SAMPLE REPORT

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PATIENT INFORMATION	SAMPLE	REFERRING PHYSICIAN
Name: John Smith	**Date Collected:** August 24, 2020	**Name:** Jane Doe, MD
DOB: October 9, 1973	**Date Received:** August 25, 2020	**Institution:** Admera Test
Age: 46	**Case ID:** PRPHL20-003350	
Sex: Male	**Source:** Buccal Swabs	
Address: 126 Corporate Blvd. South Plainfield, NJ 07080		

Current Medications and Medications of Interest

John Smith

PGxOne™ Plus

CONSIDER ALTERNATIVE

Carbamazepine

DRUG MANAGEMENT

Tacrolimus

Mercaptopurine

NORMAL RESPONSE EXPECTED

Allopurinol

Carvedilol

Simvastatin

USE WITH CAUTION

Carisoprodol

Omeprazole

Only selected drugs are listed here due to limited space.

Please refer to Patient Specific Genotype Results table for comprehensive illustration of drugs in each action category.

Laboratory Director: Dr. James Dermody CLIS ID: 0005783 CLIA ID: 31D2038676 PFI ID: 8972
Medical Director: Ruben Bonilla Guerrero, MD, DABMG, FACMG, FAACC, MB(ASCP), CGMBS

SAMPLE REPORT

PGxOne™ Plus

Table of Contents

Why would the cover page quadrant(s) be empty?

Empty Quadrant: Quadrants' content consists of cross-referencing medications we report, and the medications provided as part of the patient's current medications list or the provider's medications of interest. Therefore, when a current medication, a medication of interest does not appear in any quadrat, or all quadrants are empty, it means it is not part of the medications we report. Such medication(s) will be listed in the "no or limited pharmacogenomics evidence table" in Section I of the report. However, if the medication has an asterisk (*) next to it, it means that further informative content regarding that medication is available in RxVision.

Gene-Drug Interaction Types:

Consider Alternative: refers to gene-drug pairs in which the interaction between a drug and one or several genes may result in a clinically severe and potentially deadly adverse drug reaction(s) and lack of efficacy. Most medications included in this gene-drug pair category still can be used. However, please exercise extreme caution and clinical judgment, read the corresponding gene-drug interaction for your patient, and follow FDA recommendations.

Use With Caution: refers to gene-drug pairs in which the interaction between a drug and one or several genes may result in a mild adverse drug reaction(s) and lack of efficacy. Most medications included in this gene-drug pair category still can be used. However, please exercise caution and clinical judgment, read the corresponding gene-drug interaction for your patient, and follow FDA recommendations.

Drug Management: refers to gene-drug pairs in which a negative drug response (adverse drug reaction(s) and lack of efficacy) might be preventable by adjusting the medication to the patient's individual needs based on pharmacogenomic results and any other non-genetic factors of your knowledge. Please exercise caution and clinical judgment, read the corresponding gene-drug interaction for your patient, and follow FDA recommendations.

Normal Response Expected: refers to gene-drug pairs in which the corresponding drug response (adverse drug reaction(s) risk and efficacy) shall correlate with the FDA label description and is like that of the general population. Keep in mind that all drugs come with associated risks and should be taken into consideration when prescribing any medication. Please exercise caution and clinical judgment, read the corresponding gene-drug interaction for your patient, and follow FDA recommendations.

Pharmacogenomics (PGx) results **DO NOT REPRESENT MEDICAL ADVICE** and they **SHOULD NOT** replace standard protocol-based pharmacological care. PGx testing provides additional information regarding drug response based on the patient's genetic make-up associated with pharmacokinetics, pharmacodynamics, and other biological processes with the intent to provide insights regarding medications efficacy and adverse drug reactions.

ONLY a patient's healthcare provider can make decisions regarding medication selections, medication dosage, medication additions, medication replacements, and stopping medications.

Note to Patient:

While these are your results, YOU should not make any changes to your medications, unless directly instructed by your healthcare provider.

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I. Current Medications and Medications of Interest

John Smith

CARDIOLOGY

DrugClass: Alpha and Beta Adrenergic Blocker

MOA: Nonselective Beta Adrenergic Blocker and Alpha 1 Adrenergic Blocker

Drug Impacted	Source	Gene	Genotype	Patient Impact
Carvedilol	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to carvedilol. Physicians should follow FDA label recommendations.

CARDIOLOGY

DrugClass: Antilipemic Agent

MOA: HMG-CoA Reductase Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Simvastatin	FDA	SLCO1B1	*1/*1	Average Risk of Toxicity/ADR

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to simvastatin. However, physicians may monitor patients for myopathy symptoms (muscle pain and tenderness) and if necessary, could adjust the dose as needed based on the patient's clinical presentation, creatine kinase (CK) levels, cholesterol levels, and renal function. Physicians should follow FDA label recommendations.

DERMATOLOGY

DrugClass: Immunosuppressant Agent

MOA: Calcineurin Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Tacrolimus	FDA	CYP3A5	*1A/*1A	Normal Metabolizer/Decreased Efficacy

Gene-Drug Interaction: **INCREASE DOSE**

Patients with this genotype have lower systemic tacrolimus concentrations and lower probability of achieving target concentrations. Measure drug concentrations and adjust dosage based on trough whole blood tacrolimus concentrations. Physicians should follow FDA label recommendations.

GASTROENTEROLOGY

DrugClass: Acid Reducing Agent

MOA: Proton Pump Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Omeprazole	FDA	CYP2C19	*1/*17	Rapid Metabolizer/Decreased Efficacy

Gene-Drug Interaction: **USE WITH CAUTION**

Patients with this genotype have an increased CYP2C19 activity. Therefore, please proceed with caution as they may experience therapeutic failure. Physicians should follow FDA label recommendations.

NEUROLOGY

DrugClass: Anticonvulsant

MOA: Voltage-Activated Na+ Channel Regulator

Drug Impacted	Source	Gene	Genotype	Patient Impact
Carbamazepine	FDA	HLA-B	Negative (See Methodology page)	Average Risk of Toxicity
		HLA-A	Negative/*3101	Increased Risk of Toxicity

Gene-Drug Interaction: **CONSIDER ALTERNATIVES** — **Increased Risk of Toxicity**

Patients with this genotype have an increased risk of developing serious and sometimes fatal dermatologic reactions, including Toxic Epidermal Necrolysis (TEN) and Stevens Johnson Syndrome (SJS), after carbamazepine treatment. According to the FDA label, carbamazepine should not be used in patients positive for HLA-B*1502 unless the benefits clearly outweigh the risks. Genotyping is not a substitute for clinical vigilance. Physicians should follow FDA label recommendations.

I. Current Medications and Medications of Interest

John Smith

ONCOLOGY

DrugClass: Antineoplastic Agent

MOA: DNA and RNA Synthesis Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Mercaptopurine	FDA	TPMT	*2/*2	Poor Metabolizer
		NUDT15	c.415C>T Negative, CC	Normal Metabolizer
Gene-Drug Interaction: DECREASE DOSE				**Increased Risk of Toxicity**

Patients with this genotype have an increased risk of severe and life-threatening myelotoxicity if receiving conventional doses of mercaptopurine due to higher systemic active metabolite concentrations. According to the FDA label, patients with this genotype typically tolerate 10% or less of the standard mercaptopurine dosage because of the risk of increased toxicity, and initial dosage should be reduced in patients who are known to have homozygous TPMT or NUDT15 deficiency. Refer to FDA labeling for specific dosage recommendations. Please monitor complete blood count in patients receiving mercaptopurine. Physicians should follow FDA label recommendations.

ONCOLOGY

DrugClass: Immunosuppressant Agent

MOA: Calcineurin Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Tacrolimus	FDA	CYP3A5	*1A/*1A	Normal Metabolizer/Decreased Efficacy

Gene-Drug Interaction: INCREASE DOSE

Patients with this genotype have lower systemic tacrolimus concentrations and lower probability of achieving target concentrations. Measure drug concentrations and adjust dosage based on trough whole blood tacrolimus concentrations. Physicians should follow FDA label recommendations.

PAIN MANAGEMENT

DrugClass: Muscle Relaxant

MOA: Intraneuronal Activity in Descending Reticular Formation and Spinal Cord Suppressant

Drug Impacted	Source	Gene	Genotype	Patient Impact
Carisoprodol	FDA	CYP2C19	*1/*17	Rapid Metabolizer/Decreased Efficacy

Gene-Drug Interaction: USE WITH CAUTION

Patients with this genotype have an increased CYP2C19 activity. Therefore, please proceed with caution as they may experience therapeutic failure. Physicians should follow FDA label recommendations.

RHEUMATOLOGY

DrugClass: **Antigout Agent**

MOA: Xanthine Oxidase Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Allopurinol	FDA	HLA-B	Negative (See Methodology page)	Average Risk of ADR
Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED** Patients with this genotype are expected to have a normal response to allopurinol. Physicians should follow FDA label recommendations.				

Medications listed below either have **no** or **limited** pharmacogenomics evidence *(* visit RxVision for additional relevant information)*

Drug(s) Impacted	
Lansoprazole*	**Pegloticase***
Primaquine*	

Drug-Drug Interactions

John Smith

Drugs	Severity	Warning	Documentation	Clinical Management
ALLOPURINOL – MERCAPTOPURINE	S	**MAJOR** Concurrent use of ALLOPURINOL and MERCAPTOPURINE may result in increased mercaptopurine toxicity (bone marrow suppression, nausea, vomiting).	**FAIR**	Avoid the concomitant use of allopurinol and oral mercaptopurine. Allopurinol inhibits the first pass oxidative metabolism of mercaptopurine by xanthine oxidase, resulting in increased toxicity (myelosuppression, nausea, vomiting) (Prod Info PURIXAN® oral suspension, 2017). However, if coadministration is required, reduce the dose of mercaptopurine to one-third to one-fourth of the usual dose. Monitor closely and make subsequent dose adjustments on the basis of response to therapy and presence of toxicities (Prod Info DUZALLO® oral tablets, 2017). The kinetics of IV mercaptopurine are not altered by the concomitant administration of allopurinol (Zimm et al, 1983).
CARBAMAZEPINE – PRIMAQUINE PHOSPHATE	S	**MAJOR** Concurrent use of CARBAMAZEPINE and ANTIMALARIALS may result in decreased carbamazepine activity.	**FAIR**	Concomitant use of carbamazepine and an antimalarial agent may antagonize the activity of carbamazepine. If a patient has been titrated to a stable dosage of the antimalarial, and is initiated on carbamazepine, a dose adjustment may be necessary (Prod Info CARBATROL® oral extended-release capsules, 2018).
CARBAMAZEPINE – SIMVASTATIN	S	**MAJOR** Concurrent use of CARBAMAZEPINE and SIMVASTATIN may result in reduced simvastatin exposure.	**GOOD**	Monitor cholesterol levels in patients receiving concomitant therapy with carbamazepine and simvastatin. Simvastatin dose may need to be adjusted.
PEGLOTICASE – ALLOPURINOL	S	**MAJOR** Concurrent use of ALLOPURINOL and PEGLOTICASE may result in increased risk of anaphylaxis and infusion reactions .	**FAIR**	Concomitant administration of allopurinol and pegloticase should be avoided as this may blunt the rise in serum uric acid levels, and thereby increase the risk of anaphylaxis and infusion reactions. Discontinue treatment with oral urate-lowering drugs including allopurinol before initiating pegloticase therapy, and do not initiate therapy with urate-lowering agents while patients are on pegloticase therapy (Prod Info KRYSTEXXA® intravenous infusion injection, 2012).
CARBAMAZEPINE – OMEPRAZOLE	!	**MODERATE** Concurrent use of CARBAMAZEPINE and OMEPRAZOLE may result in an increased risk of carbamazepine toxicity.	**GOOD**	Monitor patients receiving concurrent carbamazepine and omeprazole therapy for signs of carbamazepine toxicity (ataxia, nystagmus, diplopia, headache, vomiting, apnea, seizures, coma). Also monitor carbamazepine serum levels. Doses of carbamazepine may need to be reduced.

Drug-Food Interactions

John Smith

PGxOne™ Plus

Drugs	Severity	Warning	Documentation	Clinical Management
CARBAMAZEPINE – GRAPEFRUIT JUICE	S	**MAJOR** Concurrent use of CARBAMAZEPINE and GRAPEFRUIT JUICE may result in increased carbamazepine bioavailability.	**GOOD**	Concomitant use of carbamazepine (a CYP3A4 substrate) with grapefruit juice, a CYP3A4 inhibitor, may increase the carbamazepine levels. If used concomitantly, monitor serum carbamazepine levels and adjust dosage as needed (Prod Info Tegretol®-XR oral extended release tablets, 2013; Prod Info Tegretol® oral chewable tablets, oral tablets, oral suspension, 2013).
SIMVASTATIN – CRANBERRY JUICE	S	**MAJOR** Concurrent use of SIMVASTATIN and CRANBERRY JUICE may result in increased risk of hepatitis and myopathy/rhabdomyolysis.	**GOOD**	Concomitant use of simvastatin and consumption of cranberry juice may lead to hepatitis, myopathy, and/or rhabdomyolysis (Goldenberg et al, 2012). When concurrent consumption occurs, instruct patients to promptly report any unexplained muscle pain or symptoms of hepatitis, such as yellow skin or eyes, dark-colored urine, or pale stools.
SIMVASTATIN – GRAPEFRUIT JUICE	S	**MAJOR** Concurrent use of SIMVASTATIN and GRAPEFRUIT JUICE may result in increased bioavailability of simvastatin resulting in an increased risk of myopathy or rhabdomyolysis.	**EXCELLENT**	Avoid consumption of grapefruit juice in patients receiving simvastatin therapy (Prod Info ZOCOR® oral tablets, 2015). Orange juice may be substituted for grapefruit juice. Alternatively, substitute an HMG-CoA reductase inhibitor (fluvastatin, pravastatin, rosuvastatin) that is not a substrate of CYP3A4 metabolism.
CARBAMAZEPINE – BLACK TEA	!	**MODERATE** Concurrent use of CARBAMAZEPINE and BLACK TEA may result in decreased carbamazepine bioavailability.	**GOOD**	Concomitant use of carbamazepine (a hepatic enzyme substrate) with black tea (a hepatic enzyme inducer), may decrease carbamazepine exposure. If used concomitantly, monitor serum carbamazepine levels (Akrawi et al, 2015).
LANSOPRAZOLE – CRANBERRY	!	**MODERATE** Concurrent use of PROTON PUMP INHIBITORS and CRANBERRY may result in reduced effectiveness of proton pump inhibitors.	**GOOD**	Advise patients to avoid regular use of cranberry juice while taking a proton pump inhibitor. Occasional use of cranberry juice is not likely to have a clinical effect on proton pump inhibitor effectiveness. The effect of cranberry extract supplements on gastric acid is not known, caution is advised.
LANSOPRAZOLE – FOOD	!	**MODERATE** Concurrent use of LANSOPRAZOLE and FOOD may result in decreased lansoprazole concentrations.	**GOOD**	Instruct patients to take lansoprazole on an empty stomach, especially the first day of treatment.
OMEPRAZOLE – CRANBERRY	!	**MODERATE** Concurrent use of PROTON PUMP INHIBITORS and CRANBERRY may result in reduced effectiveness of proton pump inhibitors.	**GOOD**	Advise patients to avoid regular use of cranberry juice while taking a proton pump inhibitor. Occasional use of cranberry juice is not likely to have a clinical effect on proton pump inhibitor effectiveness. The effect of cranberry extract supplements on gastric acid is not known, caution is advised.

Drug-Alcohol Interactions

John Smith

Drugs	Severity	Warning	Documentation	Clinical Management
TACROLIMUS – ETHANOL	S	**MAJOR** Concurrent use of TACROLIMUS and ETHANOL may result in increased tacrolimus exposure with use of oral extended-release capsule doseform; flushing or rash with administration of topical ointment.	**FAIR**	Alcohol may cause a more rapid release of the dose from the extended-release form of tacrolimus capsules (Prod Info ASTAGRAF XL(TM) oral extended-release capsules, 2013). Should patients using topical tacrolimus present with new skin complaints, evaluate for alcohol-related adverse reaction, rather than drug allergy (Knight et al, 2005). Patients should not consume alcohol during therapy with tacrolimus extended-release capsules (Prod Info ASTAGRAF XL(TM) oral extended-release capsules, 2013).

Drug-Lab Interactions

John Smith

Drugs	Severity	Warning	Documentation	Clinical Management
LANSOPRAZOLE – CHROMOGRANIN A MEASUREMENT	S	**MAJOR** LANSOPRAZOLE may result in may interfere with diagnostic investigation for neuroendocrine tumors due to serum chromogranin A (CgA) levels increase with decreases in gastric acidity.	**FAIR**	Interrupt lansoprazole for at least 14 days prior to assessing serum chromogranin A (CgA) levels, as a reduction in gastric acidity may cause increased CgA levels and result in a false positive diagnostic evaluation for neuroendocrine tumors. Consider repeat testing if initial CgA levels are high. If multiple tests are performed for monitoring purposes, use the same commercial laboratory as reference ranges may vary (Prod Info PREVACID(TM) oral delayed-release capsules, 2017; Prod Info PREVACID(TM) SoluTab oral delayed-release disintegrating tablets, 2017).
OMEPRAZOLE – CHROMOGRANIN A MEASUREMENT	S	**MAJOR** OMEPRAZOLE may result in may interfere with diagnostic investigation for neuroendocrine tumors due to serum chromogranin A (CgA) levels increase with decreases in gastric acidity.	**FAIR**	Omeprazole should be temporarily stopped at least 14 days prior to assessing serum chromogranin A (CgA) levels, as a reduction in gastric acidity may cause increased CgA levels and result in a false positive diagnostic evaluation for neuroendocrine tumors. Repeat testing should be considered if initial CgA levels are high. If multiple tests are performed for monitoring purposes, the same commercial laboratory should be used as reference ranges may vary (Prod Info PRILOSEC® oral delayed-release suspension, 2014).
CARBAMAZEPINE – TRICYCLIC ANTIDEPRESSANT MEASUREMENT	!	**MODERATE** CARBAMAZEPINE may result in false positive tricyclic antidepressant assay results with serum fluorescence-polarized immunoassay due to molecular structural similarity of carbamazepine to the tricyclic antidepressant class.	**EXCELLENT**	The molecular structural similarity of carbamazepine to tricyclic antidepressants (TCAs) can lead to falsely positive results with the serum fluorescence-polarized immunoassay but not the less sensitive urine enzyme-linked immunoassay. When an assay is positive for TCAs and there is no history of TCA use, gas chromatography/mass spectrometry (GC/MS) should be considered, as they are specific enough to differentiate between TCAs and structurally similar compounds (Saidinejad et al, 2007).
LANSOPRAZOLE – SECRETIN STIMULATION TEST	!	**MODERATE** LANSOPRAZOLE may result in risk of false positive result due to hyperresponse in gastrin secretion.	**FAIR**	Lansoprazole increases serum gastrin levels. A hyperresponse in gastrin secretion that falsely suggests gastrinoma may occur if a secretin stimulation test is performed during use of lansoprazole. Interrupt lansoprazole therapy at least 28 days before testing to allow gastrin levels to return to baseline (Prod Info PREVACID (TM) oral delayed-release capsules, 2017; Prod Info PREVACID(TM) SoluTab oral delayed-release disintegrating tablets, 2017).

Drug-Lab Interactions

John Smith

Drugs	Severity	Warning	Documentation	Clinical Management
LANSOPRAZOLE – URINE SUBSTANCE MEASUREMENT		**MODERATE** PROTON PUMP INHIBITORS may result in false-positive urine screening tests for tetrahydrocannabinol (THC) due to unknown.	**GOOD**	Proton pump inhibitors may cause false positive urine screening tests for tetrahydrocannabinol (THC). Use an alternative method to confirm positive screening tests for THC (Prod Info DEXILANT(TM) oral delayed-release capsules, 2016; Prod Info PRILOSEC® oral delayed-release capsules, 2016; Prod Info PROTONIX® I.V. intravenous injection, 2014).
OMEPRAZOLE – URINE SUBSTANCE MEASUREMENT		**MODERATE** PROTON PUMP INHIBITORS may result in false-positive urine screening tests for tetrahydrocannabinol (THC) due to unknown.	**GOOD**	Proton pump inhibitors may cause false positive urine screening tests for tetrahydrocannabinol (THC). Use an alternative method to confirm positive screening tests for THC (Prod Info DEXILANT(TM) oral delayed-release capsules, 2016; Prod Info PRILOSEC® oral delayed-release capsules, 2016; Prod Info PROTONIX® I.V. intravenous injection, 2014).

ANESTHESIOLOGY

DrugClass: Depolarizing Neuromuscular Blocker Agent

MOA: Cholinergic Receptor Agonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Succinylcholine (Anectine®; Quelicin®)	FDA	BCHE	c.293A>G Homozygous, GG	Poor Metabolizer/Increased Risk of ADR

Gene-Drug Interaction: ✖ **CONSIDER ALTERNATIVES**

Patients with this genotype have higher systemic succinylcholine concentrations due to poor plasma cholinesterase activity resulting in a higher risk of adverse reactions (neuromuscular blockade). Avoid use in poor metabolizers. Physicians should follow FDA label recommendations.

DrugClass: Musculoskeletal Agent

MOA: Non-Depolarizing Neuromuscular Blocker

Drug Impacted	Source	Gene	Genotype	Patient Impact
Mivacurium (Mivacron®)	FDA	BCHE	c.293A>G Homozygous, GG	Poor Metabolizer/Increased Risk of ADR

Gene-Drug Interaction: ✖ **CONSIDER ALTERNATIVES**

Patients with this genotype have higher systemic mivacurium concentrations due to poor plasma cholinesterase activity resulting in a higher risk of adverse reactions (neuromuscular blockade). Avoid use in poor metabolizers. Physicians should follow FDA label recommendations.

CARDIOLOGY

DrugClass: Alpha and Beta Adrenergic Blocker

MOA: Nonselective Beta Adrenergic Blocker and Alpha 1 Adrenergic Blocker

Drug Impacted	Source	Gene	Genotype	Patient Impact
Carvedilol (Coreg®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✔ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to carvedilol. Physicians should follow FDA label recommendations.

CARDIOLOGY

DrugClass: Antiarrhythmic Agent

MOA: Sodium Channel Blocker

Drug Impacted	Source	Gene	Genotype	Patient Impact
Procainamide	FDA	NAT2	*5/*6/*12/*13	Poor Metabolizer (Acetylation)

Gene-Drug Interaction: **USE WITH CAUTION**

Patients with this genotype have an altered systemic parent drug and metabolites concentration and are at an increased risk for adverse reactions due to a high exposure to procainamide. Refer to the FDA label for adverse drug interaction and specific dose recommendations associated with this medication. Physicians should follow FDA label recommendations.

DrugClass: Antiarrhythmic Agent

MOA: Sodium Channel Blocker

Drug Impacted	Source	Gene	Genotype	Patient Impact
Propafenone (Rythmol SR®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to propafenone. Physicians should follow FDA label recommendations.

DrugClass: Anticoagulant

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

Drug Impacted	Source	Gene	Genotype	Patient Impact
Warfarin (Coumadin®; Jantoven®)	FDA	CYP2C9	*1/*1	Normal Metabolizer
		VKORC1	c.-1639G>A Negative, GG	Normal Sensitivity
		CYP4F2	*1/*3	Intermediate Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED** **Average Risk of ADR**

Patients with this genotype are expected to have a normal response to warfarin. However, please consider incorporating dose adjustment increase if CYP4F2 (rs2108622) heterozygous or homozygous. It is recommended to establish an INR baseline and to monitor INR periodically until reaching a steady protective value. Physicians should follow FDA label recommendations.

CARDIOLOGY

DrugClass: Antilipemic Agent

MOA: HMG-CoA Reductase Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Rosuvastatin (Crestor®; Ezallor Sprinkle®)	FDA	SLCO1B1	*1/*1	Average Risk of Toxicity/ADR

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to rosuvastatin. However, physicians should always monitor patients for myopathy symptoms (muscle pain and tenderness) and if necessary, may adjust the dose as needed based on the patient's clinical presentation, creatine kinase (CK) levels, cholesterol levels, and renal function. Physicians should follow FDA label recommendations.

DrugClass: Antilipemic Agent

MOA: HMG-CoA Reductase Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Simvastatin (Zocor®)	FDA	SLCO1B1	*1/*1	Average Risk of Toxicity/ADR

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to simvastatin. However, physicians may monitor patients for myopathy symptoms (muscle pain and tenderness) and if necessary, could adjust the dose as needed based on the patient's clinical presentation, creatine kinase (CK) levels, cholesterol levels, and renal function. Physicians should follow FDA label recommendations.

DrugClass: Antiplatelet Agent

MOA: P2Y12 Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Clopidogrel (Plavix®)	FDA	CYP2C19	*1/*17	Rapid Metabolizer

Gene-Drug Interaction: **USE WITH CAUTION**

Patients with this genotype have an increased CYP2C19 activity. Therefore, please proceed with caution as they may result in higher systemic active metabolite concentrations, and higher antiplatelet response. Physicians should follow FDA label recommendations.

CARDIOLOGY

DrugClass: Beta Blocker

MOA: Beta-1 Adrenoceptor Antagonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Nebivolol (Bystolic®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to nebivolol. Physicians should follow FDA label recommendations.

DrugClass: Beta Blocker

MOA: Beta-Adrenergic Receptor Antagonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Metoprolol (Lopressor®; Toprol XL®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to metoprolol. Physicians should follow FDA label recommendations.

DrugClass: Beta Blocker

MOA: Nonselective Beta-Adrenergic Receptor Antagonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Propranolol (Inderal®; Inderal LA®; InnoPran XL®; Propranolol HCl Intensol®; Inderal XL®; Hemangeol®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to propranolol. Physicians should follow FDA label recommendations.

II. Comprehensive Drug List

John Smith

CARDIOLOGY

DrugClass: Peripheral Vasodilator

MOA: Calcium Channel Blocker

Drug Impacted	Source	Gene	Genotype	Patient Impact
Hydralazine (Apresoline®)	FDA	NAT2	*5/*6/*12/*13	Poor Metabolizer (Acetylation)

Gene-Drug Interaction: **USE WITH CAUTION**

Patients with this genotype have an increased risk for adverse reactions due to a high exposure to hydralazine. Refer to FDA labeling for specific dosing recommendations and adverse drug reactions associated with this medication. Physicians should follow FDA label recommendations.

DENTISTRY

DrugClass: Cholinergic Agonist

MOA: Cholinergic Receptor Agonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Cevimeline (Evoxac®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to cevimeline. Physicians should follow FDA label recommendations.

DERMATOLOGY

DrugClass: Antineoplastic Agent

MOA: DNA and RNA Synthesis Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Fluorouracil (Adrucil®; Carac®)	FDA	DPYD	*5/*5/*9A	Normal Metabolizer/Average Risk of Toxicity

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to fluorouracil. Physicians should follow FDA label recommendations.

DERMATOLOGY

DrugClass: Immunosuppressant Agent

MOA: Calcineurin Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Tacrolimus (Astagraf XL®; Prograf®; Protopic®; Envarsus XR®)	FDA	CYP3A5	*1A/*1A	Normal Metabolizer/Decreased Efficacy

Gene-Drug Interaction: **INCREASE DOSE**

Patients with this genotype have lower systemic tacrolimus concentrations and lower probability of achieving target concentrations. Measure drug concentrations and adjust dosage based on trough whole blood tacrolimus concentrations. Physicians should follow FDA label recommendations.

DrugClass: Tricyclic Antidepressant, Sleep Aid/Dermatological Agent

MOA: Serotonin and Norepinephrine Reuptake Inhibitor, Histamine Receptor Antagonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Doxepin (Silenor®; Zonalon®; Sinequan®; Prudoxin®)	FDA	CYP2D6	*1/*29	Normal Metabolizer
		CYP2C19	*1/*17	Rapid Metabolizer

Gene-Drug Interaction: **USE WITH CAUTION** — **Decreased Efficacy**

Patients with this genotype alter doxepin systemic concentrations which may compromise therapeutic success. Refer to FDA labeling for specific dosing recommendations. Physicians should follow FDA label recommendations.

ENDOCRINOLOGY

DrugClass: Endocrine Metabolic Agent

MOA: Glucosylceramide Synthase Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Eliglustat (Cerdelga®)	FDA	CYP2D6	*1/*29	Normal Metabolizer/Increased Risk of ADR

Gene-Drug Interaction: **USE WITH CAUTION**

Patients with this genotype metabolize eliglustat slower than patients with some other genotypes, which results in increased risk of cardiac arrhythmias from prolongation of the PR, QTc, and/or QRS cardiac intervals. Refer to FDA labeling for specific dosing recommendations. Physicians may adjust the dose based on patient's clinical presentation. Physicians should follow FDA label recommendations.

GASTROENTEROLOGY

DrugClass: 5-Aminosalicylic Acid Derivative

MOA: Local Chemical Mediator of Inflammatory Response Modulator and TNF Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Sulfasalazine (Azulfidine®)	FDA	NAT2	*5/*6/*12/*13	Poor Metabolizer (Acetylation)

Gene-Drug Interaction: **USE WITH CAUTION**

This medication is metabolized by acetylation. There are two main acetylating enzymes (NAT), N-acetyltransferase 1 (NAT1) and N-acetyltransferase 2 (NAT2). The clinical pharmacogenomics evidence does not specify the particular NAT enzyme carrying out the metabolism. Most medications are metabolized by NAT2. These results only represent NAT2 genotypes and its partial impact. Patients with this genotype have an increased risk for adverse reactions due to increased exposure to sulfasalazine. Refer to the FDA label for adverse drug reactions and dose recommendations associated with this medication. Physicians should follow FDA label recommendations.

DrugClass: Acid Reducing Agent

MOA: Proton Pump Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Dexlansoprazole (Dexilant®)	FDA	CYP2C19	*1/*17	Rapid Metabolizer/Decreased Efficacy

Gene-Drug Interaction: **USE WITH CAUTION**

Patients with this genotype have an increased CYP2C19 activity. Therefore, please proceed with caution as they may experience therapeutic failure. Physicians should follow FDA label recommendations.

DrugClass: Acid Reducing Agent

MOA: Proton Pump Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Esomeprazole (Nexium®)	FDA	CYP2C19	*1/*17	Rapid Metabolizer/Decreased Efficacy

Gene-Drug Interaction: **USE WITH CAUTION**

Patients with this genotype have an increased CYP2C19 activity. Therefore, please proceed with caution as they may experience therapeutic failure. Physicians should follow FDA label recommendations.

GASTROENTEROLOGY

DrugClass: Acid Reducing Agent

MOA: Proton Pump Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Omeprazole (Prilosec®)	FDA	CYP2C19	*1/*17	Rapid Metabolizer/Decreased Efficacy
Gene-Drug Interaction: USE WITH CAUTION Patients with this genotype have an increased CYP2C19 activity. Therefore, please proceed with caution as they may experience therapeutic failure. Physicians should follow FDA label recommendations.				

DrugClass: Acid Reducing Agent

MOA: Proton Pump Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Pantoprazole (Protonix®)	FDA	CYP2C19	*1/*17	Rapid Metabolizer/Decreased Efficacy
Gene-Drug Interaction: USE WITH CAUTION Patients with this genotype have an increased CYP2C19 activity. Therefore, please proceed with caution as they may experience therapeutic failure. Physicians should follow FDA label recommendations.				

DrugClass: Acid Reducing Agent

MOA: Proton Pump Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Rabeprazole (AcipHex®)	FDA	CYP2C19	*1/*17	Rapid Metabolizer/Decreased Efficacy
Gene-Drug Interaction: USE WITH CAUTION Patients with this genotype have an increased CYP2C19 activity. Therefore, please proceed with caution as they may experience therapeutic failure. Physicians should follow FDA label recommendations.				

GASTROENTEROLOGY

DrugClass: Antiemetic

MOA: Dopamine and Serotonin Receptors Blocker

Drug Impacted	Source	Gene	Genotype	Patient Impact
Metoclopramide (Reglan®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to metoclopramide. Physicians should follow FDA label recommendations.

DrugClass: Antiemetic

MOA: H1 Receptor Antagonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Meclizine (Antivert®; Bonine®; Dramamine Less Drowsy®; Motion-Time®; Travel Sickness®; Travel-Easy®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to meclizine. Physicians should follow FDA label recommendations.

GYNECOLOGY

DrugClass: Central Nervous System Agent

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

Drug Impacted	Source	Gene	Genotype	Patient Impact
Flibanserin (Addyi®)	FDA	CYP2C19	*1/*17	Rapid Metabolizer/Decreased Efficacy

Gene-Drug Interaction: ◆ **USE WITH CAUTION**

Patients with this genotype have an increased CYP2C19 activity. Therefore, please proceed with caution as they may experience therapeutic failure. Physicians should follow FDA label recommendations.

GYNECOLOGY

DrugClass: Endocrine Metabolic Agent

MOA: Gonadotropin Releasing Hormone Agonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Elagolix (Orilissa®)	FDA	SLCO1B1	*1/*1	Average Risk of Toxicity/ADR

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to elagolix. Physicians should follow FDA label recommendations.

HEMATOLOGY

DrugClass: Colony Stimulating Factor

MOA: Thrombopoietin Receptor Agonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Avatrombopag (Doptelet®)	FDA	CYP2C9	*1/*1	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to avatrombopag. Physicians should follow FDA label recommendations.

IMMUNOLOGY

DrugClass: Immunomodulatory Agent

MOA: Sphingosine-1 Phosphate Receptor Modulator

Drug Impacted	Source	Gene	Genotype	Patient Impact
Siponimod (Mayzent®)	FDA	CYP2C9	*1/*1	Normal Response

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to siponimod. Physicians should follow FDA label recommendations.

IMMUNOLOGY

DrugClass: Immunosuppressant Agent/Antirheumatic

MOA: Purine Synthesis Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Azathioprine (Azasan®; Imuran®)	FDA	TPMT	*2/*2	Poor Metabolizer
		NUDT15	c.415C>T Negative, CC	Normal Metabolizer
Gene-Drug Interaction: CONSIDER ALTERNATIVES				**Increased Risk of Toxicity**

Patients with this genotype have an increased risk of severe and life-threatening myelotoxicity if receiving conventional doses of azathioprine due to higher systemic active metabolite concentrations. According to the FDA label, physicians should consider alternative therapies in patients with homozygous deficiency in TPMT or NUDT15 because of the risk of increased toxicity. Please monitor complete blood count in patients receiving azathioprine. Physicians should follow FDA label recommendations.

INFECTIOUS DISEASES

DrugClass: Antifungal Agent

MOA: Ergosterol Synthesis Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Voriconazole (Vfend®)	FDA	CYP2C19	*1/*17	Rapid Metabolizer/Decreased Efficacy

Gene-Drug Interaction: USE WITH CAUTION

Patients with this genotype have an increased CYP2C19 activity. Therefore, please proceed with caution as they may experience therapeutic failure. Physicians should follow FDA label recommendations.

DrugClass: Antiretroviral

MOA: HIV-1 Integrase Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Raltegravir (Isentress®)	FDA	UGT1A1	*1/*28	Intermediate Metabolizer

Gene-Drug Interaction: USE WITH CAUTION

Patients with this genotype have a mildly decreased UGT1A1 activity. According to FDA, there is no evidence that UGT1A1 polymorphisms alter pharmacokinetics to a clinically meaningful extent of the medication. Physicians should follow FDA label recommendations.

INFECTIOUS DISEASES

DrugClass: Antiretroviral

MOA: Integrase Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Dolutegravir (Tivicay®)	FDA	UGT1A1	*1/*28	Intermediate Metabolizer

Gene-Drug Interaction: **USE WITH CAUTION**

Patients with this genotype have a mildly decreased UGT1A1 activity. These patients may experience a low risk of adverse events. Physicians should follow FDA label recommendations.

DrugClass: Antiretroviral

MOA: Non-Nucleoside Reverse Transcriptase Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Efavirenz (Sustiva®)	FDA	CYP2B6	*1/*1	Normal Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to efavirenz. Physicians should follow FDA label recommendations.

DrugClass: Antiretroviral

MOA: Nucleotide Reverse Transcriptase Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Abacavir (Ziagen®)	FDA	HLA-B	Negative (See Methodology page)	Average Risk of ADR

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to abacavir. Physicians should follow FDA label recommendations.

DrugClass: Antitubercular Agent

MOA: Mycolic Acid Synthesis Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Isoniazid (Nydrazid®)	FDA	NAT2	*5/*6/*12/*13	Poor Metabolizer (Acetylation)

Gene-Drug Interaction: **USE WITH CAUTION**

Patients with this genotype have an increased risk for adverse reactions due to a high exposure to isoniazid. Refer to the FDA label for adverse drug reactions and for specific dose recommendations associated with this medication. Physicians should follow FDA label recommendations.

INFECTIOUS DISEASES

DrugClass: Sulfonamide Antibiotic

MOA: Formation of Dihydrofolic Acid Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Sulfamethoxazole And Trimethoprim (Bactrim®; Septra®; Sulfatrim®)	FDA	NAT2	*5/*6/*12/*13	Poor Metabolizer (Acetylation)

Gene-Drug Interaction: **USE WITH CAUTION**

This medication is metabolized by acetylation. There are two main acetylating enzymes (NAT), N-acetyltransferase 1 (NAT1) and N-acetyltransferase 2 (NAT2). The clinical pharmacogenomics evidence does not specify the particular NAT enzyme carrying out the metabolism. Most medications are metabolized by NAT2. These results only represent NAT2 genotypes and its partial impact. Patients with this genotype are more prone to adverse drug reactions due to increased exposure to the medication. Refer to the FDA label for adverse drug reactions associated with this medication. Physicians may initiate recommended starting dose and adjust accordingly based on the patient's clinical presentation. Physicians should follow FDA label recommendations.

NEUROLOGY

DrugClass: Anticholinergic Agent

MOA: Acetylcholinesterase Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Donepezil (Aricept®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to donepezil. Physicians should follow FDA label recommendations.

DrugClass: Anticholinergic Agent

MOA: Acetylcholinesterase Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Galantamine (Razadyne®; Razadyne ER ®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to galantamine. Physicians should follow FDA label recommendations for therapy.

NEUROLOGY

DrugClass: Anticonvulsant

MOA: GABA-A Agonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Clobazam (Onfi®; Sympazan®)	FDA	CYP2C19	*1/*17	Rapid Metabolizer/Decreased Efficacy
Gene-Drug Interaction: USE WITH CAUTION Patients with this genotype have an increased CYP2C19 activity. Therefore, please proceed with caution as they may experience therapeutic failure. Physicians should follow FDA label recommendations.				

DrugClass: Anticonvulsant

MOA: Synaptic Vesicle Protein 2A Selective Affinity

Drug Impacted	Source	Gene	Genotype	Patient Impact
Brivaracetam (Briviact®)	FDA	CYP2C19	*1/*17	Rapid Metabolizer/Decreased Efficacy
Gene-Drug Interaction: USE WITH CAUTION Patients with this genotype have an increased CYP2C19 activity. Therefore, please proceed with caution as they may experience therapeutic failure. Physicians should follow FDA label recommendations.				

DrugClass: Anticonvulsant

MOA: Voltage-Activated Na+ Channel Regulator

Drug Impacted	Source	Gene	Genotype	Patient Impact
Carbamazepine (Carbatrol®; Epitol®; Equetro®; Tegretol®; Tegretol-XR®)	FDA	HLA-B	Negative (See Methodology page)	Average Risk of Toxicity
		HLA-A	Negative/*3101	Increased Risk of Toxicity
Gene-Drug Interaction: CONSIDER ALTERNATIVES				**Increased Risk of Toxicity**
Patients with this genotype have an increased risk of developing serious and sometimes fatal dermatologic reactions, including Toxic Epidermal Necrolysis (TEN) and Stevens Johnson Syndrome (SJS), after carbamazepine treatment. According to the FDA label, carbamazepine should not be used in patients positive for HLA-B*1502 unless the benefits clearly outweigh the risks. Genotyping is not a substitute for clinical vigilance. Physicians should follow FDA label recommendations.				

NEUROLOGY

DrugClass: Anticonvulsant

MOA: Voltage-Sensitive Sodium Channels Blocker

Drug Impacted	Source	Gene	Genotype	Patient Impact
Oxcarbazepine (Oxtellar®; Trileptal®)	FDA	HLA-B	Negative (See Methodology page)	Average Risk of ADR

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to oxcarbazepine. Physicians should follow FDA label recommendations.

DrugClass: Central Monoamine-Depleting Agent

MOA: Vesicular Monoamine Transporter 2 Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Deutetrabenazine (Austedo®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to deutetrabenazine. Physicians should follow FDA label recommendations.

DrugClass: Central Nervous System Agent

MOA: Potassium Channel Blocker

Drug Impacted	Source	Gene	Genotype	Patient Impact
Amifampridine (Ruzurgi®)	FDA	NAT2	*5/*6/*12/*13	Poor Metabolizer (Acetylation)

Gene-Drug Interaction: ◆ **USE WITH CAUTION**

Patients with this genotype have an increased risk for adverse reactions to amifampridine. Refer to the FDA label for adverse drug reactions associated with this medication. FDA recommends that physicians initiate treatment at the lowest recommended starting dosage in patients who are known NAT2 poor metabolizers and monitor for adverse reactions. Refer to FDA labeling for specific dosing recommendations. Physicians should follow FDA label recommendations.

NEUROLOGY

DrugClass: Central Nervous System Agent

MOA: Potassium Channel Blocker

Drug Impacted	Source	Gene	Genotype	Patient Impact
Amifampridine Phosphate (Firdapse®)	FDA	NAT2	*5/*6/*12/*13	Poor Metabolizer (Acetylation)

Gene-Drug Interaction: **USE WITH CAUTION**

Patients with this genotype have an increased risk for adverse reactions to amifampridine phosphate. Refer to the FDA label for adverse drug reactions associated with this medication. The recommended starting dosage of FIRDAPSE is 15 mg daily, taken orally in 3 divided doses. Physicians should follow FDA label recommendations.

DrugClass: Central Nervous System Agent

MOA: Selective Norepinephrine Reuptake Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Atomoxetine (Strattera®)	FDA	CYP2D6	*1/*29	Normal Metabolizer/Decreased Efficacy

Gene-Drug Interaction: **USE WITH CAUTION**

Patients with this genotype have a normal CYP2D6 activity. However, patients with this genotype may proceed with caution as they may result in reduced efficacy. Physicians should follow FDA label recommendations.

DrugClass: Central Nervous System Stimulant

MOA: Norepinephrine and Dopamine Reuptake Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Amphetamine (Dyanavel XR®; Adzenys XR-ODT®; Adzenys ER®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to amphetamine. Physicians should follow FDA label recommendations.

NEUROLOGY

DrugClass: Depolarizing Neuromuscular Blocker Agent

MOA: Cholinergic Receptor Agonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Succinylcholine (Anectine®; Quelicin®)	FDA	BCHE	c.293A>G Homozygous, GG	Poor Metabolizer/Increased Risk of ADR

Gene-Drug Interaction: ✖ **CONSIDER ALTERNATIVES**

Patients with this genotype have higher systemic succinylcholine concentrations due to poor plasma cholinesterase activity resulting in a higher risk of adverse reactions (neuromuscular blockade). Avoid use in poor metabolizers. Physicians should follow FDA label recommendations.

DrugClass: Monoamine Depletor

MOA: Vesicular Monoamine Transporter 2 Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Tetrabenazine (Xenazine®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✔ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to tetrabenazine. The maximum recommended single dose is 37.5 mg, and the recommended daily dose should not exceed 100 mg. Physicians should follow FDA label recommendations.

DrugClass: Monoamine Depletor

MOA: Vesicular Monoamine Transporter 2 Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Valbenazine (Ingrezza®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✔ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to valbenazine. Physicians should follow FDA label recommendations.

ONCOLOGY

DrugClass: Antiemetic

MOA: Cannabinoid Receptor Agonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Dronabinol (Syndros®)	FDA	CYP2C9	*1/*1	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to dronabinol. Physicians should follow FDA label recommendations.

DrugClass: Antiemetic

MOA: Dopamine and Serotonin Receptors Blocker

Drug Impacted	Source	Gene	Genotype	Patient Impact
Metoclopramide (Reglan®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to metoclopramide. Physicians should follow FDA label recommendations.

DrugClass: Antiestrogen

MOA: Selective Estrogen Receptor Modulator

Drug Impacted	Source	Gene	Genotype	Patient Impact
Tamoxifen (Soltamox®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to tamoxifen. Please consider monitoring serum levels of tamoxifen and endoxifen to ensure both are within therapeutic levels. Physicians should follow FDA label recommendations.

DrugClass: Antineoplastic Agent

MOA: BCR-ABL, c-KIT and Platelet Derived Growth Factor Receptor (PDGFR) Tyrosine Kinase Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Nilotinib (Tasigna®)	FDA	UGT1A1	*1/*28	Intermediate Metabolizer

Gene-Drug Interaction: ◆ **USE WITH CAUTION**

Patients with this genotype have a mildly decreased UGT1A1 activity. These patients may experience a low risk of hyperbilirubinemia. Physicians should follow FDA label recommendations.

ONCOLOGY

DrugClass: Antineoplastic Agent

MOA: DNA and RNA Synthesis Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Capecitabine (Xeloda®)	FDA	DPYD	*5/*5/*9A	Normal Metabolizer/Average Risk of Toxicity

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to capecitabine. Physicians should follow FDA label recommendations.

DrugClass: Antineoplastic Agent

MOA: DNA and RNA Synthesis Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Fluorouracil (Adrucil®; Carac®)	FDA	DPYD	*5/*5/*9A	Normal Metabolizer/Average Risk of Toxicity

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to fluorouracil. Physicians should follow FDA label recommendations.

DrugClass: Antineoplastic Agent

MOA: DNA and RNA Synthesis Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Mercaptopurine (Purinethol®; Purixan®)	FDA	TPMT	*2/*2	Poor Metabolizer
		NUDT15	c.415C>T Negative, CC	Normal Metabolizer

Gene-Drug Interaction: ▼ **DECREASE DOSE** — **Increased Risk of Toxicity**

Patients with this genotype have an increased risk of severe and life-threatening myelotoxicity if receiving conventional doses of mercaptopurine due to higher systemic active metabolite concentrations. According to the FDA label, patients with this genotype typically tolerate 10% or less of the standard mercaptopurine dosage because of the risk of increased toxicity, and initial dosage should be reduced in patients who are known to have homozygous TPMT or NUDT15 deficiency. Refer to FDA labeling for specific dosage recommendations. Please monitor complete blood count in patients receiving mercaptopurine. Physicians should follow FDA label recommendations.

ONCOLOGY

DrugClass: Antineoplastic Agent

MOA: Epidermal Growth Factor Receptor Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Gefitinib (Iressa®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to gefitinib. Physicians should follow FDA label recommendations.

DrugClass: Antineoplastic Agent

MOA: Fibroblast Growth Factor Receptor Kinase Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Erdafitinib (Balversa®)	FDA	CYP2C9	*1/*1	Normal Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to erdafitinib. Physicians should follow FDA label recommendations.

DrugClass: Antineoplastic Agent

MOA: Histone Deacetylase Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Belinostat (Beleodaq®)	FDA	UGT1A1	*1/*28	Intermediate Metabolizer/Increased Risk of Toxicity

Gene-Drug Interaction: **USE WITH CAUTION**

Patients with this genotype have a decreased UGT1A1 activity. Therefore, please proceed with caution as they could have an increased risk for adverse drug reactions. Refer to the FDA label for adverse drug reactions and for specific dose recommendation associated with this medication. Physicians should follow FDA label recommendations and adjust the therapy accordingly.

ONCOLOGY

DrugClass: Antineoplastic Agent

MOA: Purine Nucleotides Synthesis and Metabolism Blocker

Drug Impacted	Source	Gene	Genotype	Patient Impact
Thioguanine (Tabloid®)	FDA	TPMT	*2/*2	Poor Metabolizer
		NUDT15	c.415C>T Negative, CC	Normal Metabolizer
Gene-Drug Interaction: DECREASE DOSE				**Increased Risk of Toxicity**

Patients with this genotype have an increased risk of severe and life-threatening myelotoxicity if receiving conventional doses of thioguanine due to higher systemic active metabolite concentrations. According to the FDA label, patients with this genotype typically tolerate 10% or less of the standard thioguanine dosage because of the risk of increased toxicity, and initial dosage should be reduced in patients who are known to have homozygous TPMT or NUDT15 deficiency. Refer to FDA labeling for specific dosage recommendations. Please monitor complete blood count in patients receiving thioguanine. Physicians should follow FDA label recommendations.

DrugClass: Antineoplastic Agent

MOA: Topoisomerase I Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Irinotecan (Camptosar®; Ovivyde®)	FDA	UGT1A1	*1/*28	Intermediate Metabolizer/Increased Risk of ADR

Gene-Drug Interaction: USE WITH CAUTION

Patients with this genotype have a decreased UGT1A1 activity. Therefore, please proceed with caution as they could have an increased risk of neutropenia. Physicians should follow FDA label recommendations and adjust the therapy based on the patient's clinical presentation.

DrugClass: Antineoplastic Agent

MOA: Tyrosine Kinase Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Pazopanib (Votrient®)	FDA	UGT1A1	*1/*28	Intermediate Metabolizer
		HLA-B	Negative (See Methodology page)	Average Risk of Toxicity
Gene-Drug Interaction: NORMAL RESPONSE EXPECTED				**Average Risk of Toxicity**

Patients with this genotype have a decreased UGT1A1 activity. However, patients with this genotype are expected to have a normal response to pazopanib. Monitor liver function tests regardless of genotype. Physicians should follow FDA label recommendations for therapy.

II. Comprehensive Drug List

John Smith

ONCOLOGY

DrugClass: Immunosuppressant Agent

MOA: Calcineurin Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Tacrolimus (Astagraf XL®; Prograf®; Protopic®; Envarsus XR®)	FDA	CYP3A5	*1A/*1A	Normal Metabolizer/Decreased Efficacy

Gene-Drug Interaction: **INCREASE DOSE**

Patients with this genotype have lower systemic tacrolimus concentrations and lower probability of achieving target concentrations. Measure drug concentrations and adjust dosage based on trough whole blood tacrolimus concentrations. Physicians should follow FDA label recommendations.

PAIN MANAGEMENT

DrugClass: Muscle Relaxant

MOA: Intraneuronal Activity in Descending Reticular Formation and Spinal Cord Suppressant

Drug Impacted	Source	Gene	Genotype	Patient Impact
Carisoprodol (Soma®; Vanadom®)	FDA	CYP2C19	*1/*17	Rapid Metabolizer/Decreased Efficacy

Gene-Drug Interaction: **USE WITH CAUTION**

Patients with this genotype have an increased CYP2C19 activity. Therefore, please proceed with caution as they may experience therapeutic failure. Physicians should follow FDA label recommendations.

DrugClass: Non-Steroidal Anti-Inflammatory Drug

MOA: COX-1 and COX-2 Inhibitors

Drug Impacted	Source	Gene	Genotype	Patient Impact
Piroxicam (Feldene®)	FDA	CYP2C9	*1/*1	Normal Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to piroxicam. Physicians should follow FDA label recommendations.

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Medical Director: Ruben Bonilla Guerrero, MD, DABMG, FACMG, FAACC, MB(ASCP), CGMBS

PAIN MANAGEMENT

DrugClass: Non-Steroidal Anti-Inflammatory Drug

MOA: Cyclooxygenase 1 and 2 Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Flurbiprofen (Ansaid®)	FDA	CYP2C9	*1/*1	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to flurbiprofen. Physicians should follow FDA label recommendations.

DrugClass: Non-Steroidal Anti-Inflammatory Drug

MOA: Selective COX-2 Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Celecoxib (Celebrex®)	FDA	CYP2C9	*1/*1	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to celecoxib. Physicians should follow FDA label recommendations.

DrugClass: Opioid

MOA: MU Receptor Agonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Codeine	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to codeine. Physicians should follow FDA label recommendations.

DrugClass: Opioid

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

Drug Impacted	Source	Gene	Genotype	Patient Impact
Tramadol (Ultram®; ConZip®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to tramadol. Physicians should follow FDA label recommendations.

II. Comprehensive Drug List

John Smith

PGxOne™ Plus

PAIN MANAGEMENT

DrugClass: Opioid Dependency

MOA: Alpha-2 Adrenergic Agonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Lofexidine (Lucemyra®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to lofexidine. Physicians should follow FDA label recommendations.

PSYCHIATRY

DrugClass: Antidepressant

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

Drug Impacted	Source	Gene	Genotype	Patient Impact
Vortioxetine (Trintellix®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to vortioxetine. Physicians should follow FDA label recommendations.

DrugClass: Antidepressant

MOA: Selective Serotonin Reuptake Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Citalopram (Celexa®)	FDA	CYP2C19	*1/*17	Rapid Metabolizer/Decreased Efficacy

Gene-Drug Interaction: **USE WITH CAUTION**

Patients with this genotype have an increased CYP2C19 activity. Therefore, please proceed with caution as they may experience therapeutic failure. Physicians should follow FDA label recommendations.

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Medical Director: Ruben Bonilla Guerrero, MD, DABMG, FACMG, FAACC, MB(ASCP), CGMBS

PSYCHIATRY

DrugClass: Antidepressant

MOA: Selective Serotonin Reuptake Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Escitalopram (Lexapro®)	FDA	CYP2C19	*1/*17	Rapid Metabolizer/Decreased Efficacy

Gene-Drug Interaction: **USE WITH CAUTION**

Patients with this genotype have an increased CYP2C19 activity. Therefore, please proceed with caution as they may experience therapeutic failure. Physicians should follow FDA label recommendations.

DrugClass: Antidepressant

MOA: Selective Serotonin Reuptake Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Fluvoxamine (Luvox®; Luvox CR®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to fluvoxamine. Physicians should follow FDA label recommendations.

DrugClass: Antidepressant

MOA: Selective Serotonin Reuptake Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Paroxetine (Paxil®; Pexeva®; Brisdelle®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to paroxetine. Physicians should follow FDA label recommendations.

PSYCHIATRY

DrugClass: Antidepressant

MOA: Serotonin and Norepinephrine Reuptake Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Venlafaxine (Effexor®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to venlafaxine. Physicians should follow FDA label recommendations for therapy.

DrugClass: Antipsychotic

MOA: 5-HT-1A and D2 Receptor Partial Agonist and 5-HT-2A Receptor Antagonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Brexpiprazole (Rexulti®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to brexpiprazole. Physicians should follow FDA label recommendations for therapy.

DrugClass: Antipsychotic

MOA: 5-HT2 and Dopamine-D2 Receptor Antagonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Risperidone (Risperdal®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to risperidone. Physicians should follow FDA label recommendations.

DrugClass: Antipsychotic

MOA: Central Dopamine D2 Receptor Blocker

Drug Impacted	Source	Gene	Genotype	Patient Impact
Pimozide (Orap®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to pimozide. Physicians should follow FDA label recommendations.

PSYCHIATRY

DrugClass: Antipsychotic

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

Drug Impacted	Source	Gene	Genotype	Patient Impact
Aripiprazole (Abilify®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to aripiprazole. Physicians should follow FDA label recommendations.

DrugClass: Antipsychotic

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

Drug Impacted	Source	Gene	Genotype	Patient Impact
Aripiprazole Lauroxil (Aristada®; Aristada Initio®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to aripiprazole lauroxil. Physicians should follow FDA label recommendations.

DrugClass: Antipsychotic

MOA: D2 and 5-HT2 Receptor Antagonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Iloperidone (Fanapt®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to iloperidone. Physicians should follow FDA label recommendations.

DrugClass: Antipsychotic

MOA: D2 Receptor Blocker

Drug Impacted	Source	Gene	Genotype	Patient Impact
Thioridazine (Mellaril®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to thioridazine. Physicians should follow FDA label recommendations.

PSYCHIATRY

DrugClass: Antipsychotic

MOA: Dopamine Reuptake Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Perphenazine (Trilafon®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to perphenazine. Physicians should follow FDA label recommendations.

DrugClass: Antipsychotic

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

Drug Impacted	Source	Gene	Genotype	Patient Impact
Clozapine (Clozaril®; Versacloz®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to clozapine. Physicians should follow FDA label recommendations.

DrugClass: Benzodiazepine

MOA: GABA-A Agonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Diazepam (Valium®; Diastat AcuDial®; Diazepam Intensol®; Diastat Pediatric®)	FDA	CYP2C19	*1/*17	Rapid Metabolizer/Decreased Efficacy

Gene-Drug Interaction: **USE WITH CAUTION**

Patients with this genotype have an increased CYP2C19 activity. Therefore, please proceed with caution as they may experience therapeutic failure. Physicians should follow FDA label recommendations.

PSYCHIATRY

DrugClass: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Amitriptyline (Elavil®; Vanatrip®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to amitriptyline. Physicians should follow FDA label recommendations.

DrugClass: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Amoxapine (Asendin®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to amoxapine. Physicians should follow FDA label recommendations for therapy.

DrugClass: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Desipramine (Norpramin®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to desipramine. Physicians should follow FDA label recommendations.

DrugClass: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Imipramine (Tofranil®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to imipramine. Physicians should follow FDA label recommendations.

PSYCHIATRY

DrugClass: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Nortriptyline (Pamelor®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to nortriptyline. Physicians should follow FDA label recommendations.

DrugClass: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Protriptyline (Vivactil®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to protriptyline. Physicians should follow FDA label recommendations.

DrugClass: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Reuptake Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Trimipramine (Surmontil®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to trimipramine. Physicians should follow FDA label recommendations.

DrugClass: Tricyclic Antidepressant

MOA: Norepinephrine and Serotonin Uptake Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Clomipramine (Anafranil®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to clomipramine. Physicians should follow FDA label recommendations.

PSYCHIATRY

DrugClass: Tricyclic Antidepressant, Sleep Aid/Dermatological Agent

MOA: Serotonin and Norepinephrine Reuptake Inhibitor, Histamine Receptor Antagonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Doxepin (Silenor®; Zonalon®; Sinequan®; Prudoxin®)	FDA	CYP2D6	*1/*29	Normal Metabolizer
		CYP2C19	*1/*17	Rapid Metabolizer
Gene-Drug Interaction: USE WITH CAUTION				**Decreased Efficacy**
Patients with this genotype alter doxepin systemic concentrations which may compromise therapeutic success. Refer to FDA labeling for specific dosing recommendations. Physicians should follow FDA label recommendations.				

RHEUMATOLOGY

DrugClass: 5-Aminosalicylic Acid Derivative

MOA: Local Chemical Mediator of Inflammatory Response Modulator and TNF Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Sulfasalazine (Azulfidine®)	FDA	NAT2	*5/*6/*12/*13	Poor Metabolizer (Acetylation)

Gene-Drug Interaction: USE WITH CAUTION

This medication is metabolized by acetylation. There are two main acetylating enzymes (NAT), N-acetyltransferase 1 (NAT1) and N-acetyltransferase 2 (NAT2). The clinical pharmacogenomics evidence does not specify the particular NAT enzyme carrying out the metabolism. Most medications are metabolized by NAT2. These results only represent NAT2 genotypes and its partial impact. Patients with this genotype have an increased risk for adverse reactions due to increased exposure to sulfasalazine. Refer to the FDA label for adverse drug reactions and dose recommendations associated with this medication. Physicians should follow FDA label recommendations.

DrugClass: Antigout Agent

MOA: Xanthine Oxidase Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Allopurinol (Zyloprim®)	FDA	HLA-B	Negative (See Methodology page)	Average Risk of ADR

Gene-Drug Interaction: NORMAL RESPONSE EXPECTED

Patients with this genotype are expected to have a normal response to allopurinol. Physicians should follow FDA label recommendations.

RHEUMATOLOGY

DrugClass: Immunosuppressant Agent/Antirheumatic

MOA: Purine Synthesis Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Azathioprine (Azasan®; Imuran®)	FDA	TPMT	*2/*2	Poor Metabolizer
		NUDT15	c.415C>T Negative, CC	Normal Metabolizer
Gene-Drug Interaction: ✖ **CONSIDER ALTERNATIVES**				**Increased Risk of Toxicity**
Patients with this genotype have an increased risk of severe and life-threatening myelotoxicity if receiving conventional doses of azathioprine due to higher systemic active metabolite concentrations. According to the FDA label, physicians should consider alternative therapies in patients with homozygous deficiency in TPMT or NUDT15 because of the risk of increased toxicity. Please monitor complete blood count in patients receiving azathioprine. Physicians should follow FDA label recommendations.				

DrugClass: Non-Steroidal Anti-Inflammatory Drug

MOA: COX-1 and COX-2 Inhibitors

Drug Impacted	Source	Gene	Genotype	Patient Impact
Piroxicam (Feldene®)	FDA	CYP2C9	*1/*1	Normal Metabolizer
Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**				
Patients with this genotype are expected to have a normal response to piroxicam. Physicians should follow FDA label recommendations.				

DrugClass: Non-Steroidal Anti-Inflammatory Drug

MOA: Cyclooxygenase 1 and 2 Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Flurbiprofen (Ansaid®)	FDA	CYP2C9	*1/*1	Normal Metabolizer
Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**				
Patients with this genotype are expected to have a normal response to flurbiprofen. Physicians should follow FDA label recommendations.				

II. Comprehensive Drug List

John Smith

RHEUMATOLOGY

DrugClass: Non-Steroidal Anti-Inflammatory Drug

MOA: Selective COX-2 Inhibitor

Drug Impacted	Source	Gene	Genotype	Patient Impact
Celecoxib (Celebrex®)	FDA	CYP2C9	*1/*1	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to celecoxib. Physicians should follow FDA label recommendations.

UROLOGY

DrugClass: Alpha 1 Blocker

MOA: Selective Alpha-1A Adrenoceptor Antagonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Tamsulosin (Flomax®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to tamsulosin. Physicians should follow FDA label recommendations.

DrugClass: Anticholinergic Agent

MOA: Competitive Muscarinic Receptor Antagonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Tolterodine (Detrol®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to tolterodine. Physicians should follow FDA label recommendations.

UROLOGY

DrugClass: Anticholinergic Agent

MOA: Muscarinic Receptors Competitive Antagonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Fesoterodine (Toviaz®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to fesoterodine. Physicians should follow FDA label recommendations.

DrugClass: Anticholinergic Agent

MOA: Selective M3 Receptor Antagonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Darifenacin (Enablex®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to darifenacin. Physicians should follow FDA label recommendations.

DrugClass: Genitourinary Agent

MOA: Beta-3 Adrenergic Receptor Agonist

Drug Impacted	Source	Gene	Genotype	Patient Impact
Mirabegron (Myrbetriq®)	FDA	CYP2D6	*1/*29	Normal Metabolizer

Gene-Drug Interaction: ✓ **NORMAL RESPONSE EXPECTED**

Patients with this genotype are expected to have a normal response to mirabegron. Physicians should follow FDA label recommendations.

Genotype and Phenotype Results

John Smith

PGxOne™ Plus

Gene	Genotype	Functional Phenotype
ABCB1	c.2677T>A/c.2677T>G Compound Heterozygous AG/c.3435T>C Homozygous, CC	Poor Function
ABCC4	c.3348G>A Homozygous, AA	Increased Function
ABCG2	c.421C>A Negative, CC	Normal Function
ACE	Ace Insertion, Ins/Del (See Methodology page)	Increased Affinity
ADD1	c.1378G>T Negative, GG	Normal Affinity
ADRB2	c.46A>G Homozygous, GG	Increased Affinity
APOE	c.526C>T Negative, CC	Decreased Affinity
ATIC	c.1503+675T>C Heterozygous, TC	Increased Activity
ATM	c.175-5285G>T Heterozygous, GT	Decreased Activity
BCHE	c.293A>G Homozygous, GG	Poor Activity
CACNA1S	c.3257G>A Negative, GG/c.520C>T Negative, CC	Normal Activity
CES1	c.428G>A Negative, GG	Normal Activity
CFTR	Negative (See Methodology page)	Normal Activity
COMT	c.472G>A Heterozygous, GA	Decreased Activity
CRHR1	c.1107+111C>T Negative, CC	Decreased Affinity
CRHR2	c.184+2030T>A Homozygous, AA	Decreased Affinity
CYP2B6	*1/*1	Normal Activity
CYP2C	g.96405502G>A Negative, GG	Normal Activity
CYP2C19	*1/*17	Increased Activity
CYP2C8	*1/*1	Normal Activity
CYP2C9	*1/*1	Normal Activity
CYP2D6	*1/*29	Normal Activity
CYP3A4	*1A/*1B	Decreased Activity
CYP3A5	*1A/*1A	Normal Activity
CYP4F2	*1/*3	Decreased Activity
DPYD	*5/*5/*9A	Normal Activity
DRD2	c.811-83G>T Heterozygous, GT/c.-585A>G Negative, AA/c.2137G>A Negative, GG	Decreased Affinity
ERCC1	c.354T>C Homozygous, CC/c.*197G>T Heterozygous, GT	Increased Affinity

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Genotype and Phenotype Results

John Smith

PGxOne™ Plus

Gene	Genotype	Functional Phenotype
F2	c.*97G>A Negative, GG	Not Altered Function
F5	c.1601G>A Negative, GG	Not Activated Protein C Resistance
G6PD	c.466A>G Homozygous (Hemizygous)	Decreased Activity
GNB3	c.825C>T Homozygous, TT	Normal Affinity
GSTP1	c.313A>G Negative, AA	Normal Affinity
HLA-A	Negative/*3101	Detection of High-Risk Allele
HLA-B	Negative (See Methodology page)	High-Risk Allele Not Detected
HTR1A	c.-1019G>C Negative, GG	Normal Affinity
HTR2A	c.614-2211T>C Homozygous, CC	Poor Affinity
HTR2C	c.551-3008C>G Homozygous, GG	Normal Affinity
IFNL3/IL28B	g.39743165T>G Negative, TT/g.39738787C>T Negative, CC	Not Altered Expression
ITPA	c.94C>A Heterozygous, CA/c.124+21A>C Negative, AA	Decreased Activity
KIF6	c.2155T>C Homozygous, CC	Increased Affinity
LTC4S	c.-444A>C Negative, AA	Normal Activity
MC4R	g.57882787C>A Heterozygous, CA	Normal Affinity
MTHFR	c.665C>T Negative, CC	Normal Activity
MTRR	c.66A>G Negative, AA	Normal Activity
NAT2	*5/*6/*12/*13	Poor Activity
NEDD4L	c.49-16229G>A Homozygous, AA	Decreased Activity
NQO1	c.559C>T Negative, CC	Normal Affinity
NUDT15	c.415C>T Negative, CC	Normal Activity
OPRM1	c.118A>G Negative, AA/c.290+1050C>T Negative, CC	Decreased Affinity
POLG	c.1399G>A Negative, GG/c.2243G>C Negative, GG	Normal Activity
PTGFR	c.-562T>C Homozygous, CC	Normal Affinity
PTGS1	c.-842A>G Negative, AA	Normal Activity
RYR1	Negative (See Methodology page)	Normal Activity
SCN1A	c.603-91G>A Heterozygous, GA	Decreased Function
SLC6A4	L/L (See Methodology page)	Normal Activity

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Genotype and Phenotype Results

John Smith

Gene	Genotype	Functional Phenotype
SLCO1B1	*1/*1	Normal Function
TNF	c.-488G>A Negative, GG	Normal Expression
TPMT	*2/*2	Poor Activity
UGT1A1	*1/*28	Decreased Activity
UGT1A4	c.142T>G Negative, TT	Normal Activity
VKORC1	c.-1639G>A Negative, GG	Normal Affinity

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Assay Methodology and Limitations for PGxOne™ Plus Panel:

Pharmacogenomics testing to assess how a patient may respond to prescribed drugs was performed by massively parallel Next Generation Sequencing (NGS). PGxOne™ Plus was developed, and assessed for accuracy and precision by Admera Health, South Plainfield NJ. The sensitivity and specificity of this test is 100% and 100% respectively. The PGxOne™ Plus test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity clinical laboratory testing. The DNA testing is not a substitute for clinical monitoring.

*The panel includes genes and variants recommended by the FDA (Tables of Pharmacogenetic Associations and Table of Pharmacogenomic Biomarker in Drug Labeling), the Clinical Pharmacogenomics Implementation Consortium (CPIC), and the Association for Molecular Pathology. The following genetic variants may be detected in the assay: ABCB1 c.3435T>C, c.2677T>A, c.2677T>G; ABCC4 c.3348G>A; ABCG2 c.421C>A; ACE c.2306-119_2306-118insATACAGTCACTTTTTTTTTTTTTTTGAGACGGAGTCTCGCTCTGTCGCCC; ADD1 c.1378G>T; ADRB2 c.46A>G; APOE c.526C>T; ATIC c.1503+675T>C; ATM c.175-5285G>T; BCHE c.293A>G; CACNA1S c.3257G>A, c.520C>T; CES1 c.428G>A; CFTR c.350G>A, c.532G>A, c.1521_1523delCTT, c.1645A>C, c.1646G>A, c.1647T>G, c.1651G>A, c.1652G>A, c.3718-2477C>T, c.3731G>A, c.3752G>A, c.3763T>C, c.3846G>A, c.4046G>A; COMT c.472G>A; CRHR1 c.1107+111C>T; CRHR2 c.184+2030T>A; CYP2B6 *4, *6, *9, *16, *18; CYP2C g.96405502G>A; CYP2C19 *2, *3, *4, *5, *6, *7, *8, *9, *10, *17; CYP2C8 *3; CYP2C9 *2, *3, *4, *5, *6, *8, *9, *11, *12, *13, *14, *15, *16; CYP2D6 *2, *3, *4, *5, *6, *7, *8, *9, *10, *11, *12, *14, *17, *19, *20, *21, *29, *35, *38, *40, *41, *44, *1XN, *2XN, *4XN, *10XN, *17XN, *29XN, *35XN, *41XN; CYP3A4 *1B, *2, *3, *12, *17; CYP3A5 *3A, *3B, *6, *7; CYP4F2 *3; DPYD *2A, *3, *4, *5, *6, *7, *8, *9A, *9B, *10, *11, *12, *13, c.496A>G, c.1129-15T>C, c.2846A>T; DRD2 c.-585A>G, c.811-83G>T, c.2137G>A; ERCC1 c.*197G>T, c.354T>C; F2 c.*97G>A; F5 c.1601G>A; G6PD A-202A_376G, A-376G_968C, Santamaria, Mt. Sinai, c.262G>A, c.331C>T, c.332G>A, c.427G>A, c.466A>G, c.482G>T, c.556G>A, c.577G>A, c.578G>A, c.583A>G, c.617A>G, c.653C>T, c.682C>T, c.683G>C, c.724A>G, c.727G>T, c.961G>A, c.1000G>T, c.1039G>A, c.1043_1066del, c.1093G>A, c.1094C>A, c.1231T>C, c.1243T>C, c.1246A>G, c.1249C>T, c.1250G>A, c.1256A>G, c.1268G>A, c.1270G>C, c.1282G>A, c.1406G>C, c.1408C>T, c.1429G>A, c.1437G>C, c.1450C>T, c.1451G>A, c.1466G>C, c.1466G>T, c.1478G>A; GNB3 c.825C>T; GSTP1 c.313A>G; HLA-A *3101; HLA-B *1502, *5701, *5801; HTR1A c.-1019G>C; HTR2A c.614-2211T>C; HTR2C c.551-3008C>G; IFNL3/IL28B g.39738787C>T, g.39743165T>G; ITPA c.94C>A, c.124+21A>C; KIF6 c.2155T>C; LTC4S c.-444A>C; MC4R g.57882787C>A; MTHFR c.665C>T; MTRR c.66A>G; NAT2 *5, *6, *7, *12, *13; NEDD4L c.49-16229G>A; NQO1 c.559C>T; NUDT15 c.415C>T; OPRM1 c.118A>G, c.290+1050C>T; POLG c.1399G>A, c.2243G>C; PTGFR c.-562T>C; PTGS1 c.-842A>G; RYR1 c.103T>C, c.130C>T, c.487C>T, c.488G>T, c.742G>A, c.742G>C, c.982C>T, c.1021G>A, c.1021G>C, c.1201C>T, c.1209C>G, c.1565A>C, c.1589G>A, c.1597C>T, c.1598G>A, c.1654C>T, c.1840C>T, c.1841G>T, c.6487C>T, c.6488G>A, c.6502G>A, c.6617C>G, c.6617C>T, c.7007G>A, c.7039_7041delGAG/c.7042_7044delGAG, c.7048G>A, c.7063C>T, c.7124G>C, c.7282G>A, c.7300G>A, c.7304G>A, c.7354C>T, c.7360C>T, c.7361G>A, c.7372C>T, c.7373G>A, c.7522C>G, c.7522C>T, c.7523G>A, c.9310G>A, c.11969G>T, c.14387A>G, c.14477C>T, c.14497C>T, c.14512C>G, c.14545G>A, c.14582G>A, c.14693T>C; SCN1A c.603-91G>A; SLC6A4 5-HTTLPR L, 5-HTTLPR S; SLCO1B1 *5; TNF c.-488G>A; TPMT *2, *3A, *3B, *3C, *4; UGT1A1 *28; UGT1A4 c.142T>G; VKORC1 c.-1639G>A.*

A negative or a *1 allele result signifies the absence of the targeted alleles and does not indicate the absence of other mutations not covered by the assay. The possibility cannot be ruled out that the indicated genotypes may be present but below the limits of detection for this assay.

Healthcare professionals may utilize a courtesy consultation with a pharmacogenomics expert in Clinical Services. Please contact us at 844-4ADMERA (844.423.6372).

General Pharmacogenomics References:

1. FDA Table of Pharmacogenomic Associations:
   https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations
2. FDA Table of Pharmacogenomic Biomarkers in Drug Labeling:
   https://www.fda.gov/drugs/science-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling
3. FDA Drug Labels:
   https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm

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