

Patient XXX		F	Requesting physician		
Date of birth	01/06/1956 Sex F				
Sample type	DNA	F	Report generated	29/08/2022	
Collection date	10/06/2022		Laboratory director	Dr C. Lapucci	
Received date	28/06/2022		Contact email	cristina.lapucci@synlab.it	
Sample number	xxx				

MyPGx ® - Pharmacogenetic large screening panel (method: PCR, MassArray and MLPA)

Provided clinical information:

Clinical information	
Known problematic medication	NKDA
Relevant medical history	None

Summary of key pharmacogenetic results (predicted Poor or Ultrarapid activity):

Gene	Prediction
CYP2C19	Rapid metabolizer
VKORC1	Warfarin resistance
SLC22A1	Low function
SLCO1B3	Low function
SULT1A1	Poor metabolizer
NAT2	Poor acetylator

The detailed pharmacogenetic results are presented on the following pages.

Technical comments and limitations:

Coverage 100%. Haplotypes not determined (failed SNPs): None

PGx is a rapidly-evolving field primarily providing evidence-based predictions of how the tested individual's genetic profile may affect reaction to certain drugs. Factors such as drug-drug interaction and also age, diet, ethnicity, family and personal health history, can also impact the likelihood of exhibiting certain drug reactions, independently of genotype-based predictions.

This report is intended for use by a healthcare professional. Based on PGx results, patients should make no changes to medical care without the prior advice of and consultation with a healthcare professional [including, but not limited to, changes in dosage or frequency of medication, diet and/or exercise regimens, or pregnancy planning].

ELECTRONIC SIGNATURE	Dott.ssa Cristina Lapucci SPECIALISTA IN GENETICA MEDICA SYNLAB ITALIA	
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GENOTYPE/HAPLOTYPE/PHENOTYPE DETAIL

Gene	Genotype- Haplotype	Allele Tested	Predicted Phenotype
CYP1A1	*1/*1	*1, *2, *3, *4, *5, *6, *7, *8	Normal metabolizer
CYP1A2	*1A/*1F	*1A, *1F, *1K, *7	Normal metabolizer
CYP2A6	*1A/*9	*1A, *1B, *2, *4, *5, *6, *7, *8, *9, *11, *17, *20	Intermediate metabolizer
CYP2B6	*6/*6	*1, *6, *8, *10, *18, *28	Intermediate metabolizer
CYP2C8	*1/*1	*1, *2, *3, *4, *5, *7, *8	Normal metabolizer
CYP2C9	*1/*3	*1, *2, *3, *4, *5, *6, *8, *9, *10, *11, *12, *13, *15, *25, *27	Intermediate metabolizer
CYP2C19	*1A/*17	*1A, *1B, *2A, *3, *4, *5A, *5B, *6, *7, *8, *12, *17	Rapid metabolizer
CYP2D6	*2A/*41	*1, *2A, *3, *4A, *4M, *5, *6A, *7, *8, *9, *10, *11, *12, *14A, *14B, *17, *18, *19, *20, *21, *36, *38, *40,	Normal metabolizer
CYP2E1	*1/*7	*1, *2, *7	Normal metabolizer
CYP3A4	*1/*1	*1, *2, *6, *20, *22	Normal metabolizer
CYP3A5	*1A/*1A	*1A, *3A, *3K, *5, *6, *7	Normal metabolizer
VKORC1	H7/H7	H1, H3, H7, H9	Warfarin resistance
SLC15A2	*1/*1	*1, *509K, *284A, *350F, *409S	Normal function
SLC22A1	*420Del/*420Del	*1, *2, *3, *4, *5, *6, *220V, *283L, *287G, *341L, *408V, *420Del	Low function
SLC22A2	*1/*270A	*1, *54S, *165V, *270A, *400C, *432N	Normal function
SLC22A6	*1/*1	*1, *50H	Normal function
SLCO1B1	*1A/*1A	*1A, *1B, *2, *3, *5, *6, *9, *10, *11, *12, *13, *15	Normal function
SLCO1B3	*2331/*2331	*1, *112A, *233I	Low function
SLCO2B1	*1/*1	*1, *3	Normal function
ABCB1	*1/*2	*1, *2	Intermediate function
ABCC2	*1/*1324I	*1, *417I, *789F, *768W, *1324I, *1450S	Intermediate function
ABCG2	*1/*1	*1, *141K, *126Ter	Normal function
SULT1A1	*3/*3	*1, *2, *3, *4	Poor metabolizer
NAT1	*4/*11	*1, *5, *11, *14, *15, *17, *19, *22	Normal acetylator
NAT2	*5B/*6A or *5A/*6C or *6B/*5G or *12C/*5J	*4, *5A, *5B, *5C, *5D, *5E, *5G, *5J, *6A, *6B, *6C, *6E, *7A, *7B, *11A, *12A, *12B, *12C, *13, *14A, *14B, *14C, *14D, *14E, *14F, *14G, *19	Poor acetylator
TPMT	*1/*1	*1, *2, *3A, *3B, *3C, *4, *8	Normal metabolizer
GSTM1	*1/*1	*1, *173Asn	Normal metabolizer
GSTP1	*1A/*1A	*1A, *1B, *1C	Normal metabolizer
UGT1A1	*28(*60)/*28(*60)	*1, *6, *7, *27, *29, *60	Intermediate metabolizer
UGT2B7	*1a/*1a	*1a, 2b	Normal metabolizer
UGT2B15	*2/*2	*1, *2	Intermediate metabolizer
DPYD	*1/*2A	*1, *2A, *7, *8, *9A, *9B, *10	Intermediate metabolizer

<u>Disclaimer: Laboratory-developed</u> screening test and interpretation protocols, employing research-use only (RUO) materials. The result of the "Phenotype" shown in the table is to be considered as a generic parameter and not specific to a single drug. For a reference to a specific drug check the tables below in the report. Additional Disclaimer: MyPGx® is a registered trade mark of SYNLAB International GmbH. Patients should not initiate or modify any treatment or otherwise use the information in this report without the prior advice, consultation and supervision of a licensed healthcare professional such as a pharmacist or medical doctor.

Methodology: PCR-based RUO assays detect listed alleles, including all common and most rare variants with known clinical significance at analytical sensitivity and specificity >99%. Phenotypic predictions based on the current state of the scientific literature and PharmGKB. MLPA assay to identify CYP2D6 CNVs (deletions, duplications).

Limitations: Testing cannot detect all genetic variants, inactive or altered genes. The absence of a finding of a detectable gene or variant does not necessarily indicate patient possesses intermediate- or high-sensitivity phenotypes or that patient has an undetected variant. Drug-drug interactions may significantly modify phenotypes, especially in polymedicated patients. The lack of data in the literature and the absence of clinical reports do not allow any ambiguous variants and related phenotypic consequences to be adequately characterised. For these reasons, in the absence of this information, the result is given on the basis of haplotype frequencies.

PHARMACOGENOMICS

Genetic Markers Tested for Pharmacogenomics:

Results are arranged by drug response. Each individual report contains six sections, including: Patient's current medication (if any), Medication history, genotype/haplotype/phenotype detail, PGx report, Genomic Test Results, and Patient Information Card. Inclusion of the PGx Report indicates that the tested individual: displays decreased efficacy to the drug (yellow dots), should use the drug as directed (green dots), or exhibits increased toxicity to the drug (orange dots). Inclusion of Genomic Test Results indicates genotype, haplotype, phenotype, or presence of mutation.

Organization of Table:

- 1. Gene/Locus refers to gene or intergenic region of genetic marker location.
- 2. Marker refers to the tested marker's unique identifier.
- 3. Genotype/Haplotype refers to the particular marker's combination of nucleotides. The letter(s) on either side of the slash refer(s) to the two (2) copies of the patient DNA. Del and dashes denotes nucleotide indels in patient DNA. Empty cells indicate an absence of genotyping results.
- 4. Phenotype refers to the CYP specific drug metabolizing capabilities of an individual.

See RISKS AND LIMITATIONS on the last pages of this Report.

PGx Report - Pain Management

Type: Anti-inflammatory Agent, Analgesic, Antipyretic

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		The Nonsteroidal Antiin	flammatory Drugs (NSAIDs)			
	<u>Diclofenac</u>	UGT2B7	CYP2C9, CYP2E1, CYP3A4			
Acetic acid derivatives	<u>Nabumetone</u>	CYP1A2	CYP2C19, CYP3A4		Ø	
	<u>Indomethacin</u>	CYP2C9	CYP2C19			
	<u>Meloxicam</u>	CYP2C9	CYP1A2, CYP3A4, CYP3A5			
Enolic acid (Oxicam)	<u>Piroxicam</u>	CYP2C9	CYP3A4, CYP3A5			
derivatives	<u>Tenoxicam</u>	CYP2C9				9
	Lornoxicam	CYP2C9				9
	Etoricoxib	CYP3A4	CYP3A5, CYP2C9, CYP2D6, CYP1A2			
Selective COX-2 inhibitors (Coxibs)	<u>Parecoxib</u>	CYP2C9	CYP3A4, CYP3A5			
(COXIDS)	Celecoxib	CYP2C9	CYP2C19			
	<u>Ibuprofen</u>	CYP2C9	CYP2C19, CYP2C8, UGT2B7			
	Flurbiprofen	CYP2C9				
	<u>Ketoprofen</u>	CYP3A4	CYP2C9, CYP3A5, UGT2B7			
Propionic acid derivatives	<u>Fenoprofen</u>	CYP2C9	UGT2B7			
	Vicoprofen	CYP2D6	CYP3A4			
	<u>Naproxen</u>	CYP2C9	CYP1A2, CYP2C8, UGT2B7, SULT1A1			
Anthranilic acid derivatives (Fenamates)	Mefenamic acid	CYP2C9				Ø
The Non-NSAIDs Analgesic	Acetaminophen	UGT1A1, SULT1A1, GSHs	CYP2E1, CYP3A4, CYP3A5, CYP2D6, CYP1A2, ABCG2			

PGx Report - Pain Management

Type: Opioid

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Opioid A	nalgesics			
Opium alkaloids	<u>Morphine</u>	UGT2B7	ABCB1, UGT1A1, COMT			
Opium aikaioius	<u>Codeine</u>	CYP2D6	CYP3A4, UGT2B7, CYP3A5			
Ethers of morphine	<u>Dihydrocodeine</u>	CYP3A4	CYP2D6, CYP3A5			
Ethers of morphine	<u>Ethylmorphine</u>	CYP2D6	CYP3A4, CYP3A5		Ø	
	<u>Hydrocodone</u>	CYP2D6	CYP3A4, CYP3A5		Ø	
Semi-synthetic alkaloid	<u>Hydromorphone</u>	UGT2B7			Ø	
derivatives	<u>Oxycodone</u>	CYP3A4	CYP3A5, CYP2D6, ABCB1, UGT2B7, COMT		Ø	
	<u>Oxymorphone</u>	UGT2B7			Ø	
		Synthet	ic opioids			
	<u>Alfentanyl</u>	CYP3A4	CYP3A5, ABCB1			
Anilidopiperidine derivatives	<u>Fentanyl</u>	CYP3A4	CYP3A5, ABCB1			
	<u>Sufentanil</u>	CYP3A4	CYP3A5			
Dhanulainaridina dariyatiyas	<u>Meperidine</u>	CYP2B6	CYP3A4, CYP2C19, CYP3A5			
Phenylpiperidine derivatives	<u>Ketobemidone</u>	CYP2C9	CYP3A4, CYP3A5			Ø
	Dextropropoxyphene	CYP3A4	CYP3A5, Renal Excretion		Ø	
Diphenylpropylamine	Levacetylmethadol	CYP3A4	CYP3A5			
derivatives	<u>Methadone</u>	CYP3A4	CYP2B6, CYP2D6, CYP3A5, ABCB1, UGT2B7, COMT		Ø	
Oripavine derivatives	<u>Buprenorphine</u>	CYP3A4	CYP3A5, CYP2C8, UGT1A1, UGT2B7		Ø	
Morphinan derivatives	<u>Dextromethorphan</u>	CYP2D6	CYP3A4, CYP3A5		Ø	
	Tramadol	CYP2D6	CYP3A4, CYP2B6, CYP3A5, SLC22A1, COMT	Ø		
Others	<u>Tapentadol</u>	CYP2C9	CYP2C19, CYP2D6		Ø	
	<u>Tilidine</u>	CYP3A4	CYP2C19, CYP3A5			
Auti aniaid	<u>Methylnaltrexone</u>	CYP2D6	CYP3A4, CYP3A5			
Anti-opioid	<u>Naltrexone</u>	UGT2B7	UGT1A1			

PGx Report - Pain Management

Type: Drugs Prescribed for the Treatment of Gout, Antirheumatic

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Drugs Presci	ribed for Gout			
Uricosurics	Sulfinpyrazone	CYP2C9	CYP3A4, CYP3A5			
Mitotic inhibitors	<u>Colchicine</u>	CYP3A4	CYP3A5			
	<u>Febuxostat</u>	CYP1A2, CYP2C8	CYP2C9, UGT1A1, UGT2B7		Ø	
Xanthine oxidase inhibitors	Allopurinol	AOX1	Renal Excretion, HLA-B*5801			
	<u>Oxypurinol</u>	Renal Excretion				
Recombinant urate oxidase	Rasburicase		G6PD, CYB5R1, CYB5R2, CYB5R3, CYB5R4		Ø	
	<u>Azathioprine</u>	хо	TPMT, AOX1		Ø	
Antimetabolites	<u>Methotrexate</u>	Renal Excretion	AOX1, SLC01B1, SLC19A1, ABCC1, ABCC2, ABCC3, ABCG2		Ø	
DMARDs	<u>Leflunomide</u>	CYP1A2			Ø	
Anti-inflammatory	<u>Tofacitinib</u>	CYP3A4	CYP2C19, CYP3A5		Ø	
	Abbreviation	s: DMARDs, Disease-modifying antirhe	umatic drugs; RE, renal excretion (unch	nanged drug).		

Additional SNPs of Importance for Pain Management

Gene	Marker	Genotype	Drug	Level of Evidence	Results
COMT	rs4680	G/G	Paroxetine	3	Patients may require a higher dose

PGx Report - Internal Medicine

Type: Drugs Prescribed for the Modulation of Respiratory Function

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Resp	iratory			
Anticholinergic	<u>Umeclidinium</u>	CYP2D6				
Anticholinergic	<u>Aclidinium</u>	CYP2D6	CYP3A4, CYP3A5			
	<u>Arformoterol</u>	CYP2D6, UGT1A1	CYP2C19			
	<u>Indacaterol</u>	UGT1A1, CYP3A4	CYP3A5, CYP1A2, CYP2D6		Ø	
Beta2-adrenergic agonist	<u>Formoterol</u>	CYP2D6	CYP2C19, CYP2C9, CYP2A6		Ø	
	Salmeterol	CYP3A4	CYP3A5			
	<u>Vilanterol</u>	CYP3A4	CYP3A5		Ø	
	<u>Budesonide</u>	CYP3A4	CYP3A5		Ø	
Corticosteroid	<u>Fluticasone</u>	CYP3A4	CYP3A5		Ø	
	<u>Mometasone</u>	CYP3A4	CYP3A5		Ø	
Dhaankadi atawa i ahihitan	<u>Roflumilast</u>	CYP3A4	CYP1A2, CYP3A5		Ø	
Phosphodiesterase inhibitor	Theophylline	CYP1A2	CYP2E1			
5-lipoxygenase inhibitor	<u>Zileuton</u>	CYP1A2	CYP2C9, CYP3A4, CYP3A5		Ø	
	<u>Montelukast</u>	CYP3A4	CYP2C9, CYP3A5, SLCO2B1, ABCC1			
Leukotriene receptor-1 antagonist	<u>Pranlukast</u>	CYP3A4	CYP3A5		8	
untagonist	Zafirlukast	CYP2C9	CYP3A4, CYP3A5			
Treatment of cystic fibrosis (specifics mutations in the CFTR gene)	<u>lvacaftor</u>	СҮРЗА4	CYP3A5, CFTR		Ø	_
		Abbreviations: CFTR, Cystic fibrosis to	ransmembrane conductance regulator.			

PGx Report - Internal Medicine

Type: Antiemetic

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Antie	emetic			
Antiemetic, 5-HT3 receptor	<u>Dolasetron</u>	CYP3A4	CYP2D6, CYP3A5			
antagonist Indole derivative	<u>Tropisetron</u>	CYP3A4	CYP2D6, CYP3A5			
Antiemetic, 5-HT3 receptor antagonist Isoquinoline derivative	<u>Palonosetron</u>	CYP1A2	CYP2D6, CYP3A4, CYP3A5		Ø	
Antiemetic, 5-HT3 receptor antagonist Indazole derivative	Granisetron	СҮРЗА4	СҮРЗА5			
Antiemetic, 5-HT3 receptor antagonist	<u>Ondansetron</u>	CYP2B6	CYP1A2, CYP2D6, CYP3A4, ABCB1			
	<u>Domperidone</u>	CYP3A4	CYP3A5		Ø	
Antiemetic, dopamine-	<u>Prochlorperazine</u>	CYP2D6	CYP3A4, CYP3A5			
receptor antagonist	<u>Metoclopramide</u>	CYP2D6	CYP1A2, CYB5R1, CYB5R2, CYB5R3, CYB5R4		Ø	
Antiemetic, NK1 receptor antagonist	<u>Aprepitant</u>	CYP3A4	CYP3A5, CYP1A2, CYP2C19			
	<u>Diphenhydramine</u>	CYP2D6	CYP3A4, CYP3A5, UGT1A3, UGT1A4			
Antiemetic, H1 histamine receptor antagonist	<u>Hydroxyzine</u>	ADHs	CYP3A4, CYP3A5		Ø	
- Cooper unagomor	<u>Promethazine</u>	CYP2D6	SULTs		Ø	
Cannabinoids	<u>Dronabinol</u>	CYP2C9	CYP2C19, CYP3A4, CYP3A5			
	<u>Lorazepam</u>	UGT2B15	UGT2B7			
Benzodiazepines	Midazolam	CYP3A4	CYP3A5		0	
Anticholinergics	<u>Scopolamine</u>	CYP3A4	CYP3A5		0	
Steroids	<u>Dexamethasone</u>	CYP3A4	CYP17A1, CYP3A5		0	
		Abbreviations: 5-HT, Ser	otonin; NK1, neurokinin 1.			

PGx Report - Internal Medicine

Type: Drugs Prescribed for the Treatment of Peptic Ulcers and/or Gastro-Esophageal Reflux Disease

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity			
Histamine H2-receptor antagonists	<u>Ranitidine</u>	Renal Excretion	CYP1A2, CYP2C19, CYP3A4, CYP3A5						
	<u>Omeprazole</u>	CYP2C19	CYP3A4, CYP2C9, CYP3A5						
	<u>Dexiansoprazole</u>	CYP2C19	CYP3A4, CYP3A5						
	<u>Esomeprazole</u>	CYP2C19	CYP3A4, CYP3A5						
Proton-pump inhibitor	<u>Lansoprazole</u>	CYP3A4	CYP2C19, CYP3A5						
	<u>Rabeprazole</u>	Non Enz	CYP2C19, CYP3A4, CYP3A5		Ø				
	<u>Ilaprazole</u>	CYP3A4	CYP3A5		Ø				
	<u>Pantoprazole</u>	CYP2C19	CYP3A4, CYP2D6, CYP2C9, CYP3A5		Ø				
	Abbreviations: Non Enz, non-enzymatic metabolism.								

PGx Report - Internal Medicine

Type: Drugs Prescribed for the Treatment of Functional Gastrointestinal Disorders, Obesity

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
Acting on serotonin	<u>Alosetron</u>	CYP2C9	CYP3A4, CYP1A2			
receptors 5-HT3 antagonists	<u>Cilansetron</u>	CYP3A4	CYP2D6, CYP1A2, CYP2C19, CYP3A5			
Acting on serotonin	<u>Mosapride</u>	CYP3A4	CYP3A5		Ø	
receptors 5-HT4 agonists	<u>Prucalopride</u>	Renal Excretion	CYP3A4, CYP3A5		Ø	
·		Gastrop	rokinetic			
Serotonin 5-HT4 receptor	<u>Cisapride</u>	CYP3A4	CYP3A5			
agonist	<u>Cinitapride</u>	CYP3A4	CYP2C8, CYP3A5		Ø	
Parasympatho mimetic	<u>Itropride</u>	FMO3			Ø	
	<u>Metoclopramide</u>	CYP2D6	CYP1A2, CYB5R1, CYB5R2, CYB5R3, CYB5R4		Ø	
Dopamine antagonists	<u>Clebopride</u>	CYP3A4	CYP3A5		Ø	
	<u>Domperidone</u>	CYP3A4	CYP3A5		Ø	
·		Antipro	pulsives			
Opioids	<u>Loperamide</u>	CYP3A4	CYP2C8, CYP3A5			
Opioids	<u>Morphine</u>	UGT2B7	ABCB1, UGT1A1, COMT		Ø	
		Centrally acting	anti-obesity drugs			
Stimulant/ Amphetamine/	Sibutramine	CYP3A4	СҮРЗА5			
Appetite suppressant agent	<u>Phentermine</u>	Renal Excretion	CYP3A4, CYP3A5		Ø	
Anorectic <u>Lorcaserin</u> CYF		CYP2D6	CYP3A4, CYP3A5		Ø	

PGx Report - Internal Medicine

Type: Diabetes

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Antidiabetic S	Secretagogues			
Meglitinides	<u>Repaglinide</u>	CYP2C8	SLCO1B1, CYP3A4, CYP3A5, ABCC8			
Megittilides	<u>Nateglinide</u>	CYP2C9	CYP3A4, CYP3A5			
	<u>Chlorpropamide</u>	Renal Excretion	CYP2D6, G6PD		Ø	
Sulfonylurea 1st generation	<u>Tolazamide</u>	CYP2C9				
	<u>Tolbutamide</u>	CYP2C9	CYP2C19, CYP2C8			
	<u>Glipizide</u>	CYP2C9	G6PD			
	<u>Glyburide</u>	CYP3A4	CYP2C9, CYP2C19, CYP3A5, G6PD			
Sulfonylurea 2nd generation	Gliquidone	CYP2C9				
	<u>Gliclazide</u>	CYP2C9	CYP2C19		Ø	_
	<u>Glimepiride</u>	CYP2C9	G6PD			
	Saxagliptin	CYP3A4	CYP3A5			
DDD W4: 1:1:	<u>Alogliptin</u>	Renal Excretion	CYP2D6, CYP3A4, CYP3A5			
DPP-IV inhibitor	<u>Linagliptin</u>	Renal Excretion	CYP3A4, CYP3A5			
	Sitagliptin	CYP3A4	CYP2C8, CYP3A5			
-		Antidiabetio	Sensitizers			
Biguanides	<u>Metformin</u>	Renal Excretion			Ø	
Thiazolidinediones	<u>Pioglitazone</u>	CYP2C8	CYP3A4, CYP3A5		Ø	
iniazolidinediones	Rosiglitazone	CYP2C8	CYP2C9			
	Abbreviat	ions: DPP-IV, Dipeptidyl peptidase-4; S0	GLT2, sodium/glucose cotransporter 2 o	r gliflozins.		

PGx Report - Internal Medicine

Type: Migraine, Antihistamine, Abortifacient, Drugs Prescribed for the Treatment of Hyperparathyroidism, Dermatology

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Anti-	migraine			
	<u>Almotriptan</u>	CYP3A4	CYP2D6, CYP3A5			
	<u>Eletriptan</u>	CYP3A4	CYP3A5			
Selective serotonin (5-HT1)	<u>Frovatriptan</u>	CYP1A2				
agonists	<u>Naratriptan</u>	CYP1A2	CYP2C8, CYP2C9, CYP2D6			
	Sumatriptan	MAO	UGTs, HTR2A		Ø	
	Zolmitriptan	CYP1A2				
	<u>Dihydroergotamine</u>	CYP3A4	CYP3A5			
Ergot alkaloids	<u>Ergotamine</u>	CYP3A4	CYP3A5			
		Antih	istamines			ı
Aminoalkyl ethers <u>Diphenhydramine</u>		CYP2D6	CYP3A4, CYP3A5, UGT1A3, UGT1A4		Ø	
Substituted alkylamines <u>Chlorpheniramine</u>		CYP3A4	CYP3A5		Ø	
Phenothiazine derivatives	<u>Promethazine</u>	CYP2D6	SULTs		Ø	
	<u>Hydroxyzine</u>	ADHs	CYP3A4, CYP3A5			
Piperazine derivatives	Cyclizine	CYP2D6				
	<u>Cetirizine</u>	Renal Excretion				
	<u>Terfenadine</u>	CYP3A4	CYP3A5			
	<u>Loratadine</u>	CYP3A4, CYP2D6	CYP3A5, CYP2C8, CYP2C9		a	
Other antihistamines	<u>Fexofenadine</u>	Biliary Excretion	Renal Excretion, CYP3A4, CYP3A5, SLCO2B1		0	
	<u>Desloratadine</u>	CYP2C8			Ø	
	<u>Astemizole</u>	CYP3A4	CYP3A5			
		Treatment of second	lary hyperparathyroidism			'
Calcimimetic	<u>Cinacalcet</u>	CYP3A4	CYP2D6, CYP3A5, CYP1A2			
			rtifacient			
Progestin Antagonist	Mifepristone	CYP3A4	CYP3A5			
			gy Antipsoriatics			ı
Retinoids	<u>Etretinate</u>	CYP26A1				
	<u>Acitretin</u>	CYP26A1				
			ogy Anti-acne			I
Retinoid	<u>Isotretinoin</u>	CYP2C8	CYP2C9, CYP3A4, CYP2B6, CYP3A5			

PGx Report - Modulation of Cardiovascular Function

Type: Antiarrhythmic

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
	<u>Quinidine</u>	CYP3A4, CYP2D6	CYP2E1, CYP3A5, CYP2C9, CYP2C8		Ø	
Antiorrhythmic class la	<u>Procainamide</u>	CYP2D6	NAT2			
Antiarrhythmic class la	<u>Sparteine</u>	CYP2D6				
	<u>Disopyramide</u>	CYP3A4	CYP3A5, CYP1A2, CYP2C19		Ø	
	<u>Phenytoin</u>	CYP2C19	CYP2C9, CYP3A4, CYP3A5, CYP2D6, ABCB1, EPHX1, HLA-B*1502		Ø	
Antiarrhythmic class Ib	<u>Tocainide</u>	UGTs				
, , , , , , , , , , , , , , , , , , , ,	<u>Lidocaine</u>	CYP1A2	CYP3A4, CYP3A5			
	<u>Mexiletine</u>	CYP2D6	CYP1A2		Ø	
	<u>Propafenone</u>	CYP2D6	CYP3A4, CYP1A2, CYP3A5			
Antiarrhythmic class Ic	<u>Flecainide</u>	CYP2D6				
	<u>Encainide</u>	CYP2D6				
	<u>Carvedilol</u>	CYP2D6	UGT1A1, CYP2C9			
Antiquebuthmic close II	<u>Bisoprolol</u>	CYP2D6	CYP3A4, CYP3A5		Ø	
Antiarrhythmic class II	<u>Metoprolol</u>	CYP2D6	CYP3A4, CYP3A5		Ø	
	<u>Propranolol</u>	CYP2D6	CYP1A2, CYP2C19, CYP3A4, CYP3A5		Ø	
	<u>Amiodarone</u>	CYP3A4	CYP2C8, CYP3A5		Ø	
Antiarrhythmic class III	<u>Dronedarone</u>	CYP3A4	CYP3A5		Ø	
	<u>Dofetilide</u>	Renal Excretion	CYP3A4, CYP3A5		Ø	
Antiorphythmic class IV	<u>Diltiazem</u>	CYP3A4	CYP2C19, CYP3A5		Ø	
Antiarrhythmic class IV	<u>Verapamil</u>	CYP3A4	CYP2C8, CYP3A5, ABCB1			

PGx Report - Modulation of Cardiovascular Function

Type: Antihypertensive I

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Antihype	ertensives			
	<u>Losartan</u>	CYP2C9	CYP3A4, CYP3A5, UGT1A1			
	<u>Azilsartan</u>	CYP2C9				
Angiotensin II receptor	<u>Irbesartan</u>	CYP2C9				
antagonist	<u>Telmisartan</u>	Biliary Excretion	UGT1A1		Ø	
	<u>Olmesartan</u>	Hydrolysis	Renal Excretion, SLCO1B1			
	<u>Valsartan</u>	CYP2C9				
	<u>Captopril</u>	Renal Excretion	CYP2D6			
Angiotensin-Converting Enzyme Inhibitors	<u>Enalapril</u>	CES1, Renal Excretion	CYP3A4, CYP3A5			
Enzyme minotors	<u>Trandolapril</u>	CES1	CYP2D6, CYP2C9, Renal Excretion			
Renin inhibitors	<u>Aliskiren</u>	CYP3A4	CYP3A5, ABCB1		Ø	
Aldosterone Antagonists	<u>Eplerenone</u>	CYP3A4	CYP3A5		Ø	
Loop diuretic	<u>Torasemide</u>	CYP2C9	CYP2C8, Renal Excretion			
Thiazide-like diuretic	<u>Indapamide</u>	CYP3A4	CYP3A5		Ø	
Potassium-sparing diuretic	<u>Triamterene</u>	CYP1A2			Ø	
Vasopressin receptor antagonists	<u>Tolvaptan</u>	CYP3A4	CYP3A5		Ø	
Adrenergic release inhibitors	<u>Debrisoquine</u>	CYP2D6				
Peripheral Adrenergic Reserpine		CYP2D6				Ø
	Metoprolol	CYP2D6	CYP3A4, CYP3A5			
Beta-1 cardioselective beta- blockers	<u>Bisoprolol</u>	CYP2D6	CYP3A4, CYP3A5		Ø	
	<u>Nebivolol</u>	CYP2D6				

PGx Report - Modulation of Cardiovascular Function

Type: Antihypertensive II

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
<u>'</u>		Antihype	ertensives			
Nonselective beta-blockers	<u>Timolol</u>	CYP2D6				
Nonselective beta-blockers	<u>Propranolol</u>	CYP2D6	CYP1A2, CYP2C19, CYP3A4, CYP3A5			
Beta-blockers with alpha	<u>Carvedilol</u>	CYP2D6	UGT1A1, UGT2B4, CYP2C9			
activity	<u>Labetalol</u>	CYP2D6	CYP2C19, ABCB1, UGT1A1, UGT2B7		Ø	
Almha hiadiana	<u>Terazosin</u>	CYP3A4	CYP3A5		Ø	
Alpha blockers	<u>Doxazosin</u>	CYP2D6	CYP2C19, CYP3A4, CYP3A5			
	Clonidine	CYP2D6	CYP1A2, CYP3A4, CYP3A5			
α-2 adrenergic agonist	<u>Tizanidine</u>	CYP1A2				
		Antihypertensives Ca	lcium channel blockers			1
	<u>Amlodipine</u>	CYP3A4	СҮРЗА5			
Dibudronuridino	<u>Nifedipine</u>	CYP3A4	CYP1A2, CYP2A6, CYP3A5		Ø	
Dihydropyridine	<u>Nimodipine</u>	CYP3A4	CYP3A5		Ø	
	<u>Nicardipine</u>	CYP2C8	CYP2D6, CYP3A4, CYP3A5		Ø	
Benzothiazepine	<u>Diltiazem</u>	CYP3A4	CYP2C19, CYP3A5			
Phenylalkylamine	<u>Verapamil</u>	CYP3A4	CYP2C8, CYP3A5, ABCB1			
Nonselective	<u>Bepridil</u>	CYP3A4	CYP3A5			
'		Anti-pulmonary ar	terial hypertension			'
ERA-Dual antagonists	<u>Bosentan</u>	CYP2C9	CYP3A4, CYP3A5, SLCO1B3			
LINA-Dual alitagonists	<u>Macitentan</u>	CYP3A4	CYP2C19, CYP3A5		Ø	
Dhaanhadiaatayaaa inhibit	<u>Sildenafil</u>	CYP3A4	CYP2C9, CYP3A5		Ø	
Phosphodiesterase inhibitors	<u>Tadalafil</u>	CYP3A4	CYP3A5		Ø	
		Abbreviations: ERA, endo	thelin receptor antagonist.			

PGx Report - Modulation of Cardiovascular Function

Type: Cardiac stimulant, Vasodilator, Drugs Prescribed for the Treatment of Angina

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity		
		Cardiac s	timulants					
Digitalis glycosides	<u>Digoxin</u>	Renal Excretion	ABCB1, SLCO1B3, ABCB4					
	<u>Epinephrine</u>	MAO	COMT		Ø			
Adrenergic and	<u>Phenylephrine</u>	MAO	SULTs, UGTs					
dopaminergic agents	<u>Dopamine</u>	ALDH1A1, ALDH2	DBH, MAOA, MAOB, SULT1A3, SULT1A4, COMT		Ø			
	<u>Synephrine</u>	MAO			Ø			
		Vasodilators used	in cardiac diseases					
Organic nitrates	Isosorbide dinitrate	NAT2	NAT1					
Other Vasodilators	<u>Hydralazine</u>	NAT2	NAT1, CYP1A2, CYP3A4, CYP3A5					
Other Drugs Used in Angina								
Other carding preparations	<u>Ranolazine</u>	CYP3A4	CYP2D6, CYP3A5					
Other cardiac preparations	<u>Ivabradine</u>	CYP3A4	CYP3A5		Ø			

PGx Report - Modulation of Cardiovascular Function

Type: Dyslipidemia

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Drug Therapy for Hypercholeste	erolemia and Dyslipidemia (Liver)			•
	<u>Atorvastatin</u>	CYP3A4, SLCO1B1	ABCG2, CYP3A5, ABCB1, ABCG8, UGT1A1, UGT2B7, KIF6			
	<u>Fluvastatin</u>	CYP2C9, SLCO1B1	ABCG2, CYP3A4, CYP2C8, UGT1A1, UGT2B7			Ø
	<u>Lovastatin</u>	CYP3A4, SLCO1B1	CYP3A5, UGT1A1			
HMG CoA reductase inhibitors Statins	Cerivastatin	CYP3A4, SLCO1B1	CYP2C8, CYP3A5			
	<u>Pitavastatin</u>	UGT2B7	CYP2C9, CYP2C8, ABCB1			
	Simvastatin	CYP3A4, SLCO1B1	ABCG2, CYP3A5, ABCB1, SLCO2B1, UGT1A1, UGT2B7, KIF6		Ø	
	<u>Rosuvastatin</u>	UGT1A1	ABCG2			
MTTP inhibitors	<u>Lomitapide</u>	CYP3A4	CYP3A5, LDLR			
		Drug Therapy for Hypercholes	terolemia and Dyslipidemia (GI)			
Cholesterol absorption inhibitors	<u>Ezetimibe</u>	UGT1A1	UGT2B15			
		Drug Therapy for Hypercholesterole	mia and Dyslipidemia (Blood vessels)			
Fibrates	Gemfibrozil	CYP3A4	CYP3A5, UGT2B7, UGT1A1, UGT2B15			
Tibrates	<u>Clofibrate</u>	UGT2B7				
		Drug Therapy for famili	ial hypercholesterolemia			
Cholesterol-reducing drug (antisense oligonucleotide)	<u>Mipomersen</u>	Nuclease, Renal Excretion	LDLR			
		rosuv	astatin			

PGx Report - Modulation of Cardiovascular Function

Type: Anticoagulant, Antiplatelet

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Blood Coagulation and Antico	agulant, and Antiplatelet Drugs			
	<u>Warfarin</u>	CYP2C9, VKORC1	CYP2C19, CYP1A2, CYP3A4, EPHX1, PROC, PROS1			
Vitamin K antagonist	<u>Acenocoumarol</u>	CYP2C9, VKORC1	CYP2C19, CYP1A2			
	<u>Phenprocoumon</u>	CYP2C9, VKORC1	CYP3A4, CYP2C8		Ø	
Direct factor Xa inhibitors	<u>Rivaroxaban</u>	CYP3A4	CYP3A5		Ø	
Direct factor Aa infilbitors	<u>Apixaban</u>	CYP3A4	CYP3A5		Ø	
Antiplatelet Drugs						
ADP receptor (P2Y12) inhibitors Nucleotide/nucleo side analogs	<u>Ticagrelor</u>	СҮРЗА4	СҮРЗА5			
ADP receptor (P2Y12)	<u>Clopidogrel</u>	CYP2C19	ABCB1, ABCC3			
inhibitors Thienopyridines	<u>Prasugrel</u>	BCHE, CYP3A4	CYP2B6, CYP2C9, CYP2C19, CYP3A5, CYP2D6		Ø	
Irreversible cyclooxygenase inhibitors	GLYAT, UGTs, Renal Excretion		CYP2C9, CYP3A4, CYP3A5			
Phosphodiesterase inhibitors	Cilostazol	CYP3A4	CYP2C19, CYP3A5			
Protease-activated receptor- 1 (PAR-1) antagonists			CYP3A5		Ø	
		Abbreviations: P2Y12, p	urinergic receptor P2Y12.			

PGx Report - Psychiatry

Type: Antidepressant I

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
· ·		Antide	pressants			
	<u>Citalopram</u>	CYP2C19, CYP2D6	CYP3A4, CYP3A5, SLC6A4, HTR2A			
	<u>Escitalopram</u>	CYP3A4, CYP2C19	CYP2D6, CYP3A5, SLC6A4, HTR2C		Ø	
	<u>Dapoxetine</u>	CYP2D6	CYP3A4, CYP3A5			
SSRIs	<u>Fluoxetine</u>	CYP2D6	CYP3A4, CYP2C9, CYP3A5, CYP2C19, SLC6A4, HTR2A		Ø	
	<u>Paroxetine</u>	CYP2D6	CYP3A4, CYP1A2, CYP3A5, CYP2C9, SLC6A4, HTR2A, DRD3		Ø	
	<u>Sertraline</u>	CYP2B6	CYP2C19, CYP2C9, CYP3A4, CYP2D6, SLC6A4			
	<u>Fluvoxamine</u>	CYP2D6	CYP1A2, SLC6A4, HTR2A			
SMSs	<u>Vilazodone</u>	CYP3A4	CYP3A5, CYP2C19, CYP2D6		Ø	
	<u>Levomilnacipran</u>	CYP3A4	CYP2C8, CYP3A5, CYP2C19, CYP2D6		Ø	
	<u>Milnacipran</u>	UGTs	Renal Excretion			
SNRIs	<u>Venlafaxine</u>	CYP2D6	CYP2C19, CYP3A4, CYP2C9, CYP3A5, SLC6A3, SLC6A4, HTR2A		Ø	
	<u>Duloxetine</u>	CYP2D6	CYP1A2, HTR2A			
	<u>Atomoxetine</u>	CYP2D6	CYP2C19, CYP3A4, CYP3A5, SLC6A2		Ø	
NRIs	Reboxetine	CYP3A4	CYP3A5			
	<u>Maprotiline</u>	CYP2D6	CYP1A2			
TCAs that preferentially inhibit the reuptake of	Clomipramine	CYP2D6	CYP3A4, CYP2C19, CYP1A2, CYP2C9, SLC6A4, HTR2A		0	
serotonin	<u>Imipramine</u>	CYP1A2, CYP2D6	CYP2C19, CYP3A4, CYP3A5		Ø	
TCAs that preferentially	<u>Desipramine</u>	CYP2D6	CYP1A2, CYP2C19		Ø	
inhibit the reuptake of	<u>Nortriptyline</u>	CYP2D6	CYP1A2, CYP2C19, ABCB1, SLC6A4		Ø	
norepinephrine	<u>Protriptyline</u>	CYP2D6				

PGx Report - Psychiatry

Type: Antidepressant II

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Antidep	ressants			
TCAs that fairly balanced	<u>Amitriptyline</u>	CYP2D6	CYP3A4, CYP2C19, CYP2C9, CYP1A2, CYP2B6			
serotonin-norepinephrine reuptake inhibitors	<u>Doxepin</u>	CYP2D6, CYP2C19	CYP1A2, CYP3A4, CYP3A5			
reuptake illilibitors	<u>Dosulepin</u>	CYP2D6, CYP2C9	CYP3A4, CYP1A2, CYP3A5, CYP2C19			
T 04	<u>Mianserin</u>	CYP2D6	CYP3A4, CYP1A2, CYP2B6, CYP3A5		6	
TeCAs	<u>Amoxapine</u>	CYP2D6	CYP3A4, CYP3A5		6	
TCA with antipsychotic and sedative properties <u>Trimipramine</u>		CYP2D6	CYP2C19, CYP2C9		Ø	
MAOI	<u>Tranylcypromine</u>	MAO	CYP3A4, CYP2A6, CYP3A5, CYP2C19, CYP2D6		Ø	
	<u>Moclobemide</u>	CYP2C19	CYP2D6, CYP1A2, HTR2A		Ø	
		Atypical ant	tidepressants			
SMSs	<u>Vortioxetine</u>	CYP2D6	CYP2C9, CYP3A4, CYP3A5, UGTs, CYP2A6, CYP2C8, CYP2C19, CYP2B6			
NaSSAs	<u>Mirtazapine</u>	CYP1A2	CYP2D6, CYP3A4, CYP3A5, SLC6A4, HTR2A		Ø	
CARL	<u>Trazodone</u>	CYP3A4	CYP2D6, CYP3A5			
SARIs	<u>Nefazodone</u>	CYP2D6, CYP3A4	CYP3A5		6	
Antidepressant and smoking cessation aid	Bupropion	CYP2B6	CYP2E1, CYP3A4, CYP2D6, CYP1A2, CYP3A5			Ø
Antidepressant and anti- anxiety	<u>Buspirone</u>	СҮРЗА4	СҮРЗА5		Ø	

Abbreviations: SSRI, serotonin selective reuptake inhibitor; SMS, Serotonin modulator and stimulator; SNRI, serotonin-norepinephrine reuptake inhibitor; NRI, norepinephrine reuptake inhibitor; TCA, tricyclic antidepressant; TeCA, tetracyclic antidepressant; MAOI, monoamine oxidase inhibitor; NaSSA, noradrenergic and specific serotonergic antidepressant; SARI, serotonin antagonist and reuptake inhibitor.

Additional SNPs of Importance for the Treatment of Depression and Psychosis, and the Treatment of Alcohol and Tobacco Use Disorders

Gene	Marker	Genotype	Drug	Level of Evidence	Results
COMT	rs4680	G/G	Fluvoxamine	3	Schizophrenia patients may have a decreased risk for developing extrapyramidal symptoms
COMT	rs4680	G/G	Venlafaxine	3	Patients with Depressive Disorder may have increased response but patients with Anxiety Disorders may have a decreased response
COMT	rs4680	G/G	Paroxetine	3	Depressive patients may have a decreased response or decreased improvement

PGx Report - Psychiatry

Type: Typical Antipsychotic

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Typical ar	ntipsychotic			,
	<u>Bromperidol</u>	CYP3A4	CYP3A5			
Butyrophenones	<u>Droperidol</u>	CYP3A4	CYP3A5		Ø	
,	<u>Haloperidol</u>	UGTs, CYP3A4	CYP1A2, CYP2D6, CYP3A5, SLC6A4, HTR2C			
	<u>Chlorpromazine</u>	CYP2D6	CYP1A2, CYP3A4, CYP3A5		Ø	
Phenothiazines with aliphatic side-chain	<u>Levomepromazine</u>	CYP3A4	CYP1A2, CYP3A5			
	<u>Promazine</u>	CYP1A2	CYP3A4, CYP2C19, CYP2C9, CYP3A5			
	Cyamemazine	CYP1A2	CYP3A4, CYP2C9, CYP2C8, CYP3A5			
	<u>Fluphenazine</u>	CYP2D6				
Phenothiazines with	<u>Perphenazine</u>	CYP2D6				
piperazine structure	<u>Prochlorperazine</u>	CYP2D6	CYP3A4, CYP3A5			
	<u>Trifluoperazine</u>	CYP1A2				
Phenothiazines with piperidine structure	<u>Thioridazine</u>	CYP2D6	CYP1A2, CYP3A4, CYP2C19, CYP3A5		Ø	
Phenothiazines used as an anti-histamine, sedative, and antiemetic	<u>Promethazine</u>	CYP2D6	SULTs		Ø	
Diphenyl-butylpiperidine	<u>Pimozide</u>	CYP3A4, CYP2D6	CYP1A2, CYP3A5		Ø	
This could be a second as it is a first	<u>Thiothixene</u>	CYP1A2	CYP3A4, CYP3A5		Ø	
Thioxanthene derivative	Zuclopenthixol	CYP2D6	CYP3A4, CYP3A5		Ø	
Tricyclics	<u>Loxapine</u>	CYP1A2	CYP3A4, CYP2D6, CYP3A5		Ø	

PGx Report - Psychiatry

Type: Atypical antipsychotic

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Atypical a	ntipsychotic			
Diazepines, Oxazepines, Thiazepines and Oxepines	<u>Quetiapine</u>	CYP3A4, CYP2D6	CYP3A5, CYP1A2, CYP2C9, CYP2C19, SLC6A4			
	<u>Olanzapine</u>	CYP1A2	CYP2D6			
	<u>Asenapine</u>	CYP1A2	CYP2D6, CYP3A4, CYP3A5			
	<u>Clozapine</u>	CYP1A2, CYP2D6	CYP3A4, CYP2C9, CYP2C19, CYP3A5, CYP2A6, SLC6A3, SLC6A4, SLC1A1, HTR2C, DRD3		0	
	<u>Sertindole</u>	CYP2D6	CYP3A4, CYP3A5			
Indole derivatives	<u>Ziprasidone</u>	CYP3A4	AOX1, CYP3A5		8	
	<u>Lurasidone</u>	CYP3A4	CYP3A5		Ø	
	<u>Sulpiride</u>	Renal Excretion			Ø	
Benzamides	<u>Amisulpride</u>	Renal Excretion			%	
	<u>Aripiprazole</u>	CYP2D6	CYP3A4, CYP3A5, DRD3			
	Risperidone	CYP2D6	CYP3A4, CYP3A5, ABCB1, SLC6A4, SLC1A1, HTR2A, HTR2C, DRD3		Ø	
Other antipsychotics	<u>Iloperidone</u>	CYP2D6	CYP3A4, CYP3A5		Ø	
	<u>Paliperidone</u>	CYP2D6	CYP3A4, CYP3A5		Ø	
	<u>Zotepine</u>	CYP3A4	CYP1A2, CYP3A5, CYP2D6		%	

Additional SNPs of Importance in Treatment that Includes the Use of **Antipsychotics and for the Treatment of Autism**

Gene	Marker	Genotype	Drug	Level of Evidence	Results
COMT	rs4680	G/G	Haloperidol	3	Schizophrenia patients may have a decreased risk for developing extrapyramidal symptoms

PGx Report - Neurology

Type: Drugs Prescribed for the Treatment of ADHD, Related Drugs

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Anti ADHE	Stimulants			
A bb i	<u>Dextroamphetamine</u>	Renal Excretion, CYP2D6	DBH, FMO3, GLYAT			
Amphetamine	<u>Levoamphetamine</u>	Renal Excretion, CYP2D6	FMO3			
NDRI	<u>Dexmethylphenidate</u>	CYP2D6	Renal Excretion			
	<u>Lisdexamfetamine</u>	Hydrolysis	CYP2D6, Renal Excretion			
Psychostimulant	Methylphenidate	CYP2D6	Renal Excretion, SLC6A2, SLC6A3, SLC6A4, DRD3			Ø
		Anti ADHD N	Ion-stimulants			
NERI	<u>Atomoxetine</u>	CYP2D6	CYP2C19, CYP3A4, CYP3A5, SLC6A2			
Central alpha-2 Adrenergic Agonist	Clonidine	CYP2D6	CYP1A2, CYP3A4, CYP3A5		Ø	
	<u>Bupropion</u>	CYP2B6	CYP2E1, CYP3A4, CYP2D6, CYP1A2, CYP3A5			Ø
	<u>Imipramine</u>	CYP1A2, CYP2D6	CYP2C19, CYP3A4, CYP3A5, UGT1A3, UGT1A4		Ø	
Antidepressants	<u>Desipramine</u>	CYP2D6	CYP1A2, CYP2C19			
	Milnacipran	UGTs	Renal Excretion			
	Reboxetine	CYP3A4	CYP3A5			
Wakefulness-promoting	<u>Modafinil</u>	Hydrolysis, CYP2D6	CYP1A2, CYP3A4, CYP2B6, CYP3A5		2	
agent	<u>Armodafinil</u>	СҮРЗА4	CYP3A5		0	
		Anti-ir	nsomnia			
Melatonin Receptor Agonist	Ramelteon	CYP1A2	CYP2C19, CYP3A4, CYP3A5			
Abbrevia	tions: ADHD, Attention defici	t hyperactivity disorder; NERI; norepin	ephrine reuptake inhibitor, NDRI, norepi	nephrine-dopamine	reuptake inhibitor.	

PGx Report - Neurology

Type: Drugs Prescribed for the Treatment of Epilepsy

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Antie	pileptic			
Barbiturates	<u>Phenobarbital</u>	CYP2C19	ABCB1			
Carbamates	<u>Felbamate</u>	CYP3A4	CYP2E1, CYP3A5			
Carboxamides	<u>Carbamazepine</u>	СҮРЗА4	CYP2C8, CYP2B6, UGT2B7, CYP1A2, CYP3A5, ABCB1, HLA-B*1502, HLA- A*3101, ABCC2			
Fatty acids	<u>Tiagabine</u>	CYP3A4	CYP3A5, CYP1A2, CYP2D6, CYP2C19			
Fructose derivatives	<u>Topiramate</u>	Renal Excretion	CYPs, UGTs		Ø	
CARA	<u>Gabapentin</u>	Renal Excretion			Ø	
GABA analogs	<u>Pregabalin</u>	Renal Excretion			Ø	
Hydantoin	<u>Phenytoin</u>	CYP2C19	CYP2C9, CYP3A4, CYP3A5, CYP2D6, ABCB1, EPHX1, HLA-B*1502		Ø	
nyuantoiii	<u>Mephenytoin</u>	CYP2C19	CYP2C8, CYP2C9, CYP2B6, CYP1A2, CYP2D6			
Oxazolidinediones	<u>Trimethadione</u>	CYP2C9	CYP2E1, CYP3A4, CYP3A5			
Oxazonamediones	<u>Paramethadione</u>	CYP2C9				
Pyrimidinedione	<u>Primidone</u>	CYP2C9	CYP2C19		Ø	
	<u>Brivaracetam</u>	CYP2C19, CYP2C9	CYP3A4, CYP3A5, CYP2C8, CYP2B6		Ø	
Pyrrolidines	<u>Levetiracetam</u>	Renal Excretion			Ø	
	<u>Seletracetam</u>	Renal Excretion			Ø	
Succinimides	Ethosuximide	CYP3A4	CYP3A5, CYP2E1		Ø	
Sulfonamides	<u>Zonisamide</u>	CYP3A4	CYP2C19, CYP3A5		Ø	
Ohlo	<u>Lacosamide</u>	CYP2C9	CY2C19, CYP3A4		Ø	
Other	<u>Perampanel</u>	CYP3A4	CYP3A5		Ø	
		Abbreviations: GABA, g	amma-aminobutyric acid.			

PGx Report - Neurology

Type: Anxiolytic, Hypnotic, Sedative, Anticonvulsant, Muscle Relaxants

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Anxiolytic, Hypnotic, Sedative, Ar	nticonvulsant, and Muscle Relaxant			
	<u>Midazolam</u>	CYP3A4	CYP3A5			
Benzodiazepine Short-acting	<u>Triazolam</u>	CYP3A4	CYP3A5			
	<u>Brotizolam</u>	CYP3A4	CYP3A5			
	<u>Alprazolam</u>	CYP3A4	CYP3A5			
	<u>Bromazepam</u>	CYP1A2	CYP2D6		Ø	
Benzodiazepine	Clobazam	CYP2C19	CYP3A4, CYP3A5, CYP2B6			
	Flunitrazepam	CYP2C19	CYP2C9, CYP3A4, CYP3A5, NAT2			
	<u>Estazolam</u>	CYP3A4	CYP3A5			
	Clonazepam	CYP3A4	CYP2C19, CYP3A5, NAT2			
	Oxazepam-r	UGT2B7	UGT1A9		a	
Intermediate-acting	Oxazepam-s	UGT2B15				
	Quazepam	CYP3A4	CYP2C19, CYP3A5			
	Lormetazepam	CYP3A4	CYP3A5		0	
	Lorazepam-r	UGT2B7			2	
	<u>Lorazepam-s</u>	UGT2B15				
	Nitrazepam	CYP3A4	CYP3A5, NAT2			
	<u>Temazepam</u>	CYP2C19	CYP3A4, CYP3A5, UGT2B7		<u> </u>	
	<u>Diazepam</u>	CYP2C19, CYP3A4	CYP3A5, CYP2B6, CYP1A2		<u> </u>	
	Clorazepate	CYP3A4	CYP3A5		<u> </u>	
Benzodiazepine Long-acting	Chlordiazepoxide	CYP3A4	CYP3A5		<u> </u>	
	Flurazepam	CYP3A4	CYP3A5		<u> </u>	
	Nordazepam	CYP3A4	CYP3A5		<u> </u>	
	Zolpidem	CYP3A4	CYP3A5, CYP1A2, CYP2D6			
Nonbenzodiazepine	Zaleplon	AOX1, CYP3A4	CYP3A5			
hypnotic	Zopiclone	CYP3A4	CYP2C8, CYP2C9, CYP3A5			
	Eszopiclone	CYP3A4	CYP2E1, CYP3A5			

PGx Report - Neurology

Type: Drugs Prescribed for the Treatment of Alzheimer's and Parkinson's, Related Drugs

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Hav Increase Toxicity
		Anti-Alzhei	mer disease			
	<u>Tacrine</u>	CYP1A2	CYP2D6			
Acetylcholinesterase inhibitor	<u>Donepezil</u>	CYP2D6	CYP3A4, CYP3A5			
minotoi	<u>Galantamine</u>	CYP2D6	CYP3A4, CYP3A5			
NMDA receptor antagonist	<u>Memantine</u>	Renal Excretion	UGTs			
·		Anti-Parkinson disease	& Anti-multiple sclerosis			
Precursor of dopamine	Levodopa	AAAD	COMT, SLC22A1			
Inhibitor of MAO-B	<u>Selegiline</u>	CYP2B6	CYP2C9, CYP3A4, CYP3A5, CYP2A6, FMO3			Ø
IIIIIbitor of MAO-B	<u>Rasagiline</u>	CYP1A2			Ø	
	Bromocriptine	CYP3A4	CYP3A5			
Dopamine receptor agonists	<u>Pramipexole</u>	Renal Excretion	DRD3			
	Ropinirole	CYP1A2	UGTs, Renal Excretion			
Anticholinergics - Antimuscarinics	<u>Diphenhydramine</u>	CYP2D6	CYP3A4, CYP3A5, UGT1A3, UGT1A4		Ø	
Anti-hyperkinetic movement	<u>Tetrabenazine</u>	CYP2D6	CYP1A2		Ø	
Anti-amyotrophic lateral sclerosis drug	<u>Riluzole</u>	CYP1A2				
Anthracenedione	<u>Mitoxantrone</u>	CYP2E1				
Sphingosine 1-phosphate Receptor Modulator	Siponimod	CYP2C9	CYP3A4, CYP3A5			Ø
Selective blocker of members of voltage- activated K+ channels	<u>Dalfampridine</u>	Renal Excretion	CYP2E1		Ø	
	Al	breviations: NMDA, N-methyl-D-aspart	tate; COMT, Catechol-O-methyltransfera	se.		

Additional SNP of Importance for different Medical Condition and personality

Gene	Marker	Genotype	Results
ABCG2	rs2231142	G/G	Increased risk for Gout

PGx Report - Infectology

Type: Antibiotics

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Antibacterials: protein	synthesis inhibitors 50S			
Amphenicols	Chloramphenicol	CYP2C9	UGT2B7			
Lincosamides	<u>Clindamycin</u>	CYP3A4	CYP3A5			
·		Anti	biotic			
	Clarithromycin	CYP3A4	CYP3A5			
Macrolides	<u>Erythromycin</u>	CYP3A4				
	Telithromycin	CYP3A4	CYP3A5			
		Antibacterials: nu	cleic acid inhibitors			
DHPS inhibitor Short-acting	<u>Sulfadimidine</u>	NAT2	Renal Excretion			
sulfonamides	<u>Sulfapyridine</u>	NAT2	Renal Excretion			
OHPS inhibitor Intermediate- acting sulfonamides	Sulfamethoxazole	Renal Excretion	NAT2, CYP2C9			Ø
Anaerobic DNA inhibitors/	<u>Tinidazole</u>	CYP3A4	CYP3A5			
Nitroimidazole	Ornidazole	CYP3A4	CYP3A5			
DNA-dependent RNA	Rifampicin	CYP3A4	CYP2C8, CYP3A5, CYP2C19, CYP2A6, RE		Ø	
polymerase inhibitors	<u>Rifabutin</u>	CYP3A4	CYP1A2, CYP3A5			
	<u>Dapsone</u>	CYP2E1	NAT2, CYP3A4, CYP2C9, CYP3A5, CYP2D6, G6PD		Ø	
Other drugs against	<u>Bedaquiline</u>	CYP3A4	CYP2C8, CYP2C19, CYP3A5		Ø	
mycobacteria	<u>Isoniazid</u>	NAT2	CYP2E1, Renal Excretion			
	<u>Pyrazinamide</u>	AOX1, XDH	CYP1A2, CYP3A4, CYP3A5, RE			
		Abbreviations: DHPS, D	ihydropteroate synthase.			

PGx Report - Infectology

Type: Antimalarial, Anthelmintic, Antifungal

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Antin	nalarial			
	Chloroquine	CYP2C8	CYP3A4, CYP3A5, G6PD			
Aminoquinolines	<u>Hydroxychloroquine</u>	CYP2D6	CYP2C8, CYP3A4, CYP3A5			
Aminoquinolines	<u>Amodiaquine</u>	CYP2C8			Ø	
	<u>Primaquine</u>	CYP2D6	G6PD			
	<u>Quinine</u>	CYP3A4, CYP2D6	CYP2C19, CYP3A5, G6PD			
Methanolquinolines	<u>Mefloquine</u>	CYP3A4	CYP3A5			
	<u>Artemisinin</u>	CYP3A4	CYP2B6, CYP3A5			
	<u>Artemether</u>	CYP3A4	CYP3A5			
Artemisinin and derivatives	<u>Artesunate</u>	CYP2A6				
	Arteether	CYP3A4	CYP2B6, CYP3A5			
Biguanides	<u>Proguanil</u>	CYP2C19				
011 11 1 1 1	<u>Halofantrine</u>	CYP3A4	CYP3A5			
Other antimalarials	<u>Pentamidine</u>	CYP2C19	CYP1A2, CYP2D6			
		Anthe	elmintic			
Benzimidazoles	<u>Albendazole</u>	CYP3A4	CYP1A2, CYP3A5			
		Antif	ungals			
Imidazoles	<u>Ketoconazole</u>	CYP3A4	UGT1A1, CYP26A1			
	<u>Itraconazole</u>	CYP3A4				
Triazoles	<u>Voriconazole</u>	CYP2C19	CYP2C9, CYP3A4, CYP3A5			
	<u>Fluconazole</u>	Renal Excretion			Ø	
Allylamines	<u>Terbinafine</u>	CYP2C9	CYP1A2, CYP3A4, CYP2C8, CYP2C19			

PGx Report - Infectology

Type: Antiretroviral, Antiviral

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
	<u>Lopinavir</u>	CYP3A4	SLCO1B1, CYP3A5, ABCC1, ABCC2		Ø	
	Ritonavir	CYP3A4	CYP2D6, CYP3A5, ABCC1			
Protease inhibitor 1st	<u>Saquinavir</u>	CYP3A4	CYP3A5		Ø	
generation	<u>Indinavir</u>	CYP3A4	CYP2D6, CYP3A5, ABCC4		Ø	
	<u>Nelfinavir</u>	CYP2C19	CYP3A4, CYP3A5		Ø	
	<u>Fosamprenavir</u>	CYP3A4	CYP3A5		Ø	
	<u>Atazanavir</u>	CYP3A4	CYP3A5, ABCB1			
Protease inhibitor 2nd generation	<u>Darunavir</u>	CYP3A4	CYP3A5, SLCO3A1			
generation	<u>Tipranavir</u>	CYP3A4	CYP3A5			
	<u>Delavirdine</u>	CYP3A4	CYP2D6, CYP3A5			
NNRTI 1st generation	<u>Efavirenz</u>	CYP2B6	CYP2A6, ABCB1, SLCO3A1, ABCG2			
NNRTI 2nd generation	<u>Nevirapine</u>	CYP3A4	CYP2B6, CYP3A5, ABCB1, SLCO3A1			
	<u>Etravirine</u>	CYP3A4	CYP2C9, CYP2C19, CYP3A5		2	
	Rilpivirine	CYP3A4	CYP3A5			
Nucleoside reverse	Zidovudine	UGT2B7	Renal Excretion, SLCO3A1, ABCC1, ABCC4		Ø	
anscriptase inhibitor (NRTI)	<u>Abacavir</u>	ADH6	UGT1A1, ADK, HLA-B*5701		Ø	
Neuraminidase	<u>Zanamivir</u>	Renal Excretion			Ø	
inhibitors/release phase	<u>Peramivir</u>	Renal Excretion			Ø	
CCR5 Co-receptor Antagonist	<u>Maraviroc</u>	CYP3A4	CYP3A5		Ø	
	<u>Boceprevir</u>	CYP3A4	IFNL3, CYP3A5			
Hepatitis C Virus NS3/4A	<u>Telaprevir</u>	CYP3A4	CYP3A5, IFNL3		Ø	
Protease Inhibitor	<u>Paritaprevir</u>	CYP3A4	CYP3A5		Ø	
	Simeprevir	CYP3A4	CYP2C8, CYP2C19, CYP3A5, IFNL3		Ø	
	<u>Enfuvirtide</u>	CYP2C19	CYP2E1, CYP1A2		8	
Other authorizate	<u>Raltegravir</u>	UGT1A1	SLCO1A2			Ø
Other antivirals	<u>Elvitegravir</u>	CYP3A4	CYP3A5		Ø	
	<u>Dolutegravir</u>	UGT1A1, CYP3A4	CYP3A5			

PGx Report - Oncology, Hematology

Type: Antineoplastic I

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Alkylatir	ig agents			
Nitrogen mustard analogues	Cyclophosphamide	CYP2B6	CYP2C19, CYP3A4, CYP2C9, CYP3A5, ALDH1A1, ABCC3	Ø		
	<u>Iphosphamide</u>	CYP2B6	CYP3A4, CYP3A5			
Nitrosoureas	<u>Carmustine</u>	CYP1A2	Renal Excretion			
		Antimet	tabolites			
Folic acid analogues	Methotrexate	Renal Excretion	AOX1, SLCO1B1, SLC19A1, ABCC1, ABCC2, ABCC3, ABCG2			
	<u>Pemetrexed</u>	Renal Excretion	SLC19A1			
	<u>Mercaptopurine</u>	XO	TPMT, AOX1, SLC19A1			
	<u>Tioguanine</u>	HPRT1	TPMT		Ø	
Purine analogues	<u>Cladribine</u>	DCK	Renal Excretion			
	<u>Clofarabine</u>	DCK	Renal Excretion		Ø	
	<u>Nelarabine</u>	ADA	DCK, Renal Excretion, XO		Ø	
Pyrimidine analogues	<u>Tegafur</u>	CYP2A6	DPYD, TYMS			

PGx Report - Oncology, Hematology

Type: Antineoplastic II

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Plant alkaloids and o	other natural products			
Vinca alkaloids and	<u>Vincristine</u>	CYP3A4	CYP3A5, ABCC3			
analogues	<u>Vinblastine</u>	CYP3A4	CYP3A5		Ø	
Podophyllotoxin derivatives	Etoposide	CYP3A4	CYP3A5, CYP1A2, CYP2E1, ABCB1, UGT1A1		Ø	
	<u>Teniposide</u>	CYP2C19	CYP3A4, CYP3A5, ABCB1			
Taxanes	<u>Paclitaxel</u>	CYP2C8	CYP3A4, CYP3A5, ABCB1, SLC29A1		Ø	
Taxanes	<u>Docetaxel</u>	CYP3A4	CYP3A5, EPHX1, SLCO1B3, ABCC6		Ø	
·		Cytotoxic antibiotics a	and related substances			
Anthracyclines and related	<u>Doxorubicin</u>	ALDH1A1, ABCB1, GSTP1, NQO1	CYP3A4, CYP2B6, CYP3A5, CYP2C8, CYP2D6, ABCC2, ABCC3			
substances	<u>Mitoxantrone</u>	CYP2E1				
		Other antined	pplastic agents			
Platinum compounds	<u>Cisplatin</u>	Renal Excretion, NQO1, GSTP1	EPHX1, GSTM1, ABCB1, XPC, LRP2, SLC19A1, ABCC2, ABCC3			
Derivative of camptothecin	<u>Irinotecan</u>	UGT1A1, CYP3A4	CYP3A5, CYP2B6, SLCO1B1, SLCO1B3, ABCG2			

PGx Report - Oncology, Hematology

Type: Antineoplastic Targeted Therapy I

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Protein kinase i	nhibitor (receptor)			
	<u>Erlotinib</u>	CYP3A4	CYP1A2, CYP3A5			
Epidermal growth factor receptor (EGFR)	<u>Gefitinib</u>	CYP3A4	CYP2D6, CYP3A5, ABCG2			
	<u>Vandetanib</u>	CYP3A4	CYP3A5			
EGFR and epidermal growth	<u>Lapatinib</u>	CYP3A4, CYP2C19	CYP2C8, CYP3A5, HLA-DQA1*0201, HLA-DRB1*0701		Ø	
factor receptor (HER2)	<u>Neratinib</u>	CYP3A4	CYP3A5			
C-KIT and PDGFR	<u>Masitinib</u>	CYP3A4	CYP3A5		Ø	
FLT3	<u>Lestaurtinib</u>	CYP3A4	CYP3A5		Ø	
RET, VEGFR and EGFR	<u>Vandetanib</u>	CYP3A4	CYP3A5			
c-MET and VEGFR2	Cabozantinib	CYP3A4	CYP2C8, CYP3A5			
	<u>Axitinib</u>	CYP3A4	CYP1A2, CYP2C19, CYP3A5, UGT1A1			
	<u>Nintedanib</u>	CYP1A2	CYP2C9, CYP2C19, CYP2D6, CYP2E1		a	
	<u>Pazopanib</u>	CYP3A4, UGT1A1	CYP1A2, CYP2C8, CYP3A5		a	
Multiple targets (c-KIT,	<u>Ponatinib</u>	CYP3A4	CYP2C8, CYP2D6, CYP3A5		a	
FGFR, PDGFR and VEGFR)	Regorafenib	CYP3A4	CYP3A5		Ø	
	<u>Sorafenib</u>	CYP3A4	CYP3A5		2	
	Sunitinib	CYP3A4	CYP3A5, ABCG2		<u> </u>	
	Toceranib	CYP3A4	CYP3A5			
		Protein kinase inh	ibitor (non-receptor)			
	<u>Imatinib</u>	CYP3A4	CYP3A5, ABCB1, ABCG2		Ø	
BCR-ABL	<u>Nilotinib</u>	CYP3A4, UGT1A1	CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP3A5, ABCG2		Ø	
	<u>Dasatinib</u>	CYP3A4	CYP3A5, ABCG2			
	<u>Ponatinib</u>	CYP3A4	CYP2C8, CYP2D6, CYP3A5		Ø	
Src	<u>Bosutinib</u>	CYP3A4	CYP3A5			
	<u>Lestaurtinib</u>	CYP3A4	CYP3A5		Ø	
	Ruxolitinib	CYP3A4	CYP3A5			
Janus kinase	<u>Pacritinib</u>	CYP3A4	СҮРЗА5			
	<u>Tofacitinib</u>	CYP3A4	CYP2C19, CYP3A5		<u> </u>	

PGx Report - Oncology, Hematology

Type: Antineoplastic Targeted Therapy II

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Protein kinase inhi	bitor (non-receptor)			
EML4-ALK	<u>Ceritinib</u>	CYP3A4	CYP2C9, CYP3A5			
LML4-ALK	<u>Crizotinib</u>	CYP3A4	CYP3A5			
Bruton tyrosine kinase	<u>Ibrutinib</u>	CYP3A4	CYP2D6, CYP3A5			
BRAF inhibitor (V600E mutation-positive)	<u>Dabrafenib</u>	CYP2C8	CYP3A4, CYP3A5, G6PD		Ø	
		Other Targ	eted therapy			
mTOR Inhibitors	<u>Sirolimus</u>	CYP3A4	CYP3A5			
IIIIOK IIIIIIbitois	<u>Everolimus</u>	CYP3A4	CYP2C8, CYP3A5			
Hedgehog pathway inhibitor	<u>Vismodegib</u>	CYP2C9	CYP3A4, CYP3A5			
		Hormone antagonis	ts and related agents			
Selective estrogen receptor	<u>Toremifene</u>	CYP3A4	CYP2D6, CYP3A5			
modulators (SERM)	<u>Tamoxifen</u>	CYP2D6, CYP3A4, CYP2C9	CYP3A5, CYP2B6, CYP2C19, CYP1A2, SULT1A1, F2, F5, ABCC2			
SERD	<u>Fulvestrant</u>	CYP3A4	CYP3A5			
	<u>Flutamide</u>	CYP1A2	CYP3A4, CYP3A5		Ø	
	<u>Nilutamide</u>	CYP2C19				
Anti-androgens	<u>Bicalutamide</u>	CYP3A4	CYP3A5			
	Enzalutamide	CYP2C8	CYP3A4, CYP3A5			
	<u>Anastrozole</u>	CYP3A4	CYP3A5, UGT1A4			
Aromatase inhibitors	<u>Letrozole</u>	CYP3A4	CYP2A6, CYP3A5			
	Exemestane	CYP3A4	CYP3A5		2	
Other hormone antagonists and related agents	<u>Abiraterone</u>	СҮРЗА4	CYP3A5, SULT2A1		Ø	
		Hema	ntologic			
Thrombopoiesis Stimulating Agent	Eltrombopag	CYP1A2	CYP2C8, F5, SERPINC1			

Abbreviations: C-KIT, tyrosine-protein kinase Kit; PDGFR, Platelet-derived growth factor receptor; FLT3, FMS-like tyrosine kinase-3; RET, RET proto-oncogene; VEGFR, Vascular endothelial growth factor receptor; Src, Proto-oncogene tyrosine-protein kinase Src; EML4-ALK, echinoderm microtubule associated protein like 4 – anaplastic lymphoma kinase; BRAF, proto-oncogene B-Raf; mTOR mammalian target of rapamycin; SERD, selective estrogen receptor down-regulator.

PGx Report - Organ Transplantation

Type: Immunosuppressive, Immunomodulation

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Immunos	uppressive			
Antimetabolite	Mycophenolate mofetil	CYP3A4	CYP3A5, CYP2C8, UGT2B7, SLCO1B1, SLCO1B3, ABCC2, HPRT1		Ø	
	<u>Azathioprine</u>	XO	TPMT, AOX1			
	<u>Pimecrolimus</u>	CYP3A4	СҮРЗА5			
Calcineurin Inhibitors	<u>Tacrolimus</u>	CYP3A5	CYP3A4, ABCB1, UGT2B7			
	<u>Cyclosporine</u>	CYP3A4	CYP3A5, ABCB1, UGT2B7, ABCC2			
mTOR Inhibitors	<u>Temsirolimus</u>	CYP3A4	СҮРЗА5			
IIIION IIIIIbilois	<u>Everolimus</u>	CYP3A4	CYP2C8, CYP3A5	Ø		
		Immunor	nodulation			
Immunomodulator and anti- angiogenic	<u>Pomalidomide</u>	CYP1A2	CYP3A4, CYP2C19, CYP2D6, CYP3A5		Ø	

PGx Report - Anesthesiology

Type: Anesthetic, Muscle Relaxant

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Inhaled A	nesthetics			
	<u>Enflurane</u>	CYP2E1				
	<u>Halothane</u>	CYP2E1	CYP3A4, CYP2A6, CYP3A5			
Inhaled Agents	<u>Isoflurane</u>	CYP2E1	CYP2B6		Ø	
	<u>Methoxyflurane</u>	CYP2E1	CYP1A2, CYP2C9, CYP2D6			
	<u>Sevoflurane</u>	CYP2E1				
		Intravenous age	ents (non-opioid)			
Barbiturates	<u>Hexobarbital</u>	CYP2C19	CYP2C9, CYP2E1, CYP1A2			
barbiturates	<u>Thiamylal</u>	CYP2C9				
	<u>Diazepam</u>	CYP2C19, CYP3A4	CYP3A5, CYP2B6, CYP1A2		Ø	
Benzodiazepines	<u>Lorazepam</u>	UGT2B15	UGT2B7		Ø	
	<u>Midazolam</u>	CYP3A4	CYP3A5		Ø	
Other Anesthetics	<u>Ketamine</u>	CYP3A4	CYP2B6, CYP2C9, CYP3A5		Ø	
		Skeletal mus	scle relaxants		_	
	<u>Carisoprodol</u>	CYP2C19				
Muscle Relaxants	<u>Cyclobenzaprine</u>	CYP1A2	CYP2D6, CYP3A4, CYP3A5		Ø	
	<u>Tizanidine</u>	CYP1A2				

PGx Report - Urology

Type: Drugs Prescribed for the Treatment of Incontinence, Erectile Dysfunction, Benign Prostatic Hypertrophy

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Drugs for urinary frequ	uency and incontinence			
	<u>Oxybutynin</u>	CYP3A4	СҮРЗА5			
A satisfaction assis	<u>Tolterodine</u>	CYP2D6, CYP3A4	CYP2C9, CYP3A5, CYP2C19		Ø	
Anticholinergic	<u>Solifenacin</u>	CYP3A4	CYP3A5		Ø	
	<u>Darifenacin</u>	CYP2D6	CYP3A4, CYP3A5		Ø	
		Drugs used in er	ectile dysfunction			
	<u>Sildenafil</u>	CYP3A4	CYP2C9, CYP3A5			
	<u>Tadalafil</u>	CYP3A4	CYP3A5		Ø	
Phosphodiesterase inhibitors	<u>Vardenafil</u>	CYP3A4	CYP2C9, CYP3A5		Ø	
	<u>Avanafil</u>	CYP3A4	CYP3A5			
	<u>Udenafil</u>	CYP3A4	CYP3A5			
'		Drugs used in benign	prostatic hypertrophy			
	<u>Alfuzosin</u>	CYP3A4	CYP3A5, Renal Excretion		Ø	
Alpha-adrenoreceptor antagonists	<u>Tamsulosin</u>	CYP3A4	CYP2D6, CYP3A5, Renal Excretion		Ø	
untagonists	Silodosin	CYP3A4	UGT2B7, CYP3A5		2	
Testosterone-5-alpha	<u>Finasteride</u>	CYP3A4	CYP3A5			
reductase inhibitors	<u>Dutasteride</u>	CYP3A4	CYP3A5			

PGx Report - Endocrinology

Type: Contraceptives, Androgens, Antiandrogens, Glucocorticoid, Thyroid

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
		Hormonal co	ontraceptives			
Estrogens	<u>Ethinylestradiol</u>	CYP3A4, CYP2C9	CYP3A5, CYP2C19, CYP1A2, UGT1A1			
Estrogens	<u>Estradiol</u>	CYP1A2	CYP3A4, CYP3A5, CYP2C8, UGT1A1			
	<u>Desogestrel</u>	CYP3A4, HSD3B1	CYP3A5, CYP2C9, CYP2C19, UGT1A1		Ø	
Progestogens	<u>Dienogest</u>	CYP3A4	CYP3A5		Ø	
	Mestranol	CYP2C9				
	<u>Levonorgestrel</u>	CYP3A4	CYP3A5			
Emergency contraceptives	<u>Ulipristal</u>	CYP3A4	CYP1A2, CYP2D6, CYP3A5			
		Andr	ogens			ı
3-oxoandrosten-(4) derivatives	<u>Testosterone</u>	CYP3A4, CYP19A1	HSD3B2, CYP3A5, UGT2B15, SULTs			
			drogens			
Antiandrogens	Cyproterone	CYP3A4	CYP3A5			
			dulators of the genital system			
Colorbino colorono no contra	<u>Raloxifene</u>	UGT1A1				
Selective estrogen receptor modulators (SERMs)	<u>Bazedoxifene</u>	UGT1A1				
	<u>Ospemifene</u>	CYP3A4	CYP2C9, CYP3A5, CYP2C19, CYP2B6			
		Steroid	hormone			
	<u>Dexamethasone</u>	CYP3A4	CYP17A1, CYP3A5			
Glucocorticoids	Cortisol (hydrocortisone)	CYP3A4	CYP3A5			
	<u>Prednisone</u>	HSD11B2	CYP3A4, CYP3A5, SLC19A1, SULTs, UGTs			
	·	Thyroid	hormone			
Thyroid hormones	<u>Levothyroxine</u>	DIO2	UGT1A1, SULTs			
myroid normones	<u>Liothyronine</u>	DIO2	UGT1A1, SULTs			
	There	are additional SERMs (Tamoxifen and	Toremifene) described under antineopla	astics)		

PGx Report - Recreational Drugs

Type: Barbiturates, Benzodiazepines, Cannabinoids, Synthetic Cannabis, Dissociative Drugs, Tobacco

Drug Class	Substance	Primary Mechanism Involved	Other Mechanisms Involved	May Have Decreased Efficacy	Used As Directed	May Have Increased Toxicity
Amphetamines	3,4-methylenedioxy- methamphetamine (MDMA)	Renal Excretion, CYP2D6	CYP1A2, CYP3A4, CYP3A5			
	<u>Methamphetamine</u>	CYP2D6, Renal Excretion	DBH, FMO3, ACSM1, GLYAT, DRD3			
Barbiturates	<u>Amobarbital</u>	CYP3A4	CYP3A5, CYP2B6, CYP2C9, CYP2A6			
barbiturates	<u>Phenobarbital</u>	CYP2C19	ABCB1	Ø		
	<u>Alprazolam</u>	CYP3A4	СҮРЗА5		Ø	
Benzodiazepines	<u>Clonazepam</u>	CYP3A4	CYP2C19, CYP3A5, NAT2			
benzoulazepines	<u>Lorazepam</u>	UGT2B15	UGT2B7			
	<u>Diazepam</u>	CYP2C19, CYP3A4	CYP3A5, CYP2B6, CYP1A2			
	Cannabidiol (CBD)	CYP3A4	CYP2C19, CYP3A5			
Cannabinoids & Related Drugs	<u>Delta 9-tetra</u> <u>hydrocannabinol (△9_THC)</u>	CYP2C9	CYP2C19, CYP3A4, CYP3A5			
	Cannabinol (CBN)	CYP2C9	CYP2C19, CYP3A4, CYP3A5			
Synthetic Cannabis	<u>JWH-018</u>	CYP1A2	CYP2C9			
Synthetic Cannabis	<u>AM2201</u>	CYP1A2	CYP2C9		Ø	
Dissociative Drugs	<u>Ketamine</u>	CYP3A4	CYP2B6, CYP2C9, CYP3A5		Ø	
Dissociative Drugs	Phencyclidine (PCP)	CYP3A4	CYP3A5, CYP2A6, CYP1A2		Ø	
Ergoline derivatives	Lysergic acid diethylamide (LSD)	СҮРЗА4	CYP3A5		Ø	
Tobacco	<u>Nicotine</u>	CYP2A6	UGT2B7, CYP2B6			

Summary of pharmacogenetic results including SNP genotypes (rs), for compatibility with the CPIC Guidelines (see below) and the medical literature

Gene	Haplotype (if known)	Predicted phenotype	Marker	Genotype	Gene	Haplotype (if known)	Predicted phenotype	Marker	Genotype
			rs1048943	A/A				rs3758581	G/A
			rs1800031	T/T				rs4244285	G/G
			rs1799814	C/C				rs4986893	G/G
CYP1A1	*1/*1	Normal metabolizer	rs41279188	C/C				rs28399504	A/A
		metabolizer	rs56313657	G/G	CYP2C19		Rapid metabolizer	rs56337013	C/C
			rs72547510	-/-	CTPZC19	*1A/*17	Rapid metabolizer	rs72552267	G/G
			rs72547509	T/T				rs72558186	T/T
			rs12720461	C/C				rs41291556	T/T
CYP1A2	*1A/*1F	Normal rs762551 C/A			rs55640102	A/A			
		metabolizei	rs56107638	G/G				rs12248560	C/T
			CYP2A6_A7conversion	า				rs1080985	G/C
			rs1801272	T/T				rs35742686	A/A
			rs5031017	G/G				rs3892097	G/G
			rs4986891	G/G				CYP2D6_CNVs	2
CYP2A6	*1A/*9	Intermediate	rs5031016	T/T				rs5030655	T/T
CIFZAU	1A) 3	metabolizer	rs28399468	G/G				rs5030867	A/A
			rs28399433	G/T				rs5030865	G/G
			rs28399447	T/T				rs5030656	AAG/AAG
			rs28399454	G/G				rs1065852	C/C
			rs28399444	AA/AA	CYP2D6			rs201377835	G/G
			rs3745274	T/T				rs5030862	G/G
		Intermediate	rs12721655	A/A		*2A/*41	Normal metabolizer	rs28371706	C/C
CYP2B6	*6/*6	metabolizer	rs8192709	C/C				rs765776661	-/-
			rs28399499	T/T				rs72549353	AACT/AACT
			rs34097093	C/C				rs72549354	-/-
			rs11572103	A/A				rs72549352	-/-
			rs11572080	G/G				CYP2D7/2D6 hybrid *36	T/T
CYP2C8	*1/*1	Normal	rs10509681	T/T				rs72549351	GACT/GACT
		metabolizer	rs1058930	C/C				rs72549356	-/-
			rs72558196	A/A				rs28371725	A/G
			rs72558195	C/C				rs72549346	-/-
			rs1799853	C/C				rs72549349	G/G
			rs1057910	C/A				rs147960066	C/C
			rs56165452	T/T				rs72559710	G/G
			rs28371686	C/C	CYP2E1	*1/*7	Normal metabolizer	rs2070673	T/A
			rs9332131	A/A				rs55785340	T/T
			rs7900194	G/G				rs4646438	-/-
CYP2C9	*1/*3	Intermediate metabolizer	rs2256871	A/A	CYP3A4	*1/*1	Normal metabolizer	rs67666821	-/-
		metabolizer	rs9332130	A/A				rs35599367	C/C
			rs28371685	C/C				rs776746	T/T
			rs9332239	C/C				rs55965422	T/T
			rs72558187	T/T	CYP3A5	*1A/*1A	Normal metabolizer	rs10264272	G/G
			rs72558190	C/C	227.0	_, , _, ,		rs41303343	-/-
			rs72558188	AGAAATGGAA/AGAAATGGA				rs41279854	T/T
			rs9332094	T/T					

Summary of pharmacogenetic results including SNP genotypes (rs), for compatibility with the CPIC Guidelines (see below) and the medical literature

Gene	Haplotype (if known)	Predicted phenotype	Marker	Genotype	Gene	Haplotype (if known)	Predicted phenotype	Marker	Genotype
			rs9934438	C/C	ABCG2	*1/*1	Normal function	rs2231142	G/G
VKORC1	117/117	Morforin registance	rs9923231	C/C	ABCG2	"1/"1	Normal function	rs72552713	C/C
VKURCI	H7/H7	Warfarin resistance	rs7294	T/T				rs9282861	G/G
			rs17708472	C/C	SULT1A1	*3/*3 Poor metaboliz	Poor metabolizer	rs1801030	A/A
			rs1143672	G/G				rs72547527	G/G
SLC15A2	*1/*1	Normal function	rs2293616	G/G				rs55793712	A/A
SLCIDAZ	.1/.1	Normal function	rs2257212	C/C				rs4986989	A/T
			rs1143671	C/C				rs4986782	G/G
			rs12208357	C/C	NAT1	*4/*11	Normal acetylator	rs5030839	C/C
			rs55918055	T/T				rs56379106	C/C
			rs36103319	G/G				rs56318881	C/C
			rs4646277	C/C				rs56172717	A/A
			rs4646278	C/C				rs1801280	T/C
			rs2282143	C/C				rs1799930	G/A
SLC22A1	*420Del/*420Del	Low function	rs34130495	G/G				rs1799931	G/G
			rs628031	G/G	NAT2	*5B/*6A or *5A/*6C or	Poor acetylator	rs1799929	C/T
			rs72552763	GAT/-	NAIZ	*6B/*5G or *12C/*5J	rooi acetylatoi	rs1208	A/G
			rs4646281	AAGTTGGT/AAGTTGGT				rs1041983	C/T
			rs34305973	T/T				rs1801279	G/G
			rs35167514	A/A				rs1805158	C/C
			rs34059508	G/G				rs1800462	G/G
			rs8177504	C/C				rs1800460	G/G
			rs8177508	A/A	TPMT	*1/*1	Normal metabolizer	rs1142345	A/A
SLC22A2	*1/*270A	Normal function	rs316019	G/T				rs1800584	G/G
			rs8177516	C/C				rs56161402	G/G
			rs8177517	A/A				rs4680	G/G
SLC22A6	*1/*1	Normal function	rs11568626	G/G	COMT			rs165599	G/G
			rs2306283	A/A				rs737865	A/G
			rs56101265	T/T	GSTP1	*1A/*1A	Normal metabolizer	rs1695	A/A
			rs56061388	T/T	03111	IA, IA	Normal metabolizer	rs1138272	C/C
			rs72559745	A/A				rs4148323	G/G
SLCO1B1	*1A/*1A	Normal function	rs4149056	T/T			Intermediate	rs34993780	T/T
			rs55901008	T/T	UGT1A1	*28(*60)/*28(*60)	metabolizer	rs35350960	C/C
			rs59502379	G/G				rs55750087	C/C
			rs56199088	A/A				rs4124874	G/G
			rs55737008	A/A	UGT2B7	*1a/*1a	Normal metabolizer	rs7662029	G/G
SLCO1B3	*233I/*233I	Low function	rs4149117	G/G	OGTZB7	10/ 10	Normal metabolizer	rs7668258	C/C
		LOW TUTTECTOTT	rs7311358	A/A	UGT2B15	*2/*2	Intermediate	rs1902023	A/A
SLCO2B1	*1/*1	Normal function	rs2306168	C/C		-, -	metabolizer		
			rs1045642	G/A				rs3918290	C/T
ABCB1	*1/*2	Intermediate function	rs2032582					rs72549309	TCAT/TCAT
ADCDI	1/ 2	c.mediate function	rs1128503	G/A	DP\/D	41 (42 A	Intermediate	rs1801266	C/C
			rs3213619	T/T	DPYD	*1/*2A	metabolizer	rs1801265	T/T
			rs717620	C/C				rs1801267	C/C
			rs2273697	G/G				rs1801268	G/G
ABCC2	*1/*1324I	Intermediate function	rs56220353	C/C					
			rs56199535	C/C					
			rs3740066	C/T					

Clinical Pharmacogenetics Implementation Consortium (CPIC) and Royal Dutch Association for the Advancement of Pharmacy - Pharmacogenetics Working Group (DPWG)

Medications Affected by Patient Genetic Results

Clinical Annotation for rs2231142 (ABCG2)

Allopurinol and Gout Evidence Level 2B Efficacy Genotype: G/G

Patients with gout may have improved response when treated with allopurinol as compared to patients with the GT or TT genotype.

- https://www.pharmgkb.org/clinicalAnnotation/1447982582

Clinical Annotation for CYP2C19*1, *2, *3, *4, *5, *6, *8

Haplotype: *1A/*17 Evidence Level 1A Efficacy,

Toxicity/ADR

-- https://www.pharmgkb.org/clinicalAnnotation/1043858794

Clopidogrel

Clinical Annotation for rs4149056 (SLCO1B1)

Simvastatin, Muscular Diseases Genotype: T/T Evidence Level 1A

and Central Core Myopathy

Toxicity/ADR

Patients may have a lower risk of simvastatin-related myopathy as compared to patients with the CC or CT genotype.

Clinical Annotation for CYP2C9*1, *2, *3

Warfarin, Cardiovascular **Haplotype:** *1/*3 Evidence Level 1A Dosage **Diseases and Heart Diseases**

Patients may require a lower dose of warfarin as compared to patients with the *1/*1 diplotype.

-- https://www.pharmgkb.org/clinicalAnnotation/981238341

Clinical Annotation for rs9923231 (VKORC1)

Warfarin Genotype: C/C Evidence Level 1A Dosage

Patients may require an increased dose of warfarin as compared to patients with the CT or TT genotype.

https://www.pharmgkb.org/variant/rs9923231?previousQuery=rs9923231

Clinical Annotation for rs7294 (VKORC1)

Warfarin Genotype: T/T Evidence Level 1B Dosage

Patients treated with warfarin may require a higher dose as compared to patients with the CC genotype.

https://www.pharmgkb.org/clinicalAnnotation/655384733

Clinical Annotation for rs1045642 (ABCB1)

Digoxin Evidence Level 2A Genotype: G/A

Patients may have decreased metabolism and increased serum concentration of digoxin as compared to patients with the GG genotype.

- https://www.pharmgkb.org/clinicalAnnotation/981204372

Clinical Annotation for rs2032582 (ABCB1)

Simvastatin and Evidence Level 2A Efficacy Hypercholesterolemia

https://www.pharmgkb.org/clinicalAnnotation/1150414901

Clinical Annotation for rs4149056 (SLCO1B1)

Cerivastatin and Genotype: T/T Evidence Level 2A

Rhabdomyolysis Toxicity/ADR

Patients may have a lower risk of cerivastatin-related rhabdomyolysis as compared to patients with the CC or CT genotype. Cerivastatin was withdrawn from the market because of 52 deaths attributed to drug-related rhabdomyolysis that lead to kidney failure.

-- https://www.pharmgkb.org/clinicalAnnotation/981344897

Clinical Annotation for rs4149056 (SLCO1B1)

Pravastatin Genotype: T/T Evidence Level 2A

Metabolism/PK

Patients may have decreased plasma concentrations of pravastatin as compared to patients with the CC or CT genotype.

Clinical Annotation for rs4149056 (SLCO1B1)

Rosuvastatin and Evidence Level 2A Genotype: T/T Hypercholesterolemia

Patients may have lower plasma concentrations of rosuvastatin as compared to patients with the CC genotype. No association is seen between genotypes of this variant and change in LDL-cholesterol levels in response to rosuvastatin treatment.

https://www.pharmgkb.org/clinicalAnnotation/981345350

Clinical Annotation for rs7294 (VKORC1)

Acenocoumarol and Genotype: T/T Evidence Level 2A Dosage phenprocoumon

Patients may require an increased dose of phenprocoumon or acenocoumarol as compared to patients with the CT or CC genotype, although this has been contradicted in some studies.

-- https://www.pharmgkb.org/clinicalAnnotation/1445585748

Clinical Annotation for rs2231142 (ABCG2)

Rosuvastatin, Genotype: G/G Evidence Level 2B Efficacy Hypercholesterolemia and

Patients treated with rosuvastatin 1) may have lower plasma concentrations of rosuvastatin 2) may have a reduced response to treatment as determined by a lower reduction in LDL-C as compared to patients with the TT genotype.

https://www.pharmgkb.org/clinicalAnnotation/1154221922

Myocardial Infarction

Clinical Annotation for rs1045642 (ABCB1)

Ondansetron Evidence Level 2A Efficacy Genotype: G/A

Patients may have increased likelihood of nausea and vomiting shortly after being treated with treated with ondansetron as compared to patients with AA genotype. -- https://www.pharmgkb.org/clinicalAnnotation/1183632195

Clinical Annotation for rs2032582 (ABCB1)

Ondansetron Evidence Level 2A Efficacy

-- https://www.pharmgkb.org/clinicalAnnotation/1183632200

Clinical Annotation for rs10509681 (CYP2C8)

Rosiglitazone Genotype: T/T Evidence Level 2A Dosage

Patients may have decreased metabolism of rosiglitazone, a larger change in HbA1c, and an increased risk of edema as compared to patients with the CC (CYP2C8*3/*3) or CT (CYP2C8*3/*1) genotype. One study found no association with blood glucose levels.

-- https://www.pharmgkb.org/clinicalAnnotation/655384653

Clinical Annotation for CYP2C19*1, *2, *3

Evidence Level 1A Sertraline and Major **Haplotype:** *1A/*17 **Depressive Disorder** Metabolism/PK

-- https://www.pharmgkb.org/clinicalAnnotation/1183619004

Clinical Annotation for CYP2C19*1, *17, *2, *3, *4

Citalopram, escitalopram and Haplotype: *1A/*17 Evidence Level 1A Efficacy, **Major Depressive Disorder**

Patients treated with citalogram or escitalogram may have an increased drug clearance/metabolism as compared to patients with CYP2C19*1/*1 genotype.

https://www.pharmgkb.org/clinicalAnnotation/1183620386

Clinical Annotation for rs1902023 (UGT2B15)

Lorazepam and oxazepam Genotype: A/A Evidence Level 2B

Subjects may have decreased clearance of oxazepam or lorazepam as compared to subjects with the CC genotype.

https://www.pharmgkb.org/clinicalAnnotation/655387798

Toxicity/ADR

Clinical Annotation for CYP2C19*1, *17, *2, *3

Voriconazole and Mycoses

Haplotype: *1A/*17

Evidence Level 1B

Metabolism/PK

Patients may have increased metabolism of voriconazole as compared to patients with the CYP2C19*1/*1 diplotype (extensive metabolizers), the CYP2C19*1/*2 or *1/*3 diplotypes (intermediate/heterozygous extensive metabolizers), or the CYP2C19*2/*2, *2/*3 or *3/*3 diplotypes (poor metabolizers, or may have decreased metabolism as compared to patients with the CYP2C19*17/*17 diplotype (ultrarapid metabolizers). Though several studies have found no association, the majority report an association.

- https://www.pharmgkb.org/clinicalAnnotation/1183689217

Clinical Annotation for rs1045642 (ABCB1)

Nevirapine and HIV Infections

Haplotype: *1/*2 Evidence Level 2A

Toxicity/ADR

Patients with HIV-1 infection who are treated with nevirapine may have a decreased, but not absent, risk for nevirapine hepatotoxicity as compared to patients with the GG genotype, it is not clear what the influence of one A allele with the G allele is.

-- https://www.pharmgkb.org/clinicalAnnotation/655386244

Clinical Annotation for rs3745274 (CYP2B6)

Nevirapine and HIV Infections

Genotype: T/T

Evidence Level 2A

Patients with HIV infection may have decreased clearance of and increased exposure to nevirapine as compared to patients with the GG genotype. -- https://www.pharmgkb.org/clinicalAnnotation/981202294

Clinical Annotation for rs28399499 (CYP2B6)

Nevirapine and HIV

Genotype: T/T

Evidence Level 2A

Patients may have decreased plasma drug exposure when treated with nevirapine as compared to patients with the CC or CT genotype.

https://www.pharmgkb.org/clinicalAnnotation/981201854

Clinical Annotation for rs28399499 (CYP2B6)

Efavirenz and HIV

Genotype: T/T

Evidence Level 2A

Metabolism/PK

Patients may have decreased plasma drug exposure when treated with efavirenz as compared to patients with the CC or CT genotype.

-- https://www.pharmgkb.org/clinicalAnnotation/981201844

Clinical Annotation for NAT2*12, NAT2*13, NAT2*14, NAT2*4, NAT2*5, NAT2*6, NAT2*7

Isoniazid and Tuberculosis

Haplotype: *5B/*6A or *5A/*6C or *6B/*5G or

Evidence Level 2A

-- https://www.pharmgkb.org/clinicalAnnotation/982030222

Clinical Annotation for rs3918290 (DPYD)

Capecitabine, fluorouracil, Pyrimidine analogues, tegafur and Neoplasms

Genotype: C/T

*12C/*5J

Evidence Level 1A

Toxicity/ADR, Metabolism/PK

Cancer patients treated with fluoropyrimidine-based chemotherapy may have 1) DPYD deficiency and decreased clearance of fluoropyrimidine drugs and 2) be at risk for severe or even fatal drug toxicity as compared to patients with the CC genotype (DPYD *1/*1). Fluoropyrimidines are often used in combination chemotherapy such as FOLFOX (fluorouracil, leucovorin and oxaliplatin), FOLFIRI (fluorouracil, leucovorin and irinotecan) or FEC (fluorouracil, epirubicin and cyclophosphamide) or with other drugs such as bevacizumab, cetuximab, raltitrexed. The combination and delivery of the drug may influence risk for toxicity. https://www.pharmgkb.org/clinicalAnnotation/827843617

Clinical Annotation for TPMT*1, *2, *3A, *3B, *3C, *4

Azathioprine, mercaptopurine, purine analogues and thioguanine

Haplotype: *1/*1

Evidence Level 1A

Toxicity/ADR

Patients treated with thiopurine drugs and purine analogues: 1) may have increased inactivation of thiopurines due to normal TPMT activity and 2) may have a decreased risk for toxicity when receiving thiopurine drugs and purine analogues as compared to patients with a non-functional allele (e.g. *2, *3A, *3B, *3C, *4). Patients with the *1/*1 genotype may still be at risk for toxicity when taking thiopurine drugs and purine analogues based upon their genotypes.

-- https://www.pharmgkb.org/clinicalAnnotation/1184648909

Clinical Annotation for rs1695 (GSTP1)

Platinum compounds and Genotype: A/A Evidence Level 2A

Toxicity/ADR Neoplasms

Cancer patients treated with platinum-based drugs may have the highest risk of toxicity as compared to patients with the AG or GG genotype. - https://www.pharmgkb.org/clinicalAnnotation/63788

Clinical Annotation for rs1045642 (ABCB1)

Methotrexate, Burkitt Lymphoma, Drug Toxicity, T-Cel Lymphomal, Precursor Cell Lymphoblastic Leukemia-Lymphoma and Toxic liver

disease

Haplotype: *1/*2 Evidence Level 2A

Toxicity/ADR

Evidence Level 2A Efficacy

Patients with lymphoma or leukemia who are treated with methotrexate may have an increased risk of toxicity as compared to patients with the GG genotype, or a decreased risk of toxicity as compared to patients with the AA genotype.

-- https://www.pharmgkb.org/clinicalAnnotation/1296599132

Clinical Annotation for rs1695 (GSTP1)

Genotype: A/A

Fluorouracil, oxaliplatin and **Colorectal Neoplasms**

Patients with colorectal cancer who are treated with fluorouracil and oxaliplatin may have poorer treatment outcome (reduced responsiveness, lower overall survival time, increased risk of death) as compared to patients with the GG genotype.

https://www.pharmgkb.org/clinicalAnnotation/827847788

Clinical Annotation for rs1695 (GSTP1)

Cyclophosphamide, epirubicin Genotype: A/A Evidence Level 2A and Breast Neoplasms

Toxicity/ADR Patients with Breast Neoplasms who are treated with cyclophosphamide and epirubicin may have 1) increased drug response 2) decreased severity of toxicity as

compared to patients with GG genotype. Some patients were additionally treated with fluorouracil.

-- https://www.pharmgkb.org/clinicalAnnotation/981238323

Clinical Annotation for rs4148323 (UGT1A1)

SN-38 and Neoplasms Evidence Level 2A Genotype: G/G

Cancer patients may have increased metabolism of SN-38 when treated with irinotecan as compared to patients with the AA genotype. SN-38 is the active metabolite of irinotecan, and is glucuronidated by UGT1A1. One in vitro study found increased enzyme activity for the G allele compared to the A allele.

https://www.pharmgkb.org/clinicalAnnotation/982047955

Clinical Annotation for rs4148323 (UGT1A1)

Evidence Level 2A **Irinotecan and Neoplasms** Genotype: G/G

Cancer patients treated with irinotecan-based regimens may have a decreased risk of neutropenia as compared to patients with the AA genotype. https://www.pharmgkb.org/clinicalAnnotation/981201713

Clinical Annotation for rs776746 (CYP3A5)

Tacrolimus, heart Genotype: T/T Evidence Level 1A Dosage, transplantation, hemopoietic Metabolism/PK

stem cell transplant, Kidney Transplantation and lung

transplantation

Patients who are recipients of a kidney, heart, lung or hematopoeitic stem cell transplant, or have other diseases, who are treated with tacrolimus may have increased metabolism of tacrolimus resulting in decreased exposure, and may require a higher dose as compared to patients with the CC genotype.

-- https://www.pharmgkb.org/clinicalAnnotation/981203719

Clinical Annotation for rs776746 (CYP3A5)

Tacrolimus and liver Genotype: *T/T* Evidence Level 2A Dosage,

transplantation Metabolism/PK

Patients who are recipients of a liver transplantation from a donor with the TT genotype may have increased metabolism of tacrolimus resulting in decreased exposure,

and may require a higher dose as compared to patients who receive a liver transplantation from a donor with the CC (*3/*3) genotype. https://www.pharmgkb.org/clinicalAnnotation/982046323

Clinical Annotation for rs776746 (CYP3A5)

Tacrolimus and transplant rejection

Evidence Level 2A Efficacy

Patients who are recipients of kidney or hematopoietic stem cell transplant who are treated with tacrolimus may have an increased risk of transplant rejection as compared to patients with the CC genotype.
-- https://www.pharmgkb.org/clinicalAnnotation/981203808

Clinical Annotation for rs776746 (CYP3A5)

Sirolimus and Transplantation

Genotype: T/T

Genotype: T/T

Genotype: G/G

Evidence Level 2A Dosage

Patients who are recipients of transplants may have increased metabolism of sirolimus and require a higher dose as compared to patients with the CC genotype. https://www.pharmgkb.org/clinicalAnnotation/981203936

Clinical Annotation for rs4680 (COMT)

Nicotine and Tobacco Use Disorder

Evidence Level 2A Efficacy

Patients treated with nicotine replacement therapy may have a decreased likelihood of smoking cessation and increased risk of relapse as compared to patients with the AA genotype: However, some contradictory evidence exists. -- https://www.pharmgkb.org/clinicalAnnotation/981202618

RISKS AND LIMITATIONS

Risk of Laboratory Technical Problems or Laboratory Error

Standard and effective procedures are in place at testing laboratory to protect against and prevent both technical and operational problems although problems may still occur. Errors can occur due to improper sample collection by patients and physicians. Damage to sample can occur during shipment due to such issues as improper paperwork, mislabeled/misaddressed packaging, loss/delay in receipt of sample at certified testing lab, etc. Issues which may prevent the lab from obtaining results include, but are not limited to: contamination of DNA sample; human &/or testing system error; results which cannot be interpreted; and, mislabeling of DNA sample.

When such issues are encountered, the lab may request a new sample. Re-testing does not guarantee that results will be obtained.

There is a statistically small percentage of inaccurate reporting that may include, but is not limited to such issues as: a false report that a genotype is present. Such errors may cause, but is not limited to: incorrect decisions/recommendations on medical treatment; incorrect decisions/recommendations on diet and/or fitness plans. In cases where laboratory error is suspected or is proven to have occurred, the patient's healthcare professional may recommend/request additional evaluation/testing. Additional testing may be recommended/requested to verify results for any reason presented by patient's healthcare professional.

Limitations

PGx testing primarily provides evidence-based predictions of how the tested individual's genetic profile may affect reaction to certain drugs. It may also reveal possibly-altered response to selected diet, exercise, and/or nutritional factors, and/or the risks for certain common health conditions, and/or information concerning the tested individual's near or ancient ancestry. Based on PGx test results, patients should make no changes to medical care [including, but not limited to, changes in dosage or frequency of medication, diet and/or exercise regimens, or pregnancy planning] without the prior advice of and consultation with a healthcare professional.

Genetic testing is an evolving science. Current testing protocols and results are based on the current/existing developments, information and testing techniques known at this time.

In the future, new variants may be identified and/or more research may be developed on the significance of currently identified variants that will drive changes in the interpretation of previously obtained genetic testing results. Current testing may not include identification of certain variants associated with: diet, exercise or nutrition; disease; and/or, drug response due to these issues.

Factors such as age, diet, ethnicity, family health history, and/or personal health, not related to genetics can also impact the likelihood of developing certain conditions or exhibiting certain drug reactions. Therefore, patients may not always exhibit and/or require the specific diet, nutrition and/or exercise, disease, or drug response expected or consistent with his/her genetic test results.

The genetic associations of certain conditions, particularly those related to diet and exercise, have only been observed/studied in Caucasian populations only. This limitation means that interpretations and recommendations are made in the context of Caucasian-only studies and results may or may not be relevant to those tested who are non-Caucasian or mixed ethnicity individuals.

Healthcare professionals may recommend additional testing to be performed by an independent laboratory or consult with an outside, independent genetic counselor or healthcare professional.

Examples of different levels of evidence for PGx SNPs

Level of Evidence	Marker	Gene	Drugs
1A	rs1142345	TPMT	Azathioprine, Mercaptopurine, Thioguanine
1A	rs3918290	DPYD	Fluorouracil, Capecitabine, Tegafur, Pyrimidine analogues
1A	rs16947	CYP2D6	Amitriptyline, Codeine, Nortriptyline, Paroxetine
1A	rs9923231	VKORC1	Warfarin
1A	rs4149056	SLCO1B1	Simvastatin
1B	rs16947	CYP2D6	Tramadol
1B	rs9923231	VKORC1	Acenocoumarol
2A	rs1801280	NAT2	Isoniazid
2A	rs16947	CYP2D6	Flecainide, Doxepin, Desipramine, Atomoxetine, Risperidone, Clomipramine, Imipramine, Venlafaxine
2A	rs4149056	SLCO1B1	Cerivastatin, Pravastatin, Rosuvastatin
2A	rs1045642	ABCB1	Digoxin, Nevirapine, Methotrexate
3	rs9282861	SULT1A1	Conjugated estrogens
3	rs16947	CYP2D6	Timolol, Carvedilol, Haloperidol, Aripiprazole, Metoprolol, Citalopram, Escitalopram, Tamoxifen
3	rs9923231	VKORC1	Phenprocoumon
3	rs4149056	SLCO1B1	Repaglinide, Irinotecan, Mycophenolate mofetil, Atorvastatin, Methotrexate, Olmesartan
3	rs1045642	ABCB1	Paclitaxel, Phenytoin, Fluorouracil, Dicloxacillin, Capecitabine, Nortriptyline, Oxaliplatin, Verapamil, Fexofenadine, Atorvastatin, Simvastatin, Sirolimus, Talinolol, Tamoxifen, Morphine, Efavirenz, Vincristine, Imatinib, Olanzapine, Risperidone, Cyclosporine, Tacrolimus, Atazanavir, Phenobarbital, Codeine, Clopidogrel, Etoposide, Oxaliplatin
4	rs16947	CYP2D6	Methylphenidate, Bufuralol
4	rs4149056	SLCO1B1	Lopinavir, Atrasentan
4	rs1045642	ABCB1	Carbamazepine

Level 1A Annotation for a variant-drug combination in a CPIC or medical society-endorsed PGx guideline, or implemented at a PGRN site or in another major health system.

Level 1B Annotation for a variant-drug combination where the preponderance of evidence shows an association. The association must be replicated in more than one cohort with significant pvalues, and preferably will have a strong effect size

Level 2A Annotation for a variant-drug combination that qualifies for level 2A where the variant is within a VIP (Very Important Pharmacogene) as defined by PharmGKB. The variants in level 2A are in known pharmacogenes, so functional significance is more likely.

Level 2B Annotation for a variant-drug combination with moderate evidence of an association. The association must be replicated but there may be some studies that do not show statistical significance, and/or the effect size may be small.

Level 3 Annotation for a variant-drug combination based on a single significant (not yet replicated) or annotation for a variant-drug combination evaluated in multiple studies but lacking clear evidence of an association.

Level 4 Annotation based on a case report, non-significant study or in vitro, molecular or functional assay evidence only.

Patient Information Card

An easily portable summary of the report patients can share with their medical professionals. (Please cut along dotted line.)

CYP1A1	*1/*1	Normal metabolizer
CYP1A2	*1A/*1F	Normal metabolizer
CYP2A6	*1A/*9	Intermediate metabolizer
CYP2B6	*6/*6	Intermediate metabolizer
CYP2C8	*1/*1	Normal metabolizer
CYP2C9	*1/*3	Intermediate metabolizer
CYP2C19	*1A/*17	Rapid metabolizer
CYP2D6	*2A/*41	Normal metabolizer
CYP2E1	*1/*7	Normal metabolizer
CYP3A4	*1/*1	Normal metabolizer
CYP3A5	*1A/*1A	Normal metabolizer
VKORC1	H7/H7	Warfarin resistance
SLC15A2	*1/*1	Normal function
SLC22A1	*420Del/*420Del	Low function
SLC22A2	*1/*270A	Normal function
SLC22A6	*1/*1	Normal function
SLCO1B1	*1A/*1A	Normal function
SLCO1B3	*2331/*2331	Low function
SLCO2B1	*1/*1	Normal function
ABCB1	*1/*2	Intermediate function
ABCC2	*1/*1324I	Intermediate function
ABCG2	*1/*1	Normal function
SULT1A1	*3/*3	Poor metabolizer
NAT1	*4/*11	Normal acetylator
NAT2	*5B/*6A or *5A/*6C or *6B/*5G or *12C/*5J	Poor acetylator
TPMT	*1/*1	Normal metabolizer
GSTM1	*1/*1	Normal metabolizer
GSTP1	*1A/*1A	Normal metabolizer
UGT1A1	*28(*60)/*28(*60)	Intermediate metabolizer
UGT2B7	*1a/*1a	Normal metabolizer
UGT2B15	*2/*2	Intermediate metabolizer
DPYD	*1/*2A	Intermediate metabolizer