Pharmacogenomics Actionable & Research Review

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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.

Name:	John Doe	**Report ID:**	PhDLabs
Date of Birth:	1960-01-01	**Issue Date:**	10/07/25

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I. Pharmacogenomics Genetic Summary

Gene	Genotype(s)	Phenotype(s)
CYP2B6	*1/*6	Intermediate Metabolizer
CYP2C19	*1/*17	Rapid Metabolizer
CYP2C9	*1/*9	Intermediate Metabolizer
CYP2D6	*2/*34	Normal Metabolizer
CYP3A5	*1/*3	Intermediate Metabolizer

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

Gene	Genotype(s)/Individual Impact
ABCB1	c.3645T>C Homozygous, GG c.1446T>C Homozygous, GG c.3095G>A(T) Negaive, CC
ABCG2	c.421C>A Negative, GG
ADRB2	c.46G>A Heterozygous, AG
APOE	E3/E3
COMT	c.472G>A Heterozygous, GG
CYP1A2	*1D/*1F or *1A/*1V
CYP2C	g.94645745G>A Negative, GG
CYP3A4	*1B/*1B
CYP4F2	c.1297G>A Homozygous, TT

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

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.

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
CARDIOLOGY	**GASTROENTEROLOGY**	**INFECTIOUS DISEASES**	**DERMATOLOGY**	**PAIN MANAGEMENT**
Antilipemic Simvastatin	**Acid Reducing Agent** Omeprazole	**Antifungal** Voriconazole	**Immunosuppressant** Tacrolimus	**Non-Steroidal Anti-Inflammatory Drug** Celecoxib
Beta-Blocker Metoprolol			**IMMUNOLOGY**	**RHEUMATOLOGY**
PSYCHIATRY			**Immunosuppressant** Tacrolimus	**Non-Steroidal Anti-Inflammatory Drug** Celecoxib
Antidepressant Paroxetine				
Antipsychotic Brexpiprazole Thioridazine				
Tricyclic Antidepressant Desipramine				

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

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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) — Normal Response Expected

This individual has a normal SLCO1B1 function but a decreased CYP2C9 enzymatic activity that does not affect the pharmacokinetics of simvastatin.

This individual has an average risk of simvastatin-induced myopathy.

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 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) — Normal Response Expected

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

Gene: CYP2D6 — Robust

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) — Increase Dose

This individual has a lower probability of achieving target tacrolimus concentrations and may result in a higher rejection risk.

The starting dose may need to be increased, but should not exceed the total starting dose of 0.3 mg/kg/day.

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 faster than individuals with some other genotypes.

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.

Physicians may initiate the recommended starting dose and potentially increase the dose for the treatment of H. pylori infection and erosive esophagitis while 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 individuals 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) — Increase Dose

This individual has a lower probability of achieving target tacrolimus concentrations and may result in a higher rejection risk.

The starting dose may need to be increased, but should not exceed the total starting dose of 0.3 mg/kg/day.

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 faster, which may reduce the probability of pharmacotherapy success.

For adult individuals, an alternative therapy may be required. For pediatric individuals, physicians may initiate the recommended standard of care dosing and adjust the dose based on the individual's clinical presentation.

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) — Decrease Dose

This individual metabolizes celecoxib slower, which can lead to an increased risk of adverse events due to increased systemic concentrations.

The adverse events may include gastrointestinal bleeding, heart failure, edema, and renal toxicity.

Physicians may use the lowest effective dosage for the shortest duration and adjust the dose based on the individual's clinical presentation while closely monitoring for adverse events.

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) — Normal Response Expected

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

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 average 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.

Drug Class: Antipsychotic

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

Brexpiprazole (Rexulti) — Normal Response Expected

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

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)

Normal Response Expected

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

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) — Normal Response Expected

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

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) — Decrease Dose

This individual metabolizes celecoxib slower, which can lead to an increased risk of adverse events due to increased systemic concentrations.

The adverse events may include gastrointestinal bleeding, heart failure, edema, and renal toxicity.

Physicians may use the lowest effective dosage for the shortest duration and adjust the dose based on the individual's clinical presentation while closely monitoring for adverse events.

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) — Normal Response Expected

The individual is expected to have a normal response to carvedilol.

Desipramine/Thioridazine/Paroxetine/Celecoxib - Increased carvedilol levels produce dizziness.

Paroxetine/Fluconazole/Voriconazole - May enhance the beta-blocking activity and further slow the heart rate or cardiac conduction. Monitor for signs of bradycardia or heart block.

Gene: CYP2D6 — **Robust**

Drug Class: Alpha and Beta Adrenergic Blocker
MOA: Nonselective Beta Adrenergic Blocker and Alpha 1 Adrenergic Blocker

Labetalol (Normodyne, Trandate)

This individual may have normal therapeutic levels of labetalol and may have an average risk of adverse events.

Gene: CYP2D6 — **Developing**

Drug Class: Antiarrhythmic
MOA: Sodium and Potassium ATPase Pump Inhibitor

Digoxin (Digitek, Digox, Lanoxin, Lanoxin Pediatric)

This individual may have increased metabolism and decreased serum concentrations of digoxin.

Gene: ABCB1 — **Developing**

Drug Class: Antiarrhythmic
MOA: Sodium Channel Blocker

Flecainide (Tambocor)

This individual may have normal therapeutic levels of flecainide and may have an average risk of adverse events.

Gene: CYP2D6 — **Developing**

Drug Class: Antiarrhythmic
MOA: Sodium Channel Blocker

Propafenone (Rythmol SR) — Normal Response Expected

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - May result in cardiac arrhythmias and exaggerated beta-adrenergic blocking activity. Simultaneous use with both a CYP3A4 and CYP2D6 inhibitor should be avoided.

Omeprazole - Decreased propafenone plasma levels.

Fluconazole/Grapefruit Juice/Voriconazole - Increased risk of adverse events. Simultaneous use with both a CYP3A4 and CYP2D6 inhibitor should be avoided.

Paroxetine - May result in cardiac arrhythmias and exaggerated beta-adrenergic blocking activity.

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 decreased exposure to dabigatran.

Grapefruit Juice - Adjust dose appropriately in patients with renal impairment receiving concomitant P-gp inhibitors.

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 normal sensitivity to acenocoumarol.

Gene: VKORC1 ✓ **Developing**

Carriers of two copies (homozygous) of CYP4F2 variants have higher levels of active vitamin K likely requiring an increased dose.

Gene: CYP4F2 ! **Developing**

This individual metabolizes acenocoumarol slower, which may have an increased risk of over-anticoagulation. This individual may be at increased risk of bleeding, as well.

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 normal sensitivity to phenprocoumon and a decreased risk of adverse events (bleeding, over-anticoagulation, or increased time above therapeutic range).

Gene: VKORC1 ✓ **Developing**

Carriers of two copies (homozygous) of CYP4F2 variants have higher levels of active vitamin K likely requiring an increased 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 at a slightly increased risk of bleeding during warfarin therapy due to altered systemic concentrations.

CYP4F2 (c.1297G>A Homozygous, TT)

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.

Omeprazole - Decreased INR. Closely monitor INR.

Paroxetine/Fluconazole/Grapefruit Juice/Voriconazole - Increased INR. Closely monitor INR.

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

Drug Class: Antihypertensive

MOA: Angiotensin II Receptor Antagonist

Irbesartan (Avapro) !

This individual metabolizes irbesartan slower, causing increased plasma concentrations of irbesartan.

Gene: CYP2C9 **Developing**

PHD LABORATORY

Cardiology

Drug Class: Antihypertensive **MOA:** Angiotensin II Receptor Antagonist

Losartan (Cozaar) !

This individual metabolizes losartan slower, which may result in the decreased apparent oral clearance of losartan and decreased plasma concentration of losartan active metabolite.

Paroxetine/Fluconazole/Voriconazole - The pharmacodynamic consequences of concomitant use have not been examined.

Gene: CYP2C9 **Developing**

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

Atorvastatin (Lipitor) — Normal Response Expected

This individual has a normal SLCO1B1 function but a decreased CYP2C9 enzymatic activity that does not affect the pharmacokinetics of atorvastatin.

This individual has an average risk of atorvastatin-induced myopathy.

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.

Fluconazole/Grapefruit Juice/Voriconazole - Increased risk of myopathy and rhabdomyolysis.

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) — Decrease Dose

This individual has a normal SLCO1B1 function but a decreased CYP2C9 enzymatic activity.

This individual may experience a subsequent increase in fluvastatin concentrations, which may translate to an increased risk of fluvastatin-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 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

Lovastatin (Altoprev, Mevacor) — Normal Response Expected

This individual has a normal SLCO1B1 function but a decreased CYP2C9 enzymatic activity that does not affect the pharmacokinetics of lovastatin.

This individual has an average risk of lovastatin-induced myopathy.

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.

Grapefruit Juice/Voriconazole - Increased risk of myopathy. Concomitant use should be avoided.

Fluconazole - Elevated plasma levels of lovastatin.

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) — Normal Response Expected

This individual has a normal SLCO1B1 function but a decreased CYP2C9 enzymatic activity that does not affect the pharmacokinetics of pitavastatin.

This individual has an average risk of pitavastatin-induced myopathy.

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**

PHD LABORATORY

Cardiology

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

Pravastatin (Pravachol) — Normal Response Expected

This individual has a normal SLCO1B1 function but a decreased CYP2C9 enzymatic activity that does not affect the pharmacokinetics of pravastatin.

This individual has an average risk of pravastatin-induced myopathy.

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) — Normal Response Expected

This individual has a SLCO1B1 and an ABCG2 normal function.

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

This individual has an average risk of rosuvastatin-induced myopathy.

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 faster leading to normal or increased clopidogrel active metabolite formation and normal or 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.

Fluconazole/Paroxetine/Voriconazole/Omeprazole/Desipramine - May lead to reduced platelet inhibition.

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.

Fluconazole/Paroxetine/Voriconazole/Omeprazole/Desipramine - There is no significant effect on the pharmacokinetics of the active metabolite of prasugrel.

Fluconazole/Grapefruit Juice/Voriconazole - CYP3A inhibitors will not have a significant effect on the pharmacokinetics of the active metabolite of prasugrel.

Voriconazole - There is not a significant effect on the pharmacokinetics of the active metabolite of prasugrel.

Gene: CYP2C19, CYP2C9, CYP3A5, CYP2B6 — **Modest**

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

! Ticagrelor (Brilinta) — Use with Caution

This individual metabolizes ticagrelor faster.

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.

Grapefruit Juice/Voriconazole - Increased risk of adverse events such as dyspnea and bleeding. Concomitant use should be avoided.

Fluconazole/Grapefruit Juice - Increased ticagrelor exposure.

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 metabolizes aspirin slower.

However, the pharmacokinetics of the drug are not significantly impacted by CYP2C9 genetic variants, and/or there is insufficient evidence to provide information regarding safety and efficacy.

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.

Grapefruit Juice/Voriconazole - Avoid the use of rivaroxaban with combined P-gp and strong CYP3A inhibitors. Increased risk of bleeding.

Grapefruit Juice - Avoid concomitant use of rivaroxaban with combined P-gp and strong CYP3A inhibitors.

Fluconazole - Increased rivaroxaban exposure.

Gene: F5 — **Modest**

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

Gene: CYP3A4 ✓ — **Developing**

PHD LABORATORY

Cardiology

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

Acebutolol — Normal Response Expected

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

Gene: CYP2D6 — Robust

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

Betaxolol — Normal Response Expected

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

Gene: CYP2D6 — Robust

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

Bisoprolol — Normal Response Expected

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

Gene: CYP2D6 — Robust

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

Nebivolol (Bystolic) — Normal Response Expected

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

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.

Desipramine/Thioridazine/Paroxetine/Celecoxib - Higher nebivolol exposure. A dose reduction may be necessary.

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) — Normal Response Expected

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

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.

Fluconazole/Paroxetine/Celecoxib/Thioridazine/Voriconazole/Omeprazole/Desipramine - Increased propranolol levels; monitor for bradycardia and hypotension.

Omeprazole - May result in reduced efficacy.

Paroxetine - Monitor for bradycardia and hypotension.

Gene: CYP2D6 — Robust

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

Timolol (Betimol)

This individual may have normal therapeutic levels of timolol.

Desipramine/Thioridazine/Paroxetine/Celecoxib - May lead systemic beta-blockade (e.g., decreased heart rate, depression).

Gene: CYP2D6 — Developing

PHD LABORATORY

Cardiology

Drug Class: Cardiovascular Agent

MOA: Cardiac Myosin Inhibitor

! Mavacamten (Camzyos)

Use with Caution

This individual may metabolize mavacamten faster, 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.

Paroxetine/Desipramine/Voriconazole/Omeprazole - Increased risk of heart failure. Dose adjustment may be required.

Fluconazole/Grapefruit Juice/Voriconazole - Increased risk of heart failure. Concomitant use is contraindicated.

Fluconazole - Increased risk of heart failure. If initiating an inhibitor, mavacamten dose reduction and additional monitoring are required.

Gene: CYP2C19 **Robust**

Dental

Drug Class: Cholinergic Agonist

MOA: Cholinergic Receptor Agonist

Cevimeline (Evoxac)

Normal Response Expected

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - Use with caution due to the increased risk of adverse events.

Fluconazole/Grapefruit Juice/Voriconazole - Cevimeline should be used with caution due to the increased risk of adverse events.

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 faster, 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 may metabolize doxepin faster, which may reduce the probability of pharmacotherapy success or increase the risk of side effects.

Alternative drug therapy may be considered. However, if doxepin is used, please monitor for drug toxicities and therapeutic response and adjust the dose accordingly.

Fluconazole/Paroxetine/Celecoxib/Thioridazine/Voriconazole/Omeprazole/Desipramine - Increased doxepin exposure.

Omeprazole - Decreased doxepin exposure.

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.

Desipramine/Thioridazine/Celecoxib - Increased risk of cardiac arrhythmias. Use of eliglustat may require dosage adjustment depending on the concomitant drug and CYP2D6 metabolizer status.

Paroxetine/Fluconazole/Grapefruit Juice/Voriconazole - Increased risk of cardiac arrhythmias. Use of eliglustat is contraindicated, to be avoided, or may require dosage adjustment depending on the concomitant drug and CYP2D6 metabolizer status.

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) — Use with Caution

This individual metabolizes nateglinide slower resulting in higher systemic concentrations, which may lead to an increased risk of hypoglycemia.

Physicians should closely monitor the individual's clinical presentation for signs of adverse reactions and adjust the dose accordingly.

Paroxetine/Fluconazole/Voriconazole - Increased risk of hypoglycemia. Dose reductions and increased frequency of glucose monitoring may be required.

Gene: CYP2C9 — Robust

Drug Class: Sulfonylurea

MOA: Insulin Release Stimulator

Glimepiride (Amaryl) !

This individual may metabolize glimepiride slower, likely causing increased plasma concentrations of glimepiride which may lead to hypoglycemia.

Paroxetine/Fluconazole/Voriconazole - Increased risk of hypoglycemia.

Gene: CYP2C9 — Developing

PHD LABORATORY

Gastroenterology

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

Dexlansoprazole (Dexilant)

Use with Caution

This individual metabolizes dexlansoprazole faster.

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.

Physicians may initiate the recommended starting dose and potentially increase the dose for the treatment of H. pylori infection and erosive esophagitis while monitoring for efficacy.

Fluconazole/Paroxetine/Voriconazole/Omeprazole/Desipramine/Grapefruit Juice - Increased dexlansoprazole exposure.

Gene: CYP2C19 **Robust**

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

Esomeprazole (Nexium)

Use with Caution

This individual metabolizes esomeprazole faster 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.

Fluconazole/Paroxetine/Voriconazole/Omeprazole/Desipramine/Grapefruit Juice - Increased esomeprazole exposure.

Gene: CYP2C19 **Robust**

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

Lansoprazole (Prevacid, Prevacid SoluTab)

Use with Caution

This individual metabolizes lansoprazole faster than individuals with some other genotypes.

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.

Physicians may initiate the recommended starting dose and potentially increase the dose for the treatment of H. pylori infection and erosive esophagitis while monitoring for efficacy.

Fluconazole/Paroxetine/Voriconazole/Omeprazole/Desipramine/Grapefruit Juice - Increased exposure of lansoprazole.

Gene: CYP2C19 **Robust**

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

Pantoprazole (Protonix)

Use with Caution

This individual metabolizes pantoprazole faster than individuals with some other genotypes.

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.

Physicians may initiate the recommended starting dose and potentially increase the dose for the treatment of H. pylori infection and erosive esophagitis while monitoring for efficacy.

Gene: CYP2C19 **Robust**

PHD LABORATORY

Gastroenterology

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

! Rabeprazole (AcipHex) — Use with Caution

The individual metabolizes rabeprazole faster 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

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

Ondansetron (Zofran, Zuplenz) — Normal Response Expected

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

Fluconazole/Paroxetine/Celecoxib/Thioridazine/Voriconazole/Omeprazole/Desipramine/Grapefruit Juice - No dose adjustment is recommended.

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 is expected to have a normal response to palonosetron.

Gene: CYP2D6 — Modest

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

Tropisetron — Normal Response Expected

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

Gene: CYP2D6 — Robust

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

! Dronabinol (Syndros, Marinol) — Use with Caution

This individual metabolizes dronabinol slower, which exposes the individual to higher dronabinol concentrations increasing the risk of adverse reactions.

The adverse events may include neuropsychiatric reactions, hemodynamic instability, seizures, and vomiting.

Physicians should closely monitor the individual's clinical presentation for signs of adverse reactions and adjust the dose accordingly.

Fluconazole/Grapefruit Juice/Voriconazole - Monitor for adverse events.

Paroxetine/Fluconazole/Voriconazole - Increased risk of adverse events. Monitor for adverse events.

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) — Normal Response Expected

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

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.

Desipramine/Thioridazine/Celecoxib - Increased metoclopramide plasma concentrations.

Paroxetine - Likely leading to an increased risk of extrapyramidal symptoms. The recommended dosage for metoclopramide is 5 mg four times daily, or 10 mg three times daily.

Gene: CYP2D6 **Robust**

Drug Class: Antiemetic **MOA:** H1 Receptor Antagonist

Meclizine (Antivert, Bonine, Dramamine Less Drowsy, Motion-Time, Travel Sickness, Travel-Easy) — Normal Response Expected

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - Monitor for adverse reactions and clinical effect accordingly.

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 faster. 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.

Paroxetine/Desipramine/Voriconazole/Omeprazole - Increased flibanserin exposure.

Fluconazole/Grapefruit Juice/Voriconazole - Increased risk for hypotension and syncope. The concomitant use is contraindicated.

Fluconazole - Increased risk of adverse events such as hypotension, syncope, and CNS depression.

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 faster.

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) — Normal Response Expected

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

Grapefruit Juice/Voriconazole - Concomitant use of elagolix 200 mg twice daily with strong CYP3A inhibitors for more than 1 month is not recommended. Limit concomitant use of elagolix 150 mg once daily and strong CYP3A inhibitors to 6 months.

Grapefruit Juice - The effect of P-gp inhibitors on the pharmacokinetics of elagolix is unknown.

Fluconazole - Increased elagolix plasma concentrations.

Gene: SLCO1B1 **Modest**

Hematology

Drug Class: Colony Stimulating Factor

MOA: Thrombopoietin Receptor Agonist

Avatrombopag (Doptelet) — Use with Caution

This individual metabolizes avatrombopag slower, which may expose the individual to higher avatrombopag concentrations increasing the risk of thrombotic and thromboembolic events.

However, this individual is not expected to have a genetic prothrombotic condition.

Physicians should closely monitor the individual's clinical presentation for signs of adverse reactions and adjust the dose accordingly.

Fluconazole/Grapefruit Juice/Voriconazole - Increased risk of toxicity. Reduce the starting dosage of avatrombopag when used concomitantly with a moderate or strong dual inhibitor of CYP2C9 and CYP3A4.

Fluconazole - Reduce the starting dosage of avatrombopag when used concomitantly with a moderate or strong dual inhibitor of CYP2C9 and CYP3A4.

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) — Normal Response Expected

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - Use with caution due to the increased risk of adverse events.

Fluconazole/Grapefruit Juice/Voriconazole - Cevimeline should be used with caution due to the increased risk of adverse events.

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) — Use with Caution

This individual metabolizes siponimod slower, which exposes the individual to higher siponimod concentrations.

This may lead to an increased risk of adverse reactions such as bradyarrhythmia, increased blood pressure, infections, and macular edema.

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

Fluconazole/Grapefruit Juice/Voriconazole - Concomitant use of siponimod with moderate CYP2C9 and moderate or strong CYP3A4 inhibitors is not recommended.

Fluconazole - Concomitant use of siponimod with moderate CYP2C9 and moderate/strong CYP3A4 inhibitors is not recommended. Administer siponimod with caution with moderate CYP2C9 inhibitors.

Paroxetine/Voriconazole - Increased siponimod plasma concentration.

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 has an average risk of toxicity such as an increased risk of bone marrow, liver, lung, and kidney toxicities when treated with methotrexate, and would not 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.

Grapefruit Juice/Voriconazole - Higher sirolimus concentrations. Avoid concomitant use with strong inhibitors of CYP3A4 and/or P-gp.

Grapefruit Juice - Avoid concomitant use with strong CYP3A4/P-gp inhibitors. The dosage may need to be adjusted.

Fluconazole - Higher sirolimus concentrations. Exercise caution when using sirolimus with drugs that are modulators of CYP3A4 and P-gp.

Gene: CYP3A5 **Developing**

PHD LABORATORY

Immunology

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

Infectious Diseases

Drug Class: Antimalarial Agent

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

Quinine Sulfate (Qualaquin)

Normal Response Expected

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

Fluconazole/Grapefruit Juice/Voriconazole - Alteration in plasma quinine concentration. Monitor for increased adverse reactions of quinine.

Gene: CYP2D6

Modest

Drug Class: Antiretroviral

MOA: Non-Nucleoside Reverse Transcriptase Inhibitor

Efavirenz (Sustiva)

Decrease Dose

This individual metabolizes efavirenz slower, which results in increased systemic concentrations of efavirenz and a greater risk for adverse reactions including QT prolongation.

A decreased dose of efavirenz may be required. Please consider conducting a baseline and subsequent electrocardiograms to evaluate QT interval status before initiating treatment.

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

Fluconazole/Grapefruit Juice/Voriconazole - Increased efavirenz plasma concentrations.

Gene: CYP2B6

Robust

Drug Class: Antiretroviral

MOA: Non-Nucleoside Reverse Transcriptase Inhibitor

Nevirapine (Viramune, Viramune XR)

This individual metabolizes nevirapine slower, which results in higher exposure to nevirapine and a greater risk of adverse effects.

The adverse effects may include Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN).

Gene: CYP2B6 !

Developing

This individual may have an increased risk for nevirapine hepatotoxicity.

Gene: ABCB1 !

Developing

PHD LABORATORY

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**

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) — Normal Response Expected

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

Desipramine/Thioridazine/Celecoxib - Higher donepezil concentrations.

Paroxetine - Increased donepezil concentrations.

Gene: CYP2D6 **Modest**

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

Galantamine (Razadyne, Razadyne ER) — Normal Response Expected

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - May increase oral bioavailability of galantamine modestly.

Fluconazole/Grapefruit Juice/Voriconazole - May increase the oral bioavailability of galantamine modestly.

Gene: CYP2D6 **Robust**

PHD LABORATORY

Neurology

Drug Class: Anticonvulsant

MOA: Sodium Channel Blocker

Fosphenytoin (Cerebyx)

Decrease Dose

Fosphenytoin is a phosphate ester prodrug that is converted to phenytoin by peripheral esterases (phosphatases).

Subsequently, phenytoin is converted into its inactive metabolite mainly by CYP2C9 (95%) in the liver. This individual metabolizes phenytoin slower, which may result in increased phenytoin serum concentrations increasing the risk of cardiac and local (Purple Glove Syndrome) toxicity.

Consider starting at the low end of the dosage range and adjusting the dose based on the individual's clinical presentation. Avoid fosphenytoin as an alternative to carbamazepine in CYP2C9*3 carriers. Serum phenytoin levels should always be monitored to verify reaching and maintaining levels within the therapeutic window.

Fluconazole/Paroxetine/Voriconazole/Omeprazole/Desipramine - Fosphenytoin is a phosphate ester prodrug that is converted to phenytoin by peripheral esterases (phosphatases). However, no drugs are known to interfere with the conversion of fosphenytoin to phenytoin.

Gene: CYP2C9, CYP2C19

Robust

Drug Class: Anticonvulsant

MOA: Sodium Channel Blocker

Phenytoin (Dilantin, Phenytek)

Decrease Dose

This individual metabolizes phenytoin slower, which may result in increased phenytoin serum concentrations increasing the risk of cardiac and local (Purple Glove Syndrome) toxicity.

Consider starting at the low end of the dosage range and adjusting the dose based on the individual's clinical presentation. Avoid phenytoin as an alternative to carbamazepine in CYP2C9*3 carriers. Serum phenytoin levels should always be monitored to verify reaching and maintaining levels within the therapeutic window.

Fluconazole/Paroxetine/Voriconazole/Omeprazole/Desipramine - Increased risk of toxicity. Monitor phenytoin serum levels.

Gene: CYP2C9, CYP2C19

Robust

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 faster.

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.

Grapefruit Juice/Voriconazole - Patients with renal or hepatic impairment who are taking strong inhibitors of CYP3A4 and CYP2C9 may have a significant increase in exposure to lacosamide. Dose reduction may be necessary.

Gene: CYP2C19

Modest

Drug Class: Anticonvulsant

MOA: Synaptic Vesicle Protein 2A Binder

Brivaracetam (Briviact)

Use with Caution

This individual metabolizes brivaracetam faster, 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

PHD LABORATORY

Neurology

Drug Class: Antimigraine

MOA: Calcitonin Gene-Related Peptide Receptor Antagonist

! Rimegepant (Nurtec) — Normal Response Expected

This individual has a decreased CYP2C9 enzymatic activity and may metabolize rimegepant slower.

However, the CYP2C9 polymorphism is not expected to significantly affect rimegepant exposure.

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

Grapefruit Juice/Voriconazole - Avoid concomitant administration.

Grapefruit Juice - Avoid another dose of rimegepant within 48 hours when administered with a potent P-gp inhibitor.

Paroxetine/Fluconazole/Voriconazole - CYP2C9 inhibition alone is not expected to significantly affect rimegepant exposure.

Fluconazole - Avoid another dose of rimegepant within 48 hours when coadministered.

Gene: CYP2C9 — Modest

Drug Class: Benzodiazepine

MOA: GABA-A Agonist

! Clobazam (Onfi, Sympazan) — Use with Caution

This individual metabolizes clobazam faster, 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.

Paroxetine/Desipramine/Voriconazole/Omeprazole - Increased exposure to N-desmethylclobazam, the active metabolite of clobazam.

Fluconazole - Increased risk of dose-related adverse events. Dose adjustments may be necessary.

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 faster than individuals with some other genotypes.

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.

Fluconazole/Paroxetine/Voriconazole/Omeprazole/Desipramine/Grapefruit Juice - Increased diazepam concentrations.

Gene: CYP2C19 — Modest

Drug Class: Benzodiazepine

MOA: GABA-A Agonist

Midazolam (Nayzilam) !

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

Fluconazole/Grapefruit Juice/Voriconazole - Elevated midazolam concentrations.

Gene: CYP3A5 — Developing

PHD LABORATORY

Neurology

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

Deutetrabenazine (Austedo) — Normal Response Expected

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

Desipramine/Thioridazine/Celecoxib - The effect on the exposure of deutetrabenazine and its metabolites has not been evaluated.

Paroxetine - Maximum recommended dose of deutetrabenazine is 36 mg per day.

Gene: CYP2D6 **Robust**

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

Tetrabenazine (Xenazine) — Normal Response Expected

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

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.

Desipramine/Thioridazine/Celecoxib - Higher exposure to the primary metabolites.

Paroxetine - The total dose of tetrabenazine should not exceed a maximum of 50 mg and the maximum single dose should not exceed 25 mg.

Gene: CYP2D6 **Robust**

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

Valbenazine (Ingrezza) — Normal Response Expected

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

Desipramine/Thioridazine/Celecoxib - Increased exposure to valbenazine's active metabolite.

Grapefruit Juice/Voriconazole - Increased risk of exposure-related adverse events. The recommended dosage is valbenazine 40 mg once daily.

Fluconazole - Increased exposure to valbenazine and its active metabolite.

Paroxetine - Increased risk of exposure-related adverse events. The recommended dosage of valbenazine is 40 mg once daily when coadministered.

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) — Normal Response Expected

This individual is expected to have a normal response to dextromethorphan and quinidine.

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) — Use with Caution

This individual metabolizes siponimod slower, which exposes the individual to higher siponimod concentrations.

This may lead to an increased risk of adverse reactions such as bradyarrhythmia, increased blood pressure, infections, and macular edema.

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

Fluconazole/Grapefruit Juice/Voriconazole - Concomitant use of siponimod with moderate CYP2C9 and moderate or strong CYP3A4 inhibitors is not recommended.

Fluconazole - Concomitant use of siponimod with moderate CYP2C9 and moderate/strong CYP3A4 inhibitors is not recommended. Administer siponimod with caution with moderate CYP2C9 inhibitors.

Paroxetine/Voriconazole - Increased siponimod plasma concentration.

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) — Normal Response Expected

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

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.

Desipramine/Thioridazine/Paroxetine/Celecoxib - Clinical significance is not well established.

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) — Normal Response Expected

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

Discontinue gefitinib if the individual has severe hepatic impairment.

Grapefruit Juice/Voriconazole - Monitor adverse reactions if concomitant use with gefitinib.

Fluconazole - Increased gefitinib plasma concentrations.

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) — Use with Caution

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

However, physicians should closely monitor individual's clinical presentation for signs of adverse reactions and adjust the dose accordingly.

Fluconazole/Grapefruit Juice/Voriconazole - Consider alternative agents or monitor closely for adverse reactions.

Paroxetine/Fluconazole/Voriconazole - Increased erdafitinib plasma concentrations.

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 faster, 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.

Fluconazole/Paroxetine/Voriconazole/Omeprazole/Desipramine - Monitor for anemia and hypoxia and reduce the dosage of belzutifan as recommended.

Gene: CYP2C19 — **Modest**

Drug Class: Antineoplastic

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

! Rucaparib (Rubraca) — Normal Response Expected

This individual has a normal CYP2D6 enzymatic activity.

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 has an average risk of toxicity such as an increased risk of bone marrow, liver, lung, and kidney toxicities when treated with methotrexate, and would not 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 may have normal therapeutic levels of timolol.

Desipramine/Thioridazine/Paroxetine/Celecoxib - May lead systemic beta-blockade (e.g., decreased heart rate, depression).

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 metabolizes aspirin slower.

However, the pharmacokinetics of the drug are not significantly impacted by CYP2C9 genetic variants, and/or there is insufficient evidence to provide information regarding safety and efficacy.

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

Gene: CYP2C9 **Robust**

PHD LABORATORY

Pain Management

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 metabolizes diclofenac slower.

However, the pharmacokinetics of the drug are not significantly impacted by CYP2C9 genetic variants, and/or there is insufficient evidence to provide information regarding safety and efficacy.

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

Paroxetine/Fluconazole/Voriconazole - Increased risk of toxicity. Use with caution; a dosage adjustment may be warranted.

Gene: CYP2C9 Robust

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

Flurbiprofen (Ansaid) — Decrease Dose

This individual metabolizes flurbiprofen slower, which exposes the individual to higher flurbiprofen concentrations.

This may lead to an increased risk of adverse reactions such as cardiovascular and gastrointestinal events.

Physicians may use the lowest effective dosage for the shortest duration and adjust the dose based on the individual's clinical presentation while closely monitoring for adverse events.

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) — Decrease Dose

This individual metabolizes ibuprofen slower, which can lead to an increased risk of adverse events due to substantially higher plasma concentrations of ibuprofen.

The adverse events may include gastrointestinal bleeding, blood pressure, and renal toxicity.

Physicians may use the lowest effective dosage for the shortest duration and adjust the dose thereafter based on the individual's clinical presentation while closely monitoring for adverse events.

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 metabolizes indomethacin slower.

However, the pharmacokinetics of the drug are not significantly impacted by CYP2C9 genetic variants, and/or there is insufficient evidence to provide information regarding safety and efficacy.

Gene: CYP2C9 Robust

PHD LABORATORY

Pain Management

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

Lornoxicam — Decrease Dose

This individual metabolizes lornoxicam slower, which can lead to an increased risk of adverse events due to substantially higher plasma concentrations of lornoxicam.

The adverse events may include gastrointestinal bleeding, blood pressure, and renal toxicity.

Physicians may use the lowest effective initial dosage and adjust the dose thereafter based on the individual's clinical presentation while closely monitoring for adverse events.

Gene: CYP2C9 Robust

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

Meloxicam (Anjeso, Mobic, Qmiiz ODT, Vivlodex) — Decrease Dose

This individual metabolizes meloxicam slower, which can lead to an increased risk of adverse events due to abnormally high plasma levels of meloxicam.

The adverse events may include gastrointestinal bleeding, heart failure, edema, and renal toxicity.

Physicians may use the lowest effective dosage for the shortest duration and adjust the dose thereafter based on the individual's clinical presentation while closely monitoring for adverse events.

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.

Paroxetine/Fluconazole/Voriconazole - Consider dose reduction and monitor for adverse events.

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 metabolizes naproxen slower.

However, the pharmacokinetics of the drug are not significantly impacted by CYP2C9 genetic variants, and/or there is insufficient evidence to provide information regarding safety and efficacy.

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) — Decrease Dose

This individual metabolizes piroxicam slower, which exposes the individual to higher piroxicam concentrations.

This may lead to an increased risk of adverse reactions such as cardiovascular thrombotic events, gastrointestinal bleeding, and renal toxicities.

Physicians may use the lowest effective dosage for the shortest duration or consider an alternative treatment based on the individual's clinical presentation while closely monitoring for adverse events.

Gene: CYP2C9 Robust

PHD LABORATORY

Pain Management

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

✕ Tenoxicam — Decrease Dose

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

The adverse events may include dyspepsia, epigastric pain, edema, fluid retention, and blurred vision.

Physicians may use the lowest effective dosage for the shortest duration or consider an alternative treatment based on the individual's clinical presentation while closely monitoring for adverse events.

Gene: CYP2C9 Robust

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

! Metamizole — Normal Response Expected

This individual metabolizes metamizole slower.

However, the pharmacokinetics of the drug are not significantly impacted by CYP2C9 genetic variants, and/or there is insufficient evidence to provide information regarding safety and efficacy.

Gene: CYP2C9 Robust

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

! Aceclofenac — Normal Response Expected

This individual metabolizes aceclofenac slower.

However, the pharmacokinetics of the drug are not significantly impacted by CYP2C9 genetic variants, and/or there is insufficient evidence to provide information regarding safety and efficacy.

Gene: CYP2C9 Robust

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

! Lumiracoxib — Normal Response Expected

This individual metabolizes lumiracoxib slower.

However, the pharmacokinetics of the drug are not significantly impacted by CYP2C9 genetic variants, and/or there is insufficient evidence to provide information regarding safety and efficacy.

Gene: CYP2C9 Robust

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

✓ Alfentanil (Alfenta) — Normal Response Expected

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.

Fluconazole/Grapefruit Juice/Voriconazole - Prolonged opioid adverse events. Monitor at frequent intervals and consider dose reduction.

Gene: COMT, OPRM1 Robust

PHD LABORATORY

Pain Management

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

Codeine — Normal Response Expected

This individual has a normal CYP2D6 enzymatic activity and may have normal therapeutic levels of the medication.

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

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.

Desipramine/Thioridazine/Paroxetine/Celecoxib - Reduced analgesic effect and/or symptoms of opioid withdrawal.

Fluconazole/Grapefruit Juice/Voriconazole - Increased or prolonged adverse reactions. Consider a dose reduction of codeine.

Gene: COMT, OPRM1, CYP2D6 **Robust**

This individual may have a normal response to codeine.

Gene: CYP3A4 **Developing**

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

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

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.

Fluconazole/Grapefruit Juice/Voriconazole - This may prolong opioid adverse reactions and exacerbate respiratory depression. Consider dosage reduction of fentanyl.

Gene: COMT, OPRM1 **Robust**

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

Hydrocodone (Hysingla ER, Zohydro ER) — Normal Response Expected

This individual has a normal CYP2D6 enzymatic activity and 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.

Desipramine/Thioridazine/Paroxetine/Celecoxib - Decreased serum concentrations of hydromorphone, the active metabolite of hydrocodone.

Fluconazole/Grapefruit Juice/Voriconazole - Increased or prolonged opioid effects. Consider dose reduction of hydrocodone.

Gene: COMT, OPRM1, CYP2D6 **Robust**

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

Hydromorphone (Dilaudid) — Normal Response Expected

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 **Robust**

PHD LABORATORY

Pain Management

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

Levomethadone — Normal Response Expected

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 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

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 Robust

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

Oliceridine (Olinvyk) — Normal Response Expected

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

Desipramine/Thioridazine/Celecoxib - Increased oliceridine plasma concentrations.

Paroxetine/Fluconazole/Grapefruit Juice/Voriconazole - Likely leading to increased or prolonged opioid effects. Less frequent dosing of oliceridine may be required.

Gene: CYP2D6 Robust

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

Oxycodone (Oxaydo, OxyCONTIN, Roxicodone, Xtampza ER) — Normal Response Expected

This individual has a normal CYP2D6 enzymatic activity and 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.

Desipramine/Thioridazine/Paroxetine/Celecoxib - No clinically significant impact to oxycodone.

Fluconazole/Grapefruit Juice/Voriconazole - Increased or prolonged opioid effects. Use with caution. Dose adjustment may be considered.

Gene: COMT, OPRM1, CYP2D6 Robust

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

Remifentanil (Ultiva) — Normal Response Expected

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 Robust

PHD LABORATORY

Pain Management

Drug Class: Opioid

MOA: MU-Opioid Receptor Agonist

Sufentanil (Dsuvia, Sufenta)

Normal Response Expected

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.

Fluconazole/Grapefruit Juice/Voriconazole - Increased or prolonged adverse drug reactions. Consider dosage reduction of sufentanil.

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)

Normal Response Expected

This individual has a normal CYP2D6 but decreased 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.

Desipramine/Thioridazine/Paroxetine/Celecoxib - May potentiate adverse events and toxicity. A dose reduction may be needed.

Fluconazole/Paroxetine/Voriconazole/Omeprazole/Desipramine/Grapefruit Juice - Prolonged opioid adverse reactions and increased risk of respiratory depression. Consider dosage reduction of methadone.

Grapefruit Juice - The pharmacokinetics of methadone will not be significantly altered.

Gene: COMT, OPRM1, CYP2D6, CYP2B6

Robust

Drug Class: Opioid

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

Tramadol (Ultram, ConZip)

Normal Response Expected

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

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

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.

Desipramine/Thioridazine/Paroxetine/Celecoxib - Reduced analgesic effect, symptoms of opioid withdrawal, and tramadol associated adverse effects.

Fluconazole/Grapefruit Juice/Voriconazole - Increased or prolonged adverse reactions. Consider dose reduction until drug effects are achieved.

Gene: CYP2D6, CYP3A4, CYP2B6, COMT, OPRM1

Robust

PHD LABORATORY

Pain Management

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

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.

Fluconazole/Grapefruit Juice/Voriconazole - Dose-reduction of one or both agents may be required.

Gene: COMT, OPRM1

Robust

Drug Class: Opioid Antagonist

MOA: Opioid Receptor Antagonist

Naltrexone (Vivitrol)

Normal Response Expected

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

Robust

Drug Class: Opioid Dependency

MOA: Alpha-2 Adrenergic Agonist

Lofexidine (Lucemyra)

Normal Response Expected

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - May lead to an increased risk of adverse events such as orthostatic hypotension and bradycardia.

Gene: CYP2D6

Robust

Psychiatry

Drug Class: Antidepressant

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

Vortioxetine (Trintellix)

Normal Response Expected

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

Desipramine/Thioridazine/Celecoxib - Higher vortioxetine plasma concentrations.

Paroxetine - Reduce the vortioxetine dose by half when coadministered.

Gene: CYP2D6

Robust

Drug Class: Antidepressant

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

Mirtazapine (Remeron)

This individual may have normal therapeutic levels of mirtazapine and may have an average risk of adverse events.

Gene: CYP2D6

Developing

PHD LABORATORY

Psychiatry

Drug Class: Antidepressant

MOA: Dopamine and Norepinephrine Reuptake Inhibitor

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

This individual metabolizes bupropion slower, which may result in decreased concentrations of hydroxybupropion, a metabolite of bupropion.

Voriconazole - Dosage adjustment of bupropion may be necessary.

Gene: CYP2B6

Developing

Drug Class: Antidepressant

MOA: Selective Serotonin Reuptake Inhibitor

! Citalopram (Celexa)

Use with Caution

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

Physicians may initiate therapy with the recommended starting dose. If the individual does not adequately respond to the recommended maintenance dosing, consider titrating to a higher maintenance dose or switching to a clinically appropriate alternative antidepressant not predominantly metabolized by CYP2C19.

Desipramine/Thioridazine/Paroxetine/Celecoxib - No clinically significant effects on citalopram metabolism when coadministered.

Fluconazole/Paroxetine/Voriconazole/Omeprazole/Desipramine - Increased risk of QT prolongation and/or ventricular arrhythmias. The maximum recommended dosage of citalopram is 20 mg once daily.

Fluconazole/Grapefruit Juice/Voriconazole - Increased citalopram concentrations.

Gene: CYP3A4, CYP2C19, CYP2D6

Robust

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

Gene: HTR2A !

Developing

Drug Class: Antidepressant

MOA: Selective Serotonin Reuptake Inhibitor

! Escitalopram (Lexapro)

Use with Caution

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

Physicians may initiate therapy with the recommended starting dose. If the individual does not adequately respond to the recommended maintenance dosing, consider titrating to a higher maintenance dose or switching to a clinically appropriate alternative antidepressant not predominantly metabolized by CYP2C19.

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.

Fluconazole/Paroxetine/Voriconazole/Omeprazole/Desipramine/Grapefruit Juice - Escitalopram is metabolized by multiple enzymes, inhibition of a single enzyme may not decrease escitalopram clearance.

Gene: CYP3A4, CYP2C19, CYP2D6

Robust

This individual may have an increased 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 is expected to have a normal response to fluoxetine.

However, 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.

Desipramine/Thioridazine/Celecoxib - Higher fluoxetine concentrations.

Paroxetine - Increased fluoxetine concentrations.

Gene: CYP2D6 **Modest**

This individual may have a decreased response.

Gene: HTR1A ! **Developing**

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

Fluvoxamine (Luvox, Luvox CR) — Normal Response Expected

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - Increased fluvoxamine plasma concentrations.

Omeprazole - Decreased fluvoxamine plasma concentrations.

Gene: CYP2D6 **Robust**

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

Sertraline (Zoloft) — Normal Response Expected

This individual is expected to have a normal response. Physicians may initiate therapy at the standard starting dose.

Gene: CYP2B6, CYP2C19 **Robust**

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

Duloxetine (Cymbalta, Drizalma Sprinkle) — Normal Response Expected

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

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - Increased duloxetine concentrations.

Omeprazole - Decreased duloxetine concentrations.

Gene: CYP2D6 **Modest**

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

Milnacipran (Savella, Savella Titration Pack)

This individual may have an increased response.

Gene: HTR1A **Developing**

PHD LABORATORY

Psychiatry

Drug Class: Antidepressant

MOA: Serotonin and Norepinephrine Reuptake Inhibitor

Venlafaxine (Effexor) — Normal Response Expected

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

Fluconazole/Grapefruit Juice/Voriconazole - Increased risk of venlafaxine toxicity. Consider reducing the dose of venlafaxine.

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) — Normal Response Expected

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

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) — Normal Response Expected

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

Iloperidone is not recommended for individuals with severe hepatic impairment.

Desipramine/Thioridazine/Celecoxib - Increased risk of QT prolongation. Use with caution.

Paroxetine/Grapefruit Juice/Voriconazole - Increased risk of QT prolongation. Iloperidone dose should be reduced by one-half.

Fluconazole - Increased risk of QT prolongation.

Gene: CYP2D6 — **Robust**

This individual may have a normal response to iloperidone.

Gene: CYP3A4 — **Developing**

Drug Class: Antipsychotic

MOA: 5-HT2A and Dopamine-D2 Receptor Antagonist

Paliperidone (Invega) — Normal Response Expected

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - There is no evidence that CYP2D6 inhibitors significantly affect the metabolism of paliperidone.

Fluconazole/Grapefruit Juice/Voriconazole - There is no evidence that CYP3A4 inhibitors significantly affect the metabolism of paliperidone.

Gene: CYP2D6 — **Modest**

PHD LABORATORY

Psychiatry

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

Quetiapine (Seroquel)

This individual may have a normal response to quetiapine.

Grapefruit Juice/Voriconazole - Reduce quetiapine dose to one-sixth.

Fluconazole - Increased quetiapine exposure.

Gene: CYP3A4 **Developing**

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

Risperidone (Risperdal) — Normal Response Expected

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

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.

Desipramine/Thioridazine/Celecoxib - Dose adjustment may be required.

Fluconazole/Grapefruit Juice/Voriconazole - Dose adjustment is not needed.

Paroxetine - Reduce the initial dose. Do not exceed a final dose of 8 mg per day of risperidone.

Gene: CYP2D6 **Modest**

This individual may have improved symptoms and increased response to risperidone.

Gene: HTR2A **Developing**

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

Gene: HTR2C **Developing**

This individual may have decreased response, a slower time until response, and an undetermined risk of hyperprolactinemia.

Gene: DRD2 **Developing**

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

Pimozide (Orap) — Normal Response Expected

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - Increased pimozide exposure.

Fluconazole/Grapefruit Juice/Voriconazole - Concomitant use is not recommended.

Paroxetine - Concomitant use of pimozide with strong CYP2D6 inhibitors is contraindicated.

Gene: CYP2D6 **Robust**

This individual may have a normal response to pimozide.

Gene: CYP3A4 **Developing**

Drug Class: Antipsychotic **MOA:** D1 and D2, Alpha 1 Adrenergic and 5-HT2 Receptor Antagonist

Zuclopenthixol

This individual may have normal therapeutic levels of zuclopenthixol and may have an average risk of adverse events.

Gene: CYP2D6 **Developing**

PHD LABORATORY

Psychiatry

Drug Class: Antipsychotic

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

Aripiprazole (Abilify) — Normal Response Expected

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

Desipramine/Thioridazine/Fluconazole/Celecoxib - The dosing may be reduced for patients who may be receiving a combination of strong, moderate, and weak inhibitors of CYP3A4 and CYP2D6.

Grapefruit Juice/Voriconazole - Administer half of the usual dose of aripiprazole. When taking strong CYP2D6 and CYP3A4 inhibitors, administer a quarter of the usual aripiprazole dose.

Paroxetine - Half of the usual dose of aripiprazole is recommended. Administer a quarter of the usual dose when taking aripiprazole with strong CYP2D6 and CYP3A4 inhibitors.

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) — Normal Response Expected

This individual is expected to have a normal response to aripiprazole lauroxil.

Desipramine/Thioridazine/Celecoxib - Increased aripiprazole exposure.

Paroxetine/Grapefruit Juice/Voriconazole - Reduce the dose of aripiprazole lauroxil to the next lower strength. No dosage adjustment is necessary in patients taking 441 mg aripiprazole lauroxil, if tolerated.

Fluconazole - Higher aripiprazole lauroxil exposure.

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) — Normal Response Expected

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

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).

Grapefruit Juice/Voriconazole - A dose reduction will be necessary.

Fluconazole - Increased exposures of cariprazine and its major active metabolite.

Gene: CYP2D6 — **Modest**

Drug Class: Antipsychotic

MOA: D2 Receptor Blocker

Perphenazine (Trilafon) — Normal Response Expected

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

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - Increased risk of adverse events. Monitor for adverse events and reduce the dose of as needed.

Gene: CYP2D6 — **Modest**

PHD LABORATORY

Psychiatry

Drug Class: Antipsychotic

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

Lurasidone (Latuda)

This individual may have a reduced response.

Gene: HTR1A — **Developing**

Drug Class: Antipsychotic

MOA: Nonselective Postsynaptic Dopaminergic D2 Receptor Blocker

Haloperidol (Haldol)

This individual may have normal therapeutic levels of haloperidol and may have an average risk of adverse events.

Desipramine/Thioridazine/Paroxetine/Celecoxib - Increased haloperidol concentrations may increase the risk of QT-prolongation.

Fluconazole/Grapefruit Juice/Voriconazole - Increased risk of QT-prolongation.

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**

Drug Class: Antipsychotic

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

Clozapine (Clozaril, Versacloz) — Normal Response Expected

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - Increased risk of adverse events. Consider reducing the dose if necessary.

Omeprazole - Reduced efficacy. Consider increasing the clozapine dose if necessary.

Fluconazole/Grapefruit Juice/Voriconazole - Monitor for adverse drug events and consider reducing the dose if necessary.

Paroxetine - Increased risk of adverse drug events. Consider reducing the dose if necessary.

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 a decreased risk of developing metabolic syndrome.

Gene: HTR2C — **Developing**

PHD LABORATORY

Psychiatry

Drug Class: Benzodiazepine **MOA:** GABA-A Agonist

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

This individual metabolizes diazepam faster than individuals with some other genotypes.

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.

Fluconazole/Paroxetine/Voriconazole/Omeprazole/Desipramine/Grapefruit Juice - Increased diazepam concentrations.

Gene: CYP2C19 **Modest**

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

Atomoxetine (Strattera) — Use with Caution

This individual metabolizes atomoxetine faster, reducing the probability of pharmacotherapy success.

In children, atomoxetine should be initiated with a dose of 0.5 mg/kg/day and increased to 1.2 mg/kg/day after 3 days. Additionally, in adults, atomoxetine should be initiated with a dose of 40 mg/day and increased to 80 mg/day after 3 days.

Desipramine/Thioridazine/Celecoxib - Higher blood levels of atomoxetine.

Paroxetine - Increased risk of adverse events. Dose adjustment of atomoxetine may be necessary.

Gene: CYP2D6 **Robust**

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

Viloxazine (Qelbree) — Normal Response Expected

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

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) — Normal Response Expected

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

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.

Fluconazole/Grapefruit Juice/Voriconazole - Altered modafinil plasma concentrations.

Gene: CYP2D6 **Modest**

This individual may have a normal response to modafinil.

Gene: CYP3A4 **Developing**

PHD LABORATORY

Psychiatry

Drug Class: Central Nervous System Stimulant

MOA: Histamine-3 (H3) Receptor Antagonist/Inverse Agonist

Pitolisant (Wakix) — Normal Response Expected

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

Desipramine/Thioridazine/Celecoxib - Higher pitolisant exposure.

Paroxetine - Initiate pitolisant at 8.9 mg daily and increase after 7 days to a maximum dose of 17.8 mg daily. If on a stable dose of pitolisant, reduce the dose by half when initiating a strong CYP2D6 inhibitor.

Gene: CYP2D6 — Robust

Drug Class: Central Nervous System Stimulant

MOA: Norepinephrine and Dopamine Reuptake Inhibitor

Amphetamine (Dyanavel XR, Adzenys XR-ODT, Adzenys ER) — Normal Response Expected

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - Initiate with lower doses and monitor frequently. Adjust amphetamine dose or use alternative therapy based on clinical response.

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

Drug Class: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor

Amitriptyline (Elavil, Vanatrip) — Consider Alternatives

This individual may metabolize amitriptyline faster, which may reduce the probability of pharmacotherapy success or increase the risk of side effects.

Alternative drug therapy may be considered. However, if amitriptyline is used, please monitor for drug toxicities and therapeutic response, and adjust the dose accordingly.

Desipramine/Thioridazine/Paroxetine/Celecoxib - Lower doses for either amitriptyline or the CYP2D6 inhibitor are recommended. Monitor amitriptyline plasma levels.

Gene: CYP2D6, CYP2C19 — Robust

Drug Class: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor

Imipramine (Tofranil) — Consider Alternatives

This individual may metabolize imipramine faster, which may reduce the probability of pharmacotherapy success or increase the risk of side effects.

Alternative drug therapy may be considered. However, if imipramine is used, please monitor for drug toxicities and therapeutic response, and adjust the dose accordingly.

Desipramine/Thioridazine/Paroxetine/Celecoxib - Lower doses for either imipramine or the CYP2D6 inhibitor are recommended. Monitor imipramine plasma levels.

Gene: CYP2D6, CYP2C19 — Robust

PHD LABORATORY

Psychiatry

Drug Class: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor

Protriptyline (Vivactil) — Normal Response Expected

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - Lower doses for either protriptyline or the CYP2D6 inhibitor are recommended. Monitor protriptyline plasma levels.

Gene: CYP2D6 — **Modest**

Drug Class: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor

Trimipramine (Surmontil) — Consider Alternatives

This individual may metabolize trimipramine faster, which reduces the probability of pharmacotherapy success or increases the risk of side effects.

Alternative drug therapy may be considered. However, if trimipramine is used, please monitor for drug toxicities and therapeutic response, and adjust the dose accordingly.

Desipramine/Thioridazine/Paroxetine/Celecoxib - Lower doses for either trimipramine or the CYP2D6 inhibitor are recommended. Monitor trimipramine plasma levels.

Gene: CYP2D6, CYP2C19 — **Robust**

Drug Class: Tricyclic Antidepressant

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

Amoxapine (Asendin) — Normal Response Expected

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - Lower doses for either amoxapine or the CYP2D6 inhibitor are recommended. Monitor amoxapine plasma levels.

Gene: CYP2D6 — **Modest**

Drug Class: Tricyclic Antidepressant

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

Nortriptyline (Pamelor) — Normal Response Expected

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - Lower doses for either nortriptyline or the CYP2D6 inhibitor are recommended. Monitor nortriptyline plasma levels.

Gene: CYP2D6 — **Robust**

PHD LABORATORY

Psychiatry

Drug Class: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Uptake Inhibitor

! Clomipramine (Anafranil) — Consider Alternatives

This individual may metabolize clomipramine faster, which may reduce the probability of pharmacotherapy success or increase the risk of side effects.

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.

- **Desipramine/Thioridazine/Paroxetine/Celecoxib** - Lower doses for either clomipramine or the CYP2D6 inhibitor are recommended. Monitor clomipramine plasma levels.
- **Omeprazole** - Decreased clomipramine plasma levels.
- **Paroxetine** - Increased clomipramine plasma concentrations; monitor clomipramine plasma levels.

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 may metabolize doxepin faster, which may reduce the probability of pharmacotherapy success or increase the risk of side effects.

Alternative drug therapy may be considered. However, if doxepin is used, please monitor for drug toxicities and therapeutic response and adjust the dose accordingly.

- **Fluconazole/Paroxetine/Celecoxib/Thioridazine/Voriconazole/Omeprazole/Desipramine** - Increased doxepin exposure.
- **Omeprazole** - Decreased doxepin exposure.

Gene: CYP2D6, CYP2C19 — Robust

Respiratory

Drug Class: Anticholinergic

MOA: M3 Receptor Inhibitor

Umeclidinium (Incruse Ellipta) — Normal Response Expected

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

Gene: CYP2D6 — Modest

Drug Class: Antitussive

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

Dextromethorphan (Robitussin, Delsym, Pediacare, Robafen)

This individual may have normal therapeutic levels of dextromethorphan and may have an average risk of adverse events.

Gene: CYP2D6 — Developing

Drug Class: Bronchodilator

MOA: Long-Acting Beta2-Adrenergic Agonist

Arformoterol (Brovana) — Normal Response Expected

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

- **Desipramine/Thioridazine/Celecoxib** - The exposure of arformoterol was not altered.
- **Paroxetine** - No dose adjustments are needed when coadministered.

Gene: CYP2D6 — Modest

PHD LABORATORY

Respiratory

Drug Class: Bronchodilator **MOA:** Long-Acting Beta2-Adrenergic Agonist

Salmeterol (Serevent Diskus)

This individual may have an increased response to salmeterol.

Fluconazole/Grapefruit Juice/Voriconazole - Increased salmeterol concentrations. Caution should be exercised.

Gene: ADRB2 **Developing**

Rheumatology

Drug Class: Antigout **MOA:** URAT1 Inhibitor

Lesinurad (Zurampic) — Use with Caution

This individual metabolizes lesinurad slower, which may expose the individual to higher lesinurad concentrations.

This may lead to an increased risk of adverse reactions such as renal and cardiovascular events.

Physicians should closely monitor the individual's clinical presentation for signs of adverse reactions and adjust the dose accordingly.

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.

Fluconazole - Increased lesinurad exposure. Use with caution.

Paroxetine/Voriconazole - Increased lesinurad exposure.

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 metabolizes aspirin slower.

However, the pharmacokinetics of the drug are not significantly impacted by CYP2C9 genetic variants, and/or there is insufficient evidence to provide information regarding safety and efficacy.

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

Gene: CYP2C9 **Robust**

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

Methotrexate (Otrexup, Rasuvo, Trexall, Xatmet)

This individual has an average risk of toxicity such as an increased risk of bone marrow, liver, lung, and kidney toxicities when treated with methotrexate, and would not benefit from methylfolate supplementation therapy.

Gene: MTHFR **Developing**

PHD LABORATORY

Rheumatology

Drug Class: Antirheumatic
MOA: Janus Associated Kinase Inhibitor

Upadacitinib (Rinvoq) — Normal Response Expected

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

Grapefruit Juice/Voriconazole - Increased risk of adverse reactions. Dosage modification for patients with atopic dermatitis, ulcerative colitis, and Crohnï¿½s disease may be required.

Fluconazole - Increased upadacitinib exposure.

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 faster, 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.

Fluconazole/Paroxetine/Voriconazole/Omeprazole/Desipramine - The pharmacological impact in terms of safety and efficacy is unknown.

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 metabolizes diclofenac slower.

However, the pharmacokinetics of the drug are not significantly impacted by CYP2C9 genetic variants, and/or there is insufficient evidence to provide information regarding safety and efficacy.

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

Paroxetine/Fluconazole/Voriconazole - Increased risk of toxicity. Use with caution; a dosage adjustment may be warranted.

Gene: CYP2C9 — **Robust**

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

Flurbiprofen (Ansaid) — Decrease Dose

This individual metabolizes flurbiprofen slower, which exposes the individual to higher flurbiprofen concentrations.

This may lead to an increased risk of adverse reactions such as cardiovascular and gastrointestinal events.

Physicians may use the lowest effective dosage for the shortest duration and adjust the dose based on the individual's clinical presentation while closely monitoring for adverse events.

Gene: CYP2C9 — **Robust**

PHD LABORATORY

Rheumatology

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)

Decrease Dose

This individual metabolizes ibuprofen slower, which can lead to an increased risk of adverse events due to substantially higher plasma concentrations of ibuprofen.

The adverse events may include gastrointestinal bleeding, blood pressure, and renal toxicity.

Physicians may use the lowest effective dosage for the shortest duration and adjust the dose thereafter based on the individual's clinical presentation while closely monitoring for adverse events.

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 metabolizes indomethacin slower.

However, the pharmacokinetics of the drug are not significantly impacted by CYP2C9 genetic variants, and/or there is insufficient evidence to provide information regarding safety and efficacy.

Gene: CYP2C9 Robust

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

Lornoxicam

Decrease Dose

This individual metabolizes lornoxicam slower, which can lead to an increased risk of adverse events due to substantially higher plasma concentrations of lornoxicam.

The adverse events may include gastrointestinal bleeding, blood pressure, and renal toxicity.

Physicians may use the lowest effective initial dosage and adjust the dose thereafter based on the individual's clinical presentation while closely monitoring for adverse events.

Gene: CYP2C9 Robust

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

Meloxicam (Anjeso, Mobic, Qmiiz ODT, Vivlodex)

Decrease Dose

This individual metabolizes meloxicam slower, which can lead to an increased risk of adverse events due to abnormally high plasma levels of meloxicam.

The adverse events may include gastrointestinal bleeding, heart failure, edema, and renal toxicity.

Physicians may use the lowest effective dosage for the shortest duration and adjust the dose thereafter based on the individual's clinical presentation while closely monitoring for adverse events.

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.

Paroxetine/Fluconazole/Voriconazole - Consider dose reduction and monitor for adverse events.

Gene: CYP2C9 Robust

PHD LABORATORY

Rheumatology

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

! Nabumetone (Relafen DS) — Normal Response Expected

This individual metabolizes nabumetone slower.

However, the pharmacokinetics of the drug are not significantly impacted by CYP2C9 genetic variants, and/or there is insufficient evidence to provide information regarding safety and efficacy.

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 metabolizes naproxen slower.

However, the pharmacokinetics of the drug are not significantly impacted by CYP2C9 genetic variants, and/or there is insufficient evidence to provide information regarding safety and efficacy.

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) — Decrease Dose

This individual metabolizes piroxicam slower, which exposes the individual to higher piroxicam concentrations.

This may lead to an increased risk of adverse reactions such as cardiovascular thrombotic events, gastrointestinal bleeding, and renal toxicities.

Physicians may use the lowest effective dosage for the shortest duration or consider an alternative treatment based on the individual's clinical presentation while closely monitoring for adverse events.

Gene: CYP2C9 Robust

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

✕ Tenoxicam — Decrease Dose

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

The adverse events may include dyspepsia, epigastric pain, edema, fluid retention, and blurred vision.

Physicians may use the lowest effective dosage for the shortest duration or consider an alternative treatment based on the individual's clinical presentation while closely monitoring for adverse events.

Gene: CYP2C9 Robust

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

! Aceclofenac — Normal Response Expected

This individual metabolizes aceclofenac slower.

However, the pharmacokinetics of the drug are not significantly impacted by CYP2C9 genetic variants, and/or there is insufficient evidence to provide information regarding safety and efficacy.

Gene: CYP2C9 Robust

PHD LABORATORY

Rheumatology

Drug Class: Non-Steroidal Anti-Inflammatory Drug

MOA: Selective COX-2 Inhibitor

! Lumiracoxib — Normal Response Expected

This individual metabolizes lumiracoxib slower.

However, the pharmacokinetics of the drug are not significantly impacted by CYP2C9 genetic variants, and/or there is insufficient evidence to provide information regarding safety and efficacy.

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 metabolizes bupropion slower, which may result in decreased concentrations of hydroxybupropion, a metabolite of bupropion.

Voriconazole - Dosage adjustment of bupropion may be necessary.

Gene: CYP2B6

Developing

Supplements

Drug Class: Vitamins

MOA: Folic Acid Agonist

L-methylfolate (Deplin)

This individual doesn't have methylenetetrahydrofolate reductase (MTHFR) deficiency.

This individual would not benefit from methylfolate supplementation therapy.

Gene: MTHFR

Developing

Toxicology

Drug Class: Opioid Antagonist

MOA: Opioid Receptor Antagonist

Naltrexone (Vivitrol) — Normal Response Expected

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

Robust

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Urology

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

Tamsulosin (Flomax) — Normal Response Expected

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

- **Desipramine/Thioridazine/Celecoxib** - Increased tamsulosin exposure.
- **Grapefruit Juice/Voriconazole** - Tamsulosin 0.4 mg should not be coadministered.
- **Fluconazole** - Use with caution, particularly at a dose higher than 0.4 mg.
- **Paroxetine** - Tamsulosin should be used with caution when coadministered, particularly at a dose higher than 0.4 mg.

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) — Normal Response Expected

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

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

- **Desipramine/Thioridazine/Paroxetine/Celecoxib** - The interaction was not tested clinically. No dose adjustments are recommended when coadministered.
- **Grapefruit Juice/Voriconazole** - Doses of fesoterodine greater than 4 mg are not recommended. The fesoterodine dose in pediatric patients >35 kg should be reduced to 4 mg once daily and is not recommended in patients weighing greater than 25 kg and up to 35 kg.
- **Fluconazole** - No dose adjustments are needed.

Gene: CYP2D6 **Modest**

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

Tolterodine (Detrol) — Normal Response Expected

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

- **Desipramine/Thioridazine/Celecoxib** - May result in higher tolterodine AUC (area under the curve) and lower Cmax and AUC of the active metabolite of tolterodine.
- **Grapefruit Juice/Voriconazole** - The recommended dose of tolterodine is 2 mg once daily.
- **Fluconazole** - Increased tolterodine exposure.
- **Paroxetine** - May result in increased tolterodine AUC (area under the curve) and decreased Cmax and AUC of the active metabolite of tolterodine.

Gene: CYP2D6 **Modest**

This individual may have a normal response to tolterodine.

Gene: CYP3A4 **Developing**

Urology

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

Darifenacin (Enablex) — Normal Response Expected

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

Desipramine/Thioridazine/Paroxetine/Celecoxib - No dosing adjustments are recommended when coadministered.

Grapefruit Juice/Voriconazole - Higher darifenacin systemic exposure. The daily dose of darifenacin should not exceed 7.5 mg.

Fluconazole - No dosing adjustments are recommended.

Gene: CYP2D6 **Modest**

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

Mirabegron (Myrbetriq) — Normal Response Expected

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

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 John Doe
Date of Birth: 1960-01-01
Report ID: PhDLabs

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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/*6	Intermediate Metabolizer
CYP2C19	*1/*17	Rapid Metabolizer
CYP2C9	*1/*9	Intermediate Metabolizer
CYP2D6	*2/*34	Normal Metabolizer
CYP3A5	*1/*3	Intermediate Metabolizer
DPYD	*1/*1	Normal Metabolizer
NUDT15	*1/*1	Normal Metabolizer
SLCO1B1	*37/*37	Normal Function
TPMT	*1/*1	Normal Metabolizer

Gene	Genotype(s)/ Individual impact
ABCB1	c.3645T>C Homozygous, GG c.1446T>C Homozygous, GG c.3095G>A(T) Negaive, CC
ABCG2	c.421C>A Negative, GG
ADRB2	c.46G>A Heterozygous, AG
APOE	E3/E3
COMT	c.472G>A Heterozygous, GG
CYP1A2	*1D/*1F or *1A/*1V
CYP2C	g.94645745G>A Negative, GG
CYP3A4	*1B/*1B
CYP4F2	c.1297G>A Homozygous, TT
DRD2	c.-31-870T>C Heterozygous, AG g.4750dup Heterozygous, -G g.4651A>G Negative, TT c.2137G>A Heterozygous, AG c.1139-134T>G Homozygous, CC
F2	c.*97G>A Negative, GG/Average Risk of ADR
F5	c.1601G>A Negative, CC/Average Risk of ADR
HTR1A	g.4555G>C Heterozygous, CG
HTR2A	c.614-2211T>C Homozygous, GG g.4692G>A Heterozygous, CT
HTR2C	g.4963C>T Negative, CC c.551-3008C>G Homozygous, GG
MTHFR	c.788C>T Negative, GG c.1409A>C Negative, TT
OPRM1	c.118A>G Negative, AA
VKORC1	g.3588G>A Negative, CC

† Cut along dotted lines

† Fold here

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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Telephone: Click Here

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Clinical Decision Support System CDSS) Access: https://www.geneticaconsulting.com/CDSS

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