhibitor

Aspirin (Ecotrin, Bayer, Asctiptin, Durlaza) — Normal Response Expected

This individual may have normal therapeutic levels of aspirin.

Avoid aspirin in individuals with severe hepatic insufficiency or severe renal failure (GFR <10 mL/min).

Gene: CYP2C9 — **Robust**

PHD LABORATORY

Rheumatology

Drug Class: Antirheumatic
MOA: Dihydrofolate Reductase Inhibitor

Methotrexate (Otrexup, Rasuvo, Trexall, Xatmet)

This individual is a carrier of a partial methylenetetrahydrofolate reductase (MTHFR) deficiency.

An autosomal recessive inborn error of metabolism featuring higher homocysteine levels and lower serum folate levels should be managed according to the standard of care for those disorders (clinical genetics and genetic counselor consults). First-degree family members of the individual (parents, siblings, offerings, and first cousins) should be clinically assessed by a geneticist and/or a genetic counselor, and seek molecular testing for the variant(s) found positive in this individual.

This individual has an intermediate risk of toxicity such as the increased risk of bone marrow, liver, lung, and kidney toxicities when treated with methotrexate for arthritis, and would benefit from methylfolate supplementation therapy.

Gene: MTHFR — **Developing**

Drug Class: Antirheumatic
MOA: Janus Associated Kinase Inhibitor

Upadacitinib (Rinvoq) — Normal Response Expected

This individual has decreased CYP2D6 enzymatic activity and may metabolize upadacitinib slower.

However, the individual is expected to have a standard response to the recommended dosing of upadacitinib.

Physicians may initiate the recommended starting dose and adjust the dose based on the individual's clinical presentation.

Gene: CYP2D6 — **Modest**

This individual may have a normal response to standard dosing of upadacitinib.

Gene: CYP3A4 — **Developing**

Drug Class: Antirheumatic
MOA: Purine Antagonist

Azathioprine (Azasan, Imuran) — Normal Response Expected

This individual is expected to have a normal response to azathioprine.

Gene: TPMT, NUDT15 — **Robust**

Drug Class: Muscle Relaxant
MOA: Intraneuronal Activity in Descending Reticular Formation and Spinal Cord Suppressant

Carisoprodol (Soma, Vanadom) — Use with Caution

This individual metabolizes carisoprodol fast, which results in decreased exposure of carisoprodol and increased exposure of meprobamate.

There is insufficient evidence of whether this translates into efficacy or adverse events. Physicians should prescribe this medication with caution and monitor for safety and efficacy.

Gene: CYP2C19 — **Modest**

Drug Class: Non-Steroidal Anti-Inflammatory Drug
MOA: Cyclooxygenase 1 and 2 Inhibitor

Diclofenac (Diclozor, Flector, Pennsaid, Voltaren, Xrylix, Cambia, Zipsor, Zorvolex) — Normal Response Expected

This individual may have normal therapeutic levels of diclofenac.

Individuals with hepatic disease may require reduced doses of diclofenac. Treatment with diclofenac is not recommended in individuals with advanced renal disease.

Gene: CYP2C9 — **Robust**

PHD LABORATORY

Rheumatology

Drug Class: Non-Steroidal Anti-Inflammatory Drug **MOA:** Cyclooxygenase 1 and 2 Inhibitor

Flurbiprofen (Ansaid)

Normal Response Expected

This individual is expected to have a normal response to flurbiprofen.

Gene: CYP2C9 Robust

Drug Class: Non-Steroidal Anti-Inflammatory Drug **MOA:** Cyclooxygenase 1 and 2 Inhibitor

Ibuprofen (Addaprin, Advil Junior Strength, Advil Migraine, Advil, Caldolor, Childrens Advil, Childrens Motrin, Dyspel, Genpril, GoodSense Ibuprofen Childrens, GoodSense Ibuprofen, IBU, Ibuprofen Childrens, Infants Advil , KS Ibuprofen, Motrin Childrens, Motrin IB, Motrin Infants Drops, NeoProfen, Provil)

Normal Response Expected

This individual is expected to have a normal response to ibuprofen.

Avoid use in individuals with advanced renal disease; discontinue use with persistent or worsening abnormal renal function tests. Additionally, use with caution in individuals with hepatic impairment; individuals with advanced hepatic disease are at an increased risk of GI bleeding with NSAIDs.

Gene: CYP2C9 Robust

Drug Class: Non-Steroidal Anti-Inflammatory Drug **MOA:** Cyclooxygenase 1 and 2 Inhibitor

Indomethacin (Indocin, Tivorbex)

Normal Response Expected

This individual may have normal therapeutic levels of indomethacin.

Gene: CYP2C9 Robust

Drug Class: Non-Steroidal Anti-Inflammatory Drug **MOA:** Cyclooxygenase 1 and 2 Inhibitor

Lornoxicam

Normal Response Expected

This individual is expected to have a normal response to lornoxicam.

Gene: CYP2C9 Robust

Drug Class: Non-Steroidal Anti-Inflammatory Drug **MOA:** Cyclooxygenase 1 and 2 Inhibitor

Meloxicam (Anjeso, Mobic, Qmiiz ODT, Vivlodex)

Normal Response Expected

This individual is expected to have a normal response to meloxicam.

The use of meloxicam in individuals with severe renal impairment is not recommended. In individuals on hemodialysis, the maximum dosage of meloxicam is 7.5 mg per day. It is recommended to use meloxicam with caution in individuals with hepatic impairment.

Gene: CYP2C9 Robust

Drug Class: Non-Steroidal Anti-Inflammatory Drug **MOA:** Cyclooxygenase 1 and 2 Inhibitor

Nabumetone (Relafen DS)

Normal Response Expected

This individual may have normal therapeutic levels of nabumetone.

Gene: CYP2C9 Robust

PHD LABORATORY

Rheumatology

Drug Class: Non-Steroidal Anti-Inflammatory Drug
MOA: Cyclooxygenase 1 and 2 Inhibitor

Naproxen (Aleve, EC-Naprosyn, EC-Naproxen, GoodSense Naproxen Sodium, Mediproxen, Naprelan, Naprosyn, Naproxen DR) — **Normal Response Expected**

This individual may have normal therapeutic levels of naproxen.

Naproxen is not recommended for use in individuals with moderate to severe and severe renal impairment (CrCl < 30 mL/min). A lower dose should be considered in individuals with renal or hepatic impairment.

Gene: CYP2C9 — **Robust**

Drug Class: Non-Steroidal Anti-Inflammatory Drug
MOA: Cyclooxygenase 1 and 2 Inhibitor

Piroxicam (Feldene) — **Normal Response Expected**

This individual is expected to have a normal response to piroxicam.

Gene: CYP2C9 — **Robust**

Drug Class: Non-Steroidal Anti-Inflammatory Drug
MOA: Cyclooxygenase 1 and 2 Inhibitor

Tenoxicam — **Normal Response Expected**

This individual is expected to have a normal response to tenoxicam.

Gene: CYP2C9 — **Robust**

Drug Class: Non-Steroidal Anti-Inflammatory Drug
MOA: Selective COX-2 Inhibitor

Aceclofenac — **Normal Response Expected**

This individual may have normal therapeutic levels of aceclofenac.

Gene: CYP2C9 — **Robust**

Drug Class: Non-Steroidal Anti-Inflammatory Drug
MOA: Selective COX-2 Inhibitor

Lumiracoxib — **Normal Response Expected**

This individual may have normal therapeutic levels of lumiracoxib.

Gene: CYP2C9 — **Robust**

Smoking Cessation

Drug Class: Smoking Cessation Aid
MOA: Dopamine and Norepinephrine Reuptake Inhibitor

Bupropion (Aplenzin, Forfivo XL, Wellbutrin SR, Wellbutrin XL)

This individual may have normal therapeutic levels of hydroxybupropion, a metabolite of bupropion.

Gene: CYP2B6 — **Developing**

PHD LABORATORY

Supplements

Drug Class: Vitamins **MOA:** Folic Acid Agonist

L-methylfolate (Deplin) !

This individual is a carrier of a partial methylenetetrahydrofolate reductase (MTHFR) deficiency.

An autosomal recessive inborn error of metabolism featuring higher homocysteine levels and lower serum folate levels should be managed according to the standard of care for those disorders (clinical genetics and genetic counselor consults). First-degree family members of the individual (parents, siblings, offerings, and first cousins) should be clinically assessed by a geneticist and/or a genetic counselor, and seek molecular testing for the variant(s) found positive in this individual.

This individual would benefit from methylfolate supplementation therapy.

Gene: MTHFR **Developing**

Toxicology

Drug Class: Opioid Antagonist **MOA:** Opioid Receptor Antagonist

Naltrexone (Vivitrol) — Normal Response Expected

This individual may have normal therapeutic levels of the medication.

However, following the initiation of this medication, physicians should still monitor individuals for analgesic effectiveness, adverse events, individual-specific factors, and adjust the dose accordingly.

Gene: COMT, OPRM1 **Robust**

Urology

Drug Class: Alpha-1 Blocker **MOA:** Selective Alpha-1A Adrenoceptor Antagonist

Tamsulosin (Flomax) ! — Use with Caution

This individual metabolizes tamsulosin slowly.

This may lead to an increased probability of adverse events due to increased systemic concentrations. The adverse events may include postural hypotension, allergic reaction, priapism, and intraoperative floppy iris syndrome.

Physicians may initiate therapy with the recommended starting dose, adjust, or consider an alternative drug therapy based on the individual's clinical presentation.

Gene: CYP2D6 **Modest**

This individual may have a normal response to tamsulosin.

Gene: CYP3A4 **Developing**

Drug Class: Anticholinergic **MOA:** Competitive Muscarinic Receptor Antagonist

Fesoterodine (Toviaz) ! — Use with Caution

This individual metabolizes fesoterodine slower, which results in increased active metabolite concentrations that may affect the QTc interval.

Similar to poor metabolizer individuals, when administering fesoterodine 28 mg to CYP2D6 normal metabolizers, the exposure to the active metabolite is similar to the exposure of CYP2D6 poor metabolizers receiving fesoterodine 8 mg together with CYP3A4 blockade. No dosing adjustments are recommended in the presence of CYP2D6 inhibitors.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation.

Dose adjustment is recommended in individuals with severe renal impairment (CrCl <30 mL/minute). Use is not recommended in individuals with severe hepatic impairment.

Gene: CYP2D6 **Modest**

PHD LABORATORY

Urology

Drug Class: Anticholinergic **MOA:** Competitive Muscarinic Receptor Antagonist

! Tolterodine (Detrol) — Use with Caution

This individual metabolizes tolterodine slower.

This may result in increased concentrations of tolterodine and reduced concentrations of the active metabolite, 5-HMT. The increased plasma concentrations of tolterodine can affect QT prolongation.

CYP2D6 metabolic status should be used to guide therapy in individuals with a known history of QT prolongation or who are taking certain antiarrhythmic medications. When using this medication, it is recommended to conduct a baseline and subsequent electrocardiograms to evaluate QT segment status.

Gene: CYP2D6 **Modest**

This individual may have a normal response to tolterodine.

Gene: CYP3A4 **Developing**

Drug Class: Anticholinergic **MOA:** Selective M3 Receptor Antagonist

! Darifenacin (Enablex) — Use with Caution

This individual metabolizes darifenacin slower, which results in higher systemic concentrations.

However, there is no mention of the clinical significance of these increased concentrations.

When using this medication, it is recommended to conduct a baseline and subsequent electrocardiograms to evaluate QT/QTc interval status.

Gene: CYP2D6 **Modest**

Drug Class: Genitourinary Agent **MOA:** Beta-3 Adrenergic Receptor Agonist

! Mirabegron (Myrbetriq) — Use with Caution

This individual may metabolize mirabegron slower, which results in higher systemic concentrations of mirabegron.

This may lead to a greater risk of adverse effects, such as hypertension, urinary retention, and angioedema.

Physicians may initiate therapy with the recommended starting dose and adjust the dose as needed based on the individual's clinical presentation while monitoring for any adverse reactions.

Mirabegron is a moderate CYP2D6 inhibitor and, when used concomitantly with drugs metabolized by CYP2D6, especially narrow therapeutic index drugs, appropriate monitoring and possible dose adjustment of those drugs may be necessary.

Mirabegron is not recommended in severe hepatic impairment or in End-Stage Renal Disease (eGFR < 15 mL/min/1.73 m2). The maximum daily dose is 25mg in individuals with severe renal impairment (eGFR 15 to 29 mL/min/1.73 m2) or moderate hepatic impairment.

Gene: CYP2D6 **Modest**

Pharmacogenomics Actionable & Research Review

Information Card

This card contains an abbreviated genetic summary specific to the individual.
It is not intended as a replacement for the complete Pharmacogenomics Educational Review.

Name test PGX 1 test PGX 1
Date of Birth: 1994-10-28
Report ID: X242900001

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This card contains information about your genetics that relate to drug metabolism. Share this with your healthcare providers before being prescribed new medications.

Pharmacogenomics Genetic Summary

Gene	Genotype(s)	Phenotype(s)
CYP2B6	*1/*5	Normal Metabolizer
CYP2C19	*17/*17	Ultrarapid Metabolizer
CYP2C9	*1/*1	Normal Metabolizer
CYP2D6	*2/*4E	Intermediate Metabolizer
CYP3A5	*3/*3	Poor Metabolizer
DPYD	*1/*1	Normal Metabolizer
NUDT15	*1/*1	Normal Metabolizer
SLCO1B1	*37/*5 or *1/*15	Decreased Function
TPMT	*1/*1	Normal Metabolizer

Gene	Genotype(s)/ Individual impact
ABCB1	c.2887T>G(A) Heterozygous, AC c.3645T>C Heterozygous, AG c.1446T>C Heterozygous, AG
ABCG2	c.421C>A Negative, GG
ADRB2	c.46G>A Negative, GG
APOE	E3/E3
COMT	c.472G>A Negative, GG
CYP1A2	*1F/*1F
CYP2C	g.94645745G>A Negative, GG
CYP3A4	*1A/*1A
CYP4F2	c.1297G>A Negative, CC
DRD2	c.-31-870T>C Heterozygous, AG g.4651A>G Heterozygous, CT c.2137G>A Heterozygous, AG c.1139-134T>G Heterozygous, AC g.4750dup Heterozygous, GdupG
F2	c.*97G>A Negative, GG/Average Risk of ADR
F5	c.1601G>A Negative, CC/Average Risk of ADR
HTR1A	g.4555G>C Negative, CC
HTR2A	c.614-2211T>C Heterozygous, AG g.4692G>A Negative, CC
HTR2C	g.4963C>T Negative, CC c.551-3008C>G Homozygous, GG
MTHFR	c.788C>T Heterozygous, AG c.1409A>C Negative, TT
OPRM1	c.118A>G Negative, AA
VKORC1	g.3588G>A Heterozygous, CT

† Cut along dotted lines

† Fold here

The results of the systematic review performed by Genetica Consulting Services (GCS) of available pharmacogenomics (PGx) actionable guidelines and research literature is presented here for your consideration. The GCS PGx Review is a tool intended to provide users with relevant medical reference information related to identified multiple factors (including gene variations) and their drug associations. This review reflects the professional opinions of the GCS team and clearly indicates content intended for clinical use and for research use. Review of the same evidence can be found with references documented at geneticaconsulting.com/refs. © 2024 Genetica Consulting Services

PHD LABORATORY

Results Dependent Content Limitations

Based on the results provided by the testing laboratory, a negative or a star 1 allele (*1) - allele, the version of a gene - result signifies the absence of the targeted alleles and does not indicate the absence of other variants not covered by the assay. The variants *allele classification and the assigned “star” *allele genotype are directly dependent on each assay content. Because of it, the possibility that another genotype(s) may be present that is out of the scope of the results provided cannot be ruled out.

The content provided in this Educational Pharmacogenomics Review is limited to the scope of the assay performed by the testing laboratory. Variant *allele classification and its corresponding genotype is based on the results provided to Genetica Consulting Services. A negative result or a star 1 allele (*1) result signifies the absence of the targeted allele(s) and does not indicate the absence of other variants not included in the assay. The possibility that other genotype(s) may be present cannot be ruled out as they are not within the scope of the results provided.

Assay limitations may result in lack of phasing (cis- or trans- allele determination) and gene-variant content that has not been fully functionally characterized. This may produce more than one genotype and metabolizer status.

Non-genetic drug interactions are sourced from Merative Micromedex®

Sources

For each of the sources below, information is curated, and consensus educational statements are generated and reviewed by the GCS didactic group.

Robust:

- FDA (Food and Drug Administration) Drug Labeling with actionable detailed pharmacogenomics content.
- Clinical Pharmacogenomics Implementation Consortium (CPIC) Guidelines.

Modest:

- FDA (Food and Drug Administration) Drug Labeling with actionable pharmacogenomics content.

Developing (Educational/Research Use Only):

- FDA (Food and Drug Administration) Drug Labeling with informative pharmacogenomics content.
- Clinical Pharmacogenomics Implementation Consortium (CPIC) without Guidelines Levels A, B, and, B/C.
- Pharmacogenomics Knowledge Database (PharmGKB) Levels, 1, 2, and selected medications level 3.

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