

Intermountain Precision Genomics

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CLIA ID Number: 46D2094383 PrecisionGenomics.org/RxMatch

This report combines (i) an analysis of the patient's DNA by Intermountain Precision Genomics, identifying relevant genetic variants that are informative for medication efficacy, safety, and dosing, with (ii) an interpretation of the identified DNA variants by Coriell Life Sciences to bring you immediately actionable clinical quidance regarding safer, more effective medications and dosages for the patient. The Medication Report section lists the type of PGx guidance present on FDA-approved drug labels. Medications with no established FDA PGx guidance are provided solely for educational purposes.

Patient: Douglas, Sex: Unknown

Practice: Intermountain Precision Geno

Date Collected: Jan 06, 2021 Date Accessioned: Jan 06, 2021 Specimen type: DNA

Sample ID: RS-21-0000053A

#### **Medication Summary**

Therapeutic Class	Standard Precautions	▲ ① Caution / Info	Change recommended
Alpha-1 Blockers	Tamsulosin		
Anti-ADHD Agents	Amphetamine Atomoxetine Dexmethylphenidate Dextroamphetamine Guanfacine Lisdexamfetamine Methylphenidate (COMT)	Clonidine Methylphenidate (ADRA2A)	
Antiarrhythmics	Flecainide Propafenone		
Anticholinergic Agents	Fesoterodine Tolterodine		
Anticoagulants		Warfarin	
Anticonvulsants	Brivaracetam Clobazam Phenytoin		
Antidementia	Donepezil		





Therapeutic Class	Standard Precautions	▲ (i) Caution / Info	Change recommended
Agents			
Antidepressants	Amitriptyline (CYP2C19, CYP2D6) Amoxapine Clomipramine (CYP2C19, CYP2D6) Desipramine Doxepin (CYP2C19, CYP2D6) Duloxetine Imipramine (CYP2C19, CYP2D6) Mirtazapine Nortriptyline Protriptyline Trazodone Trimipramine (CYP2C19, CYP2D6) Venlafaxine Vortioxetine		
Antidiabetics	Glimepiride Glyburide Saxagliptin Tolbutamide		
Antiemetics	Ondansetron		
Antifungals	Ketoconazole Voriconazole		
Antineoplastic	Cisplatin		
Antineoplastic Agents			Methotrexate
Antiplatelet Agents	Clopidogrel Prasugrel Ticagrelor		
Antipsychotics	Aripiprazole Brexpiprazole Clozapine Haloperidol Iloperidone		



Therapeutic Class	Standard Precautions	⚠ (1) Caution / Info	Change recommended
	Olanzapine Perphenazine Pimozide Quetiapine Risperidone Thioridazine		
Anxiolytics	Alprazolam Buspirone Clonazepam Diazepam		
Beta-3 Adrenergic Agonists	Mirabegron		
Beta Blockers	Carvedilol Metoprolol Nebivolol Propranolol Timolol		
Central Monoamine- Depleting Agents	Tetrabenazine		
Central Nervous System Agents	Dextromethorphan- Quinidine		
Cholinergic Agonists	Cevimeline		
Cholinesterase Inhibitors	Galantamine		
Contraceptives	Estrogen-containing oral contraceptives		
EGFR Inhibitors	Gefitinib		
Endocrine- Metabolic Agents	Eliglustat		
Estrogen Agonists/ Antagonists	Tamoxifen		





Therapeutic Class	Standard	(1) Caution / Info	
	Precautions		recommended
Hypnotics	Eszopiclone		
Immunosuppressant	EsAzathioprine Cyclosporine Mercaptopurine Sirolimus Thioguanine	Tacrolimus	
Muscle Relaxants	Carisoprodol		
Nonsteroidal Anti- Inflamatory Drugs (NSAIDs)	Celecoxib Diclofenac Flurbiprofen Ibuprofen Meloxicam Piroxicam		
Opioids	Alfentanil Buprenorphine Codeine Fentanyl Fentanyl (OPRM1) Hydrocodone Hydromorphone Morphine Oxycodone Oxycodone (CYP3A4) Sufentanil Tramadol	Oxycodone (CYP3A5)	
<b>Prokinetic agents</b>	Metoclopramide		
Proton Pump Inhibitors (PPIs)	Esomeprazole Rabeprazole	Dexlansoprazole Lansoprazole Omeprazole Pantoprazole	
Selective Serotonin Reuptake Inhibitors (SSRIs)	Citalopram Escitalopram Fluoxetine Fluvoxamine Paroxetine Sertraline		
Statins	Atorvastatin Simvastatin		



Therapeutic Class	Standard Precautions	▲ (†) Caution / Info	Change recommended
Vesicular monoamine transporter 2 inhibitor	Deutetrabenazine Valbenazine		
Xanthine Oxidase Inhibitor	Allopurinol		



#### Legend

Typical response is expected



Caution - review recommendation



Change recommended



Additional information available



Response is uncertain

#### **Clinical Evidence Level**



Strong



Moderate



**Emerging** 

#### **Medication Report Details (by therapeutic class)**

Drug		Finding	Recommendation	Concern	Evidence
Alpha-1 Blockers					
Tamsulosin (Flomax)	<b>②</b>	CYP2D6: Normal metabolizer. Two	Normal metabolizers of this medication are expected to		
FDA drug label: Actionable PGx		alleles showing normal function.	show typical response. No additional therapeutic recommendations.		



Drug		Finding	Recommendation	Concern	Evidence
Anti-ADHD Agents					
Amphetamine (Adzenys, Evekeo) FDA drug label: Not established for PGx	<b>⊘</b>	COMT(Val158Met): Normal function. Two normal function alleles.	Individuals with normal function of this gene are expected to show typical response. No additional therapeutic recommendations.		
Atomoxetine (Strattera) FDA drug label: Actionable PGx		CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Clonidine (Clonidine, Kapvay) FDA drug label: Not established for PGx		ADRA2A(C-1291G): Unknown; One variant SNP detected.	Individuals with these heterozygous alleles may present with increased risk of pharmacotherapy failure. Be alert to lack of efficacy.	Efficacy	0
Dexmethylphenidate (Focalin) FDA drug label: Not established for PGx	<b>②</b>	COMT(Val158Met): Normal function. Two normal function alleles.	Individuals with normal function of this gene are expected to show typical response. No additional therapeutic recommendations.		
Dextroamphetamine (Zenzedi, Dexedrine) FDA drug label: Not established for PGx	<b>②</b>	COMT(Val158Met): Normal function. Two normal function alleles.	Individuals with normal function of this gene are expected to show typical response. No additional therapeutic recommendations.		
Guanfacine (Tenex, Intuniv) FDA drug label: Not established for PGx		CYP3A4: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Lisdexamfetamine (Vyvanse) FDA drug label: Not established for PGx	<b>Ø</b>	COMT(Val158Met): Normal function. Two normal function alleles.	Individuals with normal function of this gene are expected to show typical response. No additional therapeutic recommendations.		



Drug	Finding	Recommendation	Concern	Evidence
Methylphenidate (ADRA2A) (Concerta, Metadate, Ritalin, Ritalin LA, Quillivant, Daytrana, Methylin)  FDA drug label: Not established for PGx	ADRA2A(C-1291G): Unknown; One variant SNP detected.	Individuals with these heterozygous alleles may present with increased risk of pharmacotherapy failure. Be alert to lack of efficacy.	Efficacy	
Methylphenidate (COMT) (Concerta, Metadate, Ritalin, Ritalin LA, Quillivant, Daytrana, Methylin)  FDA drug label: Not established for PGx	COMT(Val158Met): Normal function. Two normal function alleles.	Individuals with normal function of this gene are expected to show typical response. No additional therapeutic recommendations.		
Antiarrhythmics				
Flecainide (Tambocor)  FDA drug label: Not established for PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Propafenone (Rythmol)  FDA drug label: Actionable PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
<b>Anticholinergic Agents</b>				
Fesoterodine (Toviaz)  FDA drug label: Actionable PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Tolterodine (Detrol)  FDA drug label: Actionable PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		





Finding	Recommendation	Concern	Evidence
Multigenic: VKORC1, CYP2C9: Normal metabolizer. Two normal function alleles.	Individuals with this combination of alleles may benefit from an increased dose of Warfarin. The FDA table recommends a therapeutic dose of 5-7 mg/day.		
CYP2C19: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
CYP2C19: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
CYP2C9: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
ts			
CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
	i Multigenic: VKORC1, CYP2C9: Normal metabolizer. Two normal function alleles.  CYP2C19: Normal metabolizer. Two normal function alleles.  CYP2C19: Normal metabolizer. Two normal function alleles.  CYP2C9: Normal metabolizer. Two normal function alleles.  CYP2C9: Normal metabolizer. Two normal function alleles.	Multigenic: VKORC1, CYP2C9: Normal metabolizer. Two normal function alleles.  CYP2C19: Normal metabolizer. Two normal function alleles.  CYP2C19: Normal metabolizer. Two normal function alleles.  Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.  CYP2C19: Normal metabolizer. Two normal function alleles.  Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.  CYP2C9: Normal metabolizer. Two normal function alleles.  Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.  Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.	Multigenic: VKORC1, CYP2C9: Normal metabolizer. Two normal function alleles.  CYP2C19: Normal metabolizer. Two normal function alleles.  CYP2C19: Normal metabolizer. Two normal function alleles.  Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.  CYP2C19: Normal metabolizer. Two normal function alleles.  CYP2C19: Normal metabolizer. Two normal function alleles.  Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.  CYP2C9: Normal metabolizer. Two normal function alleles.  Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.  CYP2C9: Normal metabolizer. Two normal function alleles.  Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.



Drug		Finding	Recommendation	Concern	Evidence
Antidepressants					
Amitriptyline (CYP2C19, CYP2D6) (Elavil) FDA drug label: Not established for PGx	<b>②</b>	Multigenic: CYP2D6, CYP2C19: Normal metabolizer. Two alleles showing normal function.; Normal metabolizer. Two normal function alleles.	Individuals with this combination of alleles are expected to show typical response. No additional therapeutic recommendations.		
Amoxapine (Asendin) FDA drug label: Actionable PGx		CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Clomipramine (CYP2C19, CYP2D6) (Anafranil, Clomicalm) FDA drug label: Not established for PGx	<b>⊘</b>	Multigenic: CYP2D6, CYP2C19: Normal metabolizer. Two alleles showing normal function.; Normal metabolizer. Two normal function alleles.	Individuals with this combination of alleles are expected to show typical response. No additional therapeutic recommendations.		
Desipramine (Norpramin) FDA drug label: Actionable PGx		CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Doxepin (CYP2C19, CYP2D6) (Quitaxon, Aponal, Sinequan) FDA drug label: Actionable PGx		Multigenic: CYP2D6, CYP2C19: Normal metabolizer. Two alleles showing normal function.; Normal metabolizer. Two normal function alleles.	Individuals with this combination of alleles are expected to show typical response. No additional therapeutic recommendations.		





Drug	Finding	Recommendation	Concern	Evidence
<b>Duloxetine</b> (Cymbalta)  FDA drug label: Actionable PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Imipramine (CYP2C19, CYP2D6) (Tofranil-PM, Tofranil) FDA drug label: Actionable PGx	Multigenic: CYP2D6, CYP2C19: Normal metabolizer. Two alleles showing normal function.; Normal metabolizer. Two normal function alleles.	Individuals with this combination of alleles are expected to show typical response. No additional therapeutic recommendations.		
Mirtazapine FDA drug label: Not established for PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Typical response expected. No additional therapeutic recommendations.		
Nortriptyline (Pamelor) FDA drug label: Actionable PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Protriptyline (Vivactil) FDA drug label: Actionable PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
<b>Trazodone</b> (Oleptro, Desyrel) FDA drug label: Not established for PGx	CYP3A4: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Trimipramine (CYP2C19, CYP2D6) (Surmontil)  FDA drug label: Not established for PGx	Multigenic: CYP2D6, CYP2C19: Normal metabolizer. Two alleles showing normal function.; Normal metabolizer. Two normal function alleles.	Individuals with this combination of alleles are expected to show typical response. No additional therapeutic recommendations.		







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Drug	Finding	Recommendation	Concern	Evidence
Venlafaxine (Effexor) FDA drug label: Actionable PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Vortioxetine (Brintellix)  FDA drug label: Actionable PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Antidiabetics				
Glimepiride  FDA drug label: Not established for PGx	CYP2C9: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Glyburide (Glibenclamide)  FDA drug label: Not established for PGx	CYP2C9: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Saxagliptin (Onglyza)  FDA drug label: Not established for PGx	CYP3A4: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Tolbutamide (Orinase)  FDA drug label: Not established for PGx	CYP2C9: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Antiemetics				
Ondansetron (Zofran)  FDA drug label: Informative PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		



Drug	Finding	Recommendation	Concern	Evidence
Antifungals				
Ketoconazole (Nizoral)  FDA drug label: Not established for PGx	CYP3A4: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Voriconazole (Vfend) FDA drug label: Actionable PGx	CYP2C19: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Antineoplastic				
Cisplatin (Platinol)  FDA drug label: Not established for PGx	TPMT: *1 *1	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
<b>Antineoplastic Agents</b>				
Methotrexate (Rheumatrex, Trexall)  FDA drug label: Not established for PGx	MTHFR: Decreased function. One normal function allele and one decreased function allele.	Individuals with decreased function of this gene frequently present with significantly increased risk of side effects. This medication should be avoided.	ADR	
Antiplatelet Agents				
Clopidogrel  FDA drug label: Actionable PGx	CYP2C19: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Prasugrel  FDA drug label: Informative PGx	CYP2C19: Normal metabolizer. Two normal function alleles.	Typical response expected. No additional therapeutic recommendations.		
Ticagrelor (Brilinta)  FDA drug label: Not established for PGx	CYP3A4: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		







Drug		Finding	Recommendation	Concern	Evidence
Antipsychotics					
Aripiprazole (Abilify) FDA drug label: Actionable PGx	<b>⊘</b>	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Brexpiprazole (Rexulti) FDA drug label: Actionable PGx		CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Clozapine FDA drug label: Actionable PGx	<b>⊘</b>	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Haloperidol (Haldol) FDA drug label: Not established for PGx	<b>⊘</b>	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Iloperidone FDA drug label: Actionable PGx	<b>⊘</b>	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Olanzapine (Zalasta, Zyprexa) FDA drug label: Not established for PGx	<b>②</b>	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Typical response expected. No additional therapeutic recommendations.		
Perphenazine (Trilafon) FDA drug label: Actionable PGx	<b>⊘</b>	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Pimozide (Orap) FDA drug label: Testing required	<b>②</b>	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		



Drug	Finding	Recommendation	Concern	Evidence
Quetiapine (Seroquel)  FDA drug label: Not established for PGx	CYP3A4: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Risperidone (Risperdal)  FDA drug label: Informative PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Thioridazine  FDA drug label: Actionable PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Anxiolytics				
Alprazolam (Xanax, Niravam)  FDA drug label: Not established for PGx	CYP3A4: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Buspirone (Buspar)  FDA drug label: Not established for PGx	CYP3A4: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Clonazepam (Klonopin) FDA drug label: Not established for PGx	CYP3A4: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Diazepam  FDA drug label: Actionable PGx	CYP2C19: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		



Drug	Finding	Recommendation	Concern	Evidence
Beta-3 Adrenergic A	gonists			
Mirabegron (Myrbetriq) FDA drug label: Actionable PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Beta Blockers				
Carvedilol (Coreg) FDA drug label: Actionable PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Metoprolol (Lopressor) FDA drug label: Informative PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Nebivolol (Bystolic) FDA drug label: Informative PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Typical response expected. No additional therapeutic recommendations.		
Propranolol (Inderal) FDA drug label: Informative PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Typical response expected. No additional therapeutic recommendations.		
Timolol (Blocadren) FDA drug label: Not established for PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Central Monoamine-	Depleting Agents			
Tetrabenazine (Xenazine)  FDA drug label: Testing required	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		





Drug		Finding	Recommendation	Concern	Evidence	
Central Nervous Sys	Central Nervous System Agents					
Dextromethorphan- Quinidine (Nuedexta) FDA drug label: Testing recommended	<b>Ø</b>	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.			
<b>Cholinergic Agonist</b>	ts					
Cevimeline (Evoxac) FDA drug label: Actionable PGx	<b>⊘</b>	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.			
Cholinesterase Inhi	bito	rs				
Galantamine (Razadyne, Razadyne ER, Nivalin, Lycoremine, Reminyl) FDA drug label: Informative PGx	<b>⊘</b>	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.			
Contraceptives						
Estrogen-containing oral contraceptives  FDA drug label: Not established for PGx	<b>⊘</b>	F5: Two wild-type alleles.	Individuals with wild type alleles are expected to show typical response. No additional therapeutic recommendations.			
EGFR Inhibitors						
<b>Gefitinib</b> (Iressa) FDA drug label: Actionable PGx	<b>⊘</b>	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.			
Endocrine-Metabolic Agents						
Eliglustat  FDA drug label: Testing required	<b>⊘</b>	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.			







Drug		Finding	Recommendation	Concern	Evidence
Estrogen Agonists	s/Anta	agonists			
<b>Tamoxifen</b> (Soltamox, Nolvadex)		CYP2D6: Normal metabolizer. Two	Normal metabolizers of this medication are expected to		
FDA drug label: Actionable PGx		alleles showing normal function.	show typical response. No additional therapeutic recommendations.		
Hypnotics					
<b>Eszopicione</b> (Lunesta)	<b>②</b>	CYP3A4: Normal metabolizer. Two	Normal metabolizers of this medication are expected to		
FDA drug label: Not established for PGx		normal function alleles.	show typical response. No additional therapeutic recommendations.		



Drug		Finding	Recommendation	Concern	Evidence
Immunosuppressa	nts				
Azathioprine (Imuran) FDA drug label: Testing recommended		TPMT: *1 *1	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Cyclosporine (Gengraf, Neoral) FDA drug label: Not established for PGx		CYP3A4: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Mercaptopurine (Purinethol) FDA drug label: Testing recommended		TPMT: *1 *1	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Sirolimus (Rapamune) FDA drug label: Not established for PGx		CYP3A4: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
<b>Tacrolimus</b> (Prograf, Hecoria) <i>FDA drug label: Not</i> <i>established for PGx</i>	<b>A</b>	CYP3A5: Poor metabolizer. Two little or no function alleles.	Poor metabolizers of this medication frequently present with higher plasma concentrations of the active medication, frequently present with increased medication efficacy. No additional therapeutic recommendations.	Efficacy	
<b>Thioguanine</b> (6-TG, Tabloid, Lanvis) FDA drug label: Testing recommended	<b>⊘</b>	TPMT: *1 *1	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Muscle Relaxants					
Carisoprodol (Soma) FDA drug label: Actionable PGx	<b>⊘</b>	CYP2C19: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		







Drug		Finding	Recommendation	Concern	Evidence
Non-drug					
ABCG2		ABCG2: Normal function. Two normal function alleles.	Typical response is expected; no additional therapeutic recommendations.		
ADRA2A(C-1291G)	<b>A</b>	ADRA2A(C-1291G): Unknown; One variant SNP detected.	No additional therapeutic recommendations.		
COMT(Val158Met)	<b>⊘</b>	COMT(Val158Met): Normal function. Two normal function alleles.	Typical response is expected; no additional therapeutic recommendations.		
CYP1A2	0	CYP1A2: *1K *1N	No additional therapeutic recommendations.		
DPYD	<b>⊘</b>	DPYD: Normal metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		
G6PD	<b>⊘</b>	G6PD: Normal function. Two alleles of Class IV variants which are normal (60-150% function).	Typical response is expected; no additional therapeutic recommendations.		
GRIK4	0	GRIK4: Indeterminate function. One normal function allele and one altered function allele.	Uncertain function. One allele with normal activity and one with altered activity.		
HTR2A	0	HTR2A: Altered function. Two altered function alleles.	Altered function. Two alleles with altered activity.		
OPRM1(A118G)	0	OPRM1(A118G): Normal function.	Normal function. Two alleles with normal activity.		



Drug	Finding	Recommendation	Concern	Evidence		
Nonsteroidal Anti-Inflamatory Drugs (NSAIDs)						
Celecoxib (Celebrex) FDA drug label: Actionable PGx	CYP2C9: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.				
Diclofenac (Cataflam) FDA drug label: Not established for PGx	CYP2C9: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.				
Flurbiprofen (Ocufen) FDA drug label: Actionable PGx	CYP2C9: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.				
Ibuprofen (Motrin, Advil) FDA drug label: Not established for PGx	CYP2C9: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.				
Meloxicam (Mobic) FDA drug label: Actionable PGx	CYP2C9: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.				
Piroxicam (Feldene) FDA drug label: Actionable PGx	CYP2C9: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.				



Drug		Finding	Recommendation	Concern	Evidence
Opioids					
Alfentanil (Rapifen, Alfenta) FDA drug label: Not established for PGx	<b>Ø</b>	OPRM1(A118G): Normal function.	Individuals with normal function of this gene are expected to show typical response. No additional therapeutic recommendations.		
Buprenorphine (Butrans, Buprenex) FDA drug label: Not established for PGx		CYP3A4: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Codeine FDA drug label: Actionable PGx	<b>⊘</b>	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Fentanyl (Duragesic, Sublimaze) FDA drug label: Not established for PGx	<b>⊘</b>	CYP3A4: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Fentanyl (OPRM1) (Duragesic, Sublimaze) FDA drug label: Not established for PGx	<b>⊘</b>	OPRM1(A118G): Normal function.	Individuals with normal function of this gene are expected to show typical response. No additional therapeutic recommendations.		
Hydrocodone  FDA drug label: Not established for PGx	<b>⊘</b>	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Hydromorphone (Dilaudid) FDA drug label: Not established for PGx	<b>Ø</b>	OPRM1(A118G): Normal function.	Individuals with normal function of this gene are expected to show typical response. No additional therapeutic recommendations.		



Drug		Finding	Recommendation	Concern	Evidence
Morphine (MS-IR) FDA drug label: Not established for PGx	<b>⊘</b>	OPRM1(A118G): Normal function.	Individuals with normal function of this gene are expected to show typical response. No additional therapeutic recommendations.	Concern	
Oxycodone (Oxycontin) FDA drug label: Not established for PGx	<b>Ø</b>	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Typical response expected. No additional therapeutic recommendations.		
Oxycodone (CYP3A4) (Oxycontin) FDA drug label: Not established for PGx	<b>Ø</b>	CYP3A4: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Oxycodone (CYP3A5) (Oxycontin) FDA drug label: Not established for PGx	<b>A</b>	CYP3A5: Poor metabolizer. Two little or no function alleles.	Poor metabolizers of this medication may present with notably lower plasma concentrations of the active medication, thus an increased risk of pharmacotherapy failure. Be alert to lack of efficacy; monitor the patient's response to guide dosing.	Efficacy	0
Sufentanil (Sufenta) FDA drug label: Not established for PGx	<b>⊘</b>	OPRM1(A118G): Normal function.	Individuals with normal function of this gene are expected to show typical response. No additional therapeutic recommendations.		
<b>Tramadol</b> (Ultracet, Ultram) <i>FDA drug label:</i> <i>Actionable PGx</i>	<b>Ø</b>	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
<b>Prokinetic agents</b>					
Metoclopramide (Primperan, Reglan) FDA drug label: Actionable PGx		CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		







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Drug		Finding	Recommendation	Concern	Evidence
Proton Pump Inhib	itors	s (PPIs)			
Dexlansoprazole (Dexilant, Kapidex) FDA drug label: Actionable PGx		CYP2C19: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication may present with lower plasma concentrations of the active medication, thus an increased risk of pharmacotherapy failure. Monitor the patient's response to guide dosing; consider increasing the dose.	Efficacy	
Esomeprazole (Nexium) FDA drug label: Actionable PGx		CYP2C19: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.		
Lansoprazole (Prevacid) FDA drug label: Informative PGx	<b>A</b>	CYP2C19: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication may present with lower plasma concentrations of the active medication, thus an increased risk of pharmacotherapy failure. Monitor the patient's response to guide dosing; consider increasing the dose.	Efficacy	
Omeprazole (Prilosec, Zegerid) FDA drug label: Actionable PGx	<b>A</b>	CYP2C19: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication may present with lower plasma concentrations of the active medication, thus an increased risk of pharmacotherapy failure. Monitor the patient's response to guide dosing; consider increasing the dose.	Efficacy	
Pantoprazole (Protonix) FDA drug label: Actionable PGx	<b>A</b>	CYP2C19: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication may present with lower plasma concentrations of the active medication, thus an increased risk of pharmacotherapy failure. Monitor the patient's response to guide dosing; consider increasing the dose.	Efficacy	





Drug	Finding	Recommendation	Concern	Evidence		
Rabeprazole (Aciphex)  FDA drug label: Actionable PGx	CYP2C19: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.				
Selective Serotonin Reuptake Inhibitors (SSRIs)						
Citalopram (Celexa)  FDA drug label: Actionable PGx	CYP2C19: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.				
Escitalopram (Lexapro)  FDA drug label: Actionable PGx	CYP2C19: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.				
Fluoxetine (Prozac)  FDA drug label: Informative PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Typical response expected. No additional therapeutic recommendations.				
Fluvoxamine (Luvox)  FDA drug label: Actionable PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.				
Paroxetine (Paxil)  FDA drug label: Informative PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.				
Sertraline (Zoloft)  FDA drug label: Not established for PGx	CYP2C19: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.				



Drug	Finding	Recommendation	Concern	Evidence	
Statins					
Atorvastatin (Lipitor, Caduet)  FDA drug label: Not established for PGx	CYP3A4: Normal metabolizer. Two normal function alleles.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.			
Simvastatin (Zocor) FDA drug label: Informative PGx	SLCO1B1: Normal function. Two normal function alleles.	Individuals with normal SLCO1B1 liver uptake activity are expected to have a typical response to a standard dose of simvastatin.			
Vesicular monoamine transporter 2 inhibitor					
Deutetrabenazine (Austedo)  FDA drug label: Actionable PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.			
Valbenazine (Ingrezza) FDA drug label: Actionable PGx	CYP2D6: Normal metabolizer. Two alleles showing normal function.	Normal metabolizers of this medication are expected to show typical response. No additional therapeutic recommendations.			
Xanthine Oxidase Inhibitor					
Allopurinol (Zyloprim)  FDA drug label: Not established for PGx	ABCG2: Normal function. Two normal function alleles.	Individuals with normal function of this gene are expected to show typical response. No additional therapeutic recommendations.			



#### **Thrombosis Profile**

Tested Gene (Allele)	Genotype	Predicted Phenotype	Clinical Guidance
Prothrombin (F2)	Normal	Normal risk expected	The absence of these variant alleles
Factor V Leiden	Normal	based on the patient's genotype.	of Prothrombin (Factor II) and Factor V Leiden suggests that the patient does
MTHFR (A1298C)	Normal		not have the elevated risk of thrombosis associated with these genetic markers.
MTHFR (C677T)	Heterozygous		

#### **General Description**

Genetic analyses of three genes (four alleles) considered to increase the risk for venous thromboembolism were performed using molecular genetic techniques. The presence of the Prothrombin (Factor 2) gene allele c.\*97G>A (previously designated as 20210G>A) and Factor V Leiden allele c.1601G>A (previously designated as 1691G>A) are risk factors for venous thromboembolism. This risk may be further increased by the use of estrogen therapy, oral contraceptives, pregnancy, and surgery.

Patients who are homozygous for MTHFR C677T or MTHFR A1298C may have a further increased risk for venous thromboembolism if they also possess the Factor V Leiden c.1601G>A allele. However, the MTHFR alleles alone do not predict a significant risk for venous thromboembolism.

#### References

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- Lim MY, et al.; Thrombophilic risk of individuals with rare compound factor V Leiden and prothrombin G20210A polymorphisms: an international case series of 100 individuals. Eur J Haematol. 2016 Oct;97(4):353-60. doi: 10.1111/ ejh.12738. Epub 2016 Feb 18. PMID: 26773706.
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- Stevens SM, et al.; Guidance for the evaluation and treatment of hereditary and acquired thrombophilia. J Thromb Thrombolysis. 2016 Jan;41(1):154-64. doi: 10.1007/s11239-015-1316-1. PMID: 26780744; PMCID: PMC4715840.





#### Clinical Evidence Levels



- Includes gene-drug pairs approved by the Coriell Institute for Medical Research Pharmacogenomics Advisory Group.
- Includes gene-drug pairs supported by multiple studies documenting consistent effects of specific genetic variant(s) on clinical outcomes.
- Includes gene-drug pairs approved by the Dutch Pharmacogenetics Working Group (DPWG) and/or guidelines published in Clinical Pharmacology and Therapeutics by the Clinical Pharmacogenetics Implementation Consortium (CPIC).

#### Moderate

- Includes gene-drug pairs supported by pharmacokinetic, pharmacodynamic, or molecular/cellular functional studies showing consistent effects of genetic variant(s).
- Includes Drug product information (e.g. This interpretation is based on guidance available in the FDA (Food and Drug Administration) drug label for ABILIFY® (10/2013).
- · Includes gene-drug pairs for which potential clinical outcomes are inferred from similar gene-drug interactions approved by the Dutch Pharmacogenetics Working Group (DPWG), and/or guidelines published in Clinical Pharmacology and Therapeutics by the Clinical Pharmacogenetics Implementation Consortium (CPIC), and/or pharmacogenomic reports and submission from the Coriell Institute for Medical Research.

#### Emerging

• Includes gene-drug pairs supported by published studies of the drug, related drug, or a probing compound of interest involving limited data and/or inconsistent findings.

Disclaimer: These tests were developed and characterized by Intermountain Precision Genomics. The tests in Intermountain Precision Genomics's pharmacogenetics panel have not been approved by the Food and Drug Administration. The FDA has determined that such approval is not necessary, provided that the laboratory both (1) maintains its good standing as a clinical testing laboratory with all mandatory accrediting bodies, and (2) continually demonstrates that its testing protocols and procedures achieve a high degree of analytical accuracy. Reads are aligned to human genome reference sequence (GrCh37) using the Kailos Blue pipeline v5.4. While this test is able to detect deletions and duplications of the CYP2D6 gene, the assay has not been validated to specify the exact number of copies that may occur as a result of a duplication event in this gene. Results indicating that a duplication of CYP2D6 was detected should be interpreted with the understanding that more than three copies of the gene cannot be excluded and therefore close monitoring of patient medication response is recommended.

Limitation: This test will not detect all the known alleles that result in altered or inactive tested genes. This test does not account for all individual variations in the individual tested. Absence





of a detectable gene mutation does not rule out the possibility that a patient has different phenotypes due to the presence of an undetected polymorphism or due to other factors such as drug-drug interactions, comorbidities and lifestyle habits.

Methodology: Illumina MiSeq System sequencing.

Laboratory Certification: CLIA # 46D2094383

Laboratory Director: Jeremy Wallentine



#### **Genetic Summary**

Gene	Result	Activity †
ABCG2	G G	Normal function
ADRA2A(C-1291G)	C G	Positive
COMT(Val158Met)	G G	Normal function
CYP1A2	*1K *1N	Unknown Metabolizer
CYP2C19	*1 *1	Normal metabolizer
CYP2C9	*1 *1	Normal metabolizer
CYP2D6	*1A *2B or *34 *39; or *1A *2A	Normal metabolizer
CYP3A4	*1 *1A; or *1A *1A; or *1 *1	Normal metabolizer
CYP3A5	*3A *3A	Poor metabolizer
DPYD	*1 *1	Normal function
Factor V Leiden	Normal	See Thrombosis Profile
G6PD	B (WT) B (WT)	Normal function
GRIK4	TJC	Uncertain function
HTR2A	G G	Altered function
MTHFR	GT AT	Decreased function
MTHFR (A1298C)	Normal	See Thrombosis Profile
MTHFR (C677T)	Heterozygous	See Thrombosis Profile
OPRM1(A118G)	A G	Normal function
Prothrombin (F2)	Normal	See Thrombosis Profile
SLCO1B1	*1 *1	Normal liver uptake activity
TPMT	*1 *1	Normal metabolizer
VKORC1	*1 *2	Medium sensitivity to warfarin